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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 20-F

☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2021

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☐ **SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Date of event requiring this shell company report _____

Commission file number 001-35773

RedHill Biopharma Ltd.
(Exact name of Registrant as specified in its charter)

N/A
(Translation of Registrant's name into English)

Israel
(Jurisdiction of incorporation or organization)

21 Ha'arba'a Street, Tel Aviv 6473921, Israel
(Address of principal executive offices)

Micha Ben Chorin, Chief Financial Officer
21 Ha'arba'a Street, Tel Aviv 6473921, Israel
Tel: 972-3-541-3131; Fax: 972-3-541-3144
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Securities registered or to be registered pursuant to Section 12(b) of the Act.

Title of class	Trading Symbol(s)	Name of each exchange on which registered
American Depositary Shares, each representing ten Ordinary Shares (1)	RDHL	NASDAQ Global Market
Ordinary Shares, par value NIS 0.01 per share (2)	RDHL	NASDAQ Global Market

(1) Evidenced by American Depositary Receipts.
(2) Not for trading, but only in connection with the listing of the American Depositary Shares.

Securities registered or to be registered pursuant to Section 12(g) of the Act:

None
(Title of Class)

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None
(Title of Class)

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report: 526,842,294 Ordinary Shares

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes ☐ No ☒

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act 1934.

Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).

Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer, or an emerging growth company. See definition of "accelerated filer ," "large accelerated filer," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large Accelerated filer ☐ **Accelerated filer ☒** **Non-accelerated filer ☐**
Emerging growth company ☐

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards† provided pursuant to Section 13(a) of the Exchange Act. ☐

† The term "new or revised financial accounting standard" refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☐

International Financing Reporting Standards as issued by the International Accounting Standards Board ☒ Other ☐

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow.

Item 17 ☐ Item 18 ☐

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes ☐ No ☒

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Unless the context otherwise requires, all references to "RedHill," "we," "us," "our," the "Company" and similar designations refer to RedHill Biopharma Ltd., a limited liability company incorporated under the laws of the State of Israel, and its direct and indirect subsidiaries, including RedHill Biopharma Inc. ("RedHill U.S."), a wholly-owned subsidiary incorporated in Delaware. The term "including" means "including but not limited to", whether or not explicitly so stated. The term "NIS" refers to New Israeli Shekels, the lawful currency of the State of Israel, the terms "dollar", "US$", "$" or "U.S." refer to U.S. dollars, the lawful currency of the United States of America. Our functional and presentation currency is the U.S. dollar. Unless otherwise indicated, U.S. dollar amounts herein (other than amounts originally receivable or payable in dollars) have been translated for the convenience of the reader from the original NIS amounts at the representative rate of exchange as of March 16, 2022 ($1 = NIS 3.263). The dollar amounts presented should not be construed as representing amounts that are receivable or payable in dollars or convertible into dollars, unless otherwise indicated. Foreign currency transactions in currencies other than U.S. dollars are translated in this Annual Report into U.S. dollars using exchange rates in effect at the date of the transactions.

Unless otherwise indicated or the context requires, the term "therapeutic candidates" refers to investigational drug products that are still in development and have not been approved by the FDA or other relevant regulatory authority and the term "commercial products" means products approved by the Food and Drug Administration ("FDA") that we commercialize or promote from time to time.

FORWARD-LOOKING STATEMENTS

Some of the statements under the sections entitled "Item 3. Key Information – Risk Factors," "Item 4. Information on the Company," "Item 5. Operating and Financial Review and Prospects" and elsewhere in this Annual Report may include forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms, including "anticipates," "believes," "could," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "projects," "should," "will," "would," and similar expressions intended to identify forward-looking statements. Forward-looking statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties, many of which are beyond the Company's control and cannot be predicted or quantified. In addition, the section of this Annual Report entitled, "Item 4. Information on the Company", contains information obtained from independent industry and other sources that we may not have independently validated. You should not put undue reliance on any forward-looking statements. Unless we are required to do so under U.S. federal securities laws or other applicable laws, we do not intend to update or revise any forward-looking statements.

Factors that could cause our actual results to differ materially from those expressed or implied in such forward-looking statements include, but are not limited to:

- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- our ability to obtain additional financing;
- the commercialization and market acceptance of our commercial products;
- our ability to generate sufficient revenues from our commercial products, including obtaining commercial insurance and government reimbursement;
- our ability to advance our therapeutic candidates into clinical trials or to successfully complete our preclinical studies or clinical trials, and to complete the development of such therapeutic candidates and obtain approval for marketing by the Food and Drug Administration ("FDA") or other regulatory authorities;

- our reliance on third parties to satisfactorily conduct key portions of our commercial operations, including manufacturing and other supply chain functions, market analysis services, safety monitoring, regulatory reporting and sales data analysis and the risk that those third parties may not perform such functions satisfactorily;
- our ability to maintain an appropriate sales and marketing infrastructure;
- our ability to establish and maintain corporate collaborations;
- that our current commercial products or commercial products that we may commercialize or promote in the future may be withdrawn from the market by regulatory authorities and our need to comply with continuing laws, regulations and guidelines to maintain clearances and approvals for those products;
- our exposure to significant drug product liability claims;
- the initiation and completion of any postmarketing studies or trials;
- our ability to acquire products approved for marketing in the U.S. that achieve commercial success and to maintain our own marketing and commercialization capabilities;
- our estimates of the markets, their size, characteristics and their potential for our commercial products and therapeutic candidates and our ability to serve those markets;
- the successful commercialization of products we in-license or acquire;
- our inability to enforce claims relating to a breach of a representation and warranty by a counterparty;
- the hiring and continued employment of executives, sales personnel, and contractors;
- our receipt and timing of regulatory clarity and approvals for our commercial products and therapeutic candidates, and the timing of other regulatory filings and approvals;
- the initiation, timing, progress, and results of our research, development, manufacturing, preclinical studies, clinical trials, and other commercial efforts and therapeutic candidate development, as well as the extent and number of additional studies that we may be required to conduct;
- our ability to advance our therapeutic candidates into clinical trials or to successfully complete our preclinical studies or clinical trials, including developing a commercial companion diagnostic for the detection of Mycobacterium avium paratuberculosis ("MAP");
- our reliance on third parties to conduct key portions of our clinical trials, including data management services and the risk that those third parties may not perform such functions satisfactorily;
- our reliance on third parties to manufacture and supply our therapeutic candidates and their respective APIs with the requisite quality and manufacturing standards in sufficient quantities and within the required timeframes and at an acceptable cost;
- the research, manufacturing, clinical development, commercialization, and market acceptance of our therapeutic candidates;
- the interpretation of the properties and characteristics of our commercial products or therapeutic candidates and of the results obtained in research, preclinical studies or clinical trials;

- the implementation of our business model, strategic plans for our business, commercial products, and therapeutic candidates;
- heightened attention on the problems associated with opioids;
- the impact of other companies and technologies that compete with us within our industry;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our commercial products and therapeutic candidates, including from existing or future claims of infringement, and our ability to operate our business without infringing or violating the intellectual property rights of others;
- parties from whom we license or acquire our intellectual property defaulting in their obligations toward us;
- the failure by a licensor or a partner of ours to meet their respective obligations under our acquisition, in-license or other development or commercialization agreements or renegotiate the obligations under such agreements, or if other events occur that are not within our control, such as bankruptcy of a licensor or a partner;
- our reliance on the actions of third parties, including sublicensors and their other sublicensees, to maintain our rights under our in-licenses which are sublicenses;
- the effect of a potential occurrence of patients suffering serious adverse events using investigative drugs under our Expanded Access Program;
- our ability to implement network systems and controls that are effective at preventing cyber-attacks, malware intrusions, malicious viruses and ransomware threats;
- the effects of the economic and business environment, including unforeseeable events and the changing market conditions caused by the COVID-19 global pandemic; and
- the impact on our business of the political and security situation in Israel, the U.S. and other places in which we operate.

Summary of Risk Factors

The following is a summary of some of the principal risks we face. The list below is not exhaustive, and investors should read the "Risk Factors" section included in "Item 3. Key Information – Risk Factors" in full.

- Our pursuit of treatments for SARS-CoV-2 (the virus that causes COVID-19) infection in patients entails a high level of uncertainty. We cannot assure you that either opaganib (ABC294640; Yeliva®)("opaganib") or RHB-107 will prove to be a safe and effective treatment for COVID-19,or will be approved for marketing or Emergency Use Authorization or be granted with Expanded Access clearance by the FDA or other regulatory authorities.
- If we are successful in developing a COVID-19 therapeutic, we may need to devote significant resources to our manufacturing scale-up and large-scale deployment, including for use by the U.S. or other governments. If one of our COVID-19 therapeutic candidates is approved for marketing or for Emergency Use, we may also need to devote significant resources to further expand our U.S. and non-U.S. sales and marketing activities and increase or maintain personnel to accommodate sales in the U.S. and outside the U.S.
- The ongoing COVID-19 pandemic may adversely affect our business, revenues, results of operations and financial condition.

- Our current working capital is not sufficient to commercialize our current commercial products or to complete the research and development with respect to any or all of our therapeutic candidates. We may need to raise additional capital to achieve our strategic objectives and to execute our business plans, and our failure to raise sufficient capital or on favorable terms would significantly impair our ability to fund the commercialization of our current commercial products, therapeutic candidates, or the products we may commercialize or promote in the future, attract development or commercial partners or retain key personnel, and to fund operations and develop our therapeutic candidates.

- Our long-term capital requirements are subject to numerous risks.

- Our term loan facility imposes significant operating and financial restrictions on us, which may prevent us from capitalizing on business opportunities and may restrict our operational flexibility, and our failure to comply with the restrictive covenants in our term loan facility could have a material adverse effect on our business.

- We may be unable to generate sufficient cash flow to make the required payments under the term loan facility or to adhere to other requirements under the term loan facility.

- The indebtedness under our term loan facility is secured by substantially all of the current and future assets of RedHill U.S., all of our assets related in any material respect to Talicia®, and all of the equity interests of RedHill U.S. As a result of these security interests, such assets would only be available to satisfy claims of our general creditors or to holders of our equity securities if we were to become insolvent to the extent the value of such assets exceeded the amount of our indebtedness and other obligations. In addition, the existence of these security interests may adversely affect our financial flexibility.

- If we or our current or future development or commercialization partners are unable to obtain or maintain the FDA or other foreign regulatory clearance and approval for our commercial products or therapeutic candidates, we or our commercialization partners will be unable to commercialize our current commercial products, products we may commercialize or promote in the future or our therapeutic candidates, upon approval, if any.

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable.

ITEM 3. KEY INFORMATION

A. [Reserved]

B. Capitalization and Indebtedness

Not applicable.

C. Reasons for the Offer and Use of Proceeds

Not applicable.

D. Risk Factors

You should carefully consider the risks we describe below, in addition to the other information set forth elsewhere in this Annual Report, including our financial statements and the related notes beginning on page F-1, before you decide to buy our securities. The risks and uncertainties described below in this Annual Report on Form 20-F for the year ended December 31, 2021, are not the only risks facing us. We may face additional risks and uncertainties not currently known to us or that we currently deem to be immaterial. Any of the risks described below or incorporated by reference in this Form 20-F, and any such additional risks, could materially adversely affect our reputation, business, financial condition or results of operations. In such case, you may lose all or part of your original investment.

Risks Related to Our Development of COVID-19 Therapy and COVID-19 Impact on Our Business

Our pursuit of treatments for SARS-CoV-2 (the virus that causes COVID-19) infection in patients entails a high level of uncertainty. We cannot assure you that either opaganib or RHB-107 will prove to be a safe and effective treatment for COVID-19 or will be approved for marketing or Emergency Use Authorization by the FDA or other regulatory authorities.

In response to the global pandemic of COVID-19, we are pursuing the study of opaganib and RHB-107 as potential treatments for COVID-19. We cannot predict with certainty the safety or efficacy of opaganib or RHB-107, and we may be unable to provide a treatment that successfully treats COVID-19 and/or its symptoms in a timely manner, if at all. Furthermore, even if we successfully develop a viable therapeutic candidate, we may encounter difficulties developing and scaling up manufacturing processes suitable for production of sufficient supply for our clinical trials or for commercial use. Likewise, we may not be successful in commercializing any of the treatments we are developing for COVID-19. We have also committed financial resources and personnel to the development of opaganib and RHB-107 as potential treatments for COVID-19, which may cause delays in or otherwise negatively impact our other development programs, despite uncertainties surrounding the longevity and extent of COVID-19 as a global health concern. Our business could be negatively impacted by the continued allocation of significant resources to a global health threat that is unpredictable and could rapidly dissipate or against which our potential treatments, if developed, may not be partially or fully effective.

Further, we may make a decision to discontinue the study of opaganib and RHB-107 as potential treatments for COVID-19 for any reason, including if additional parties are successful in developing a more effective treatment or vaccine for COVID-19 or if the pandemic is effectively contained or the risk of SARS-CoV-2 infection is diminished or eliminated or if other market or business conditions and considerations support such discontinuation before we can successfully complete clinical development and obtain regulatory approval of opaganib or RHB-107 as a treatment for SARS-CoV-2 infection.

We may be unable to recoup any costs we incur in the evaluation of opaganib and RHB-107 for SARS-CoV-2 infection, and we may never recognize any revenue from the sale of opaganib or RHB-107 to treat COVID-19, even if we do receive one or more regulatory approvals.

Furthermore, the biotechnology sector is highly competitive and there are numerous companies that are currently pursuing a treatment for COVID-19 and vaccine for SARS-CoV-2. In particular, there are efforts by public and private entities to develop additional treatments or vaccines as fast as possible. To date, several SARS-CoV-2 vaccines and drugs have received marketing approval or emergency use authorization. These and other public and private entities may develop treatments that are more effective than any we may develop, may develop a COVID-19 treatment that becomes the standard-of-care or at a lower cost or earlier than we are able to, or may be more successful at commercializing their product, which will reduce or eliminate the commercial opportunity for our therapeutic candidates. Many of these other organizations are much larger than we are and have access to larger pools of capital, including government grants and support, and broader manufacturing infrastructure. We cannot guarantee that the FDA, the Secretary of the Department of Health and Human Services or other agencies around the world will continue to accept applications for emergency use authorization in connection with COVID-19. Even if we do obtain emergency use authorization or FDA (or other agency) approval for our COVID-19 therapeutic candidate, such authorization will only be effective as long as the public health emergency continues, and the Secretary of the Department of Health and Human Services or the FDA (or other agency) may declare an end to such emergency at any time. Finally, if the pandemic ends or is sufficiently controlled, patient accruals for clinical trials will likely become difficult, which will have a material adverse effect on our ability to complete the development of our COVID-19 therapeutic candidate. There are a number of uncertainties and risks associated with our development of a COVID-19 therapeutic candidate, and we cannot guarantee success or profitability and may, instead, face financial and operational hardship as a result of this pursuit.

Government involvement may limit the commercial success of our COVID-19 therapeutic candidate.

The COVID-19 pandemic has been classified as a pandemic by public health authorities, and it is possible that one or more government entities may take actions that directly or indirectly have the effect of abrogating some of our rights or opportunities. If we were to develop an anti-viral therapeutic to COVID-19, the economic value of such therapeutic to us could be limited.

Separately, various government entities, including the U.S. and or other governments, are offering incentives, such as those we received, grants and contracts to encourage additional investment by commercial organizations into preventative and therapeutic agents against COVID-19, which may have the effect of increasing the number of competitors and/or providing advantages to competitors. Accordingly, there can be no assurance that we will be able to successfully establish a competitive market share for our COVID-19 candidates.

If we are successful in developing a COVID-19 therapeutic, we may need to devote significant resources to our manufacturing scale-up and large-scale deployment, including for use by the U.S. or other governments. If one of our COVID-19 therapeutic candidates is approved for marketing or for Emergency Use, we may also need to devote significant resources to further expand our U.S. and non-U.S. sales and marketing activities and increase or maintain personnel to accommodate sales in the U.S. and outside the U.S.

In the event that the clinical studies of opaganib and/or RHB-107 as a COVID-19 therapeutic candidate are perceived to be successful, we may need to work toward the large-scale manufacturing scale-up and larger-scale deployment of the potential therapeutic through a variety of U.S. and foreign government or other agency mechanisms, such as an Expanded Access Program or an Emergency Use Authorization program. In this case, we may need to devote significant resources to this program, which would require diversion of resources from our other programs. In addition, since the path to licensure of any COVID-19 therapeutic is unclear, if use of the therapeutic is approved by the U.S. or other governments, we may have a widely used therapeutic in circulation in the U.S. or any another country prior to our full validation of the overall long-term safety and efficacy profile of our therapeutic. Unexpected safety issues in these circumstances could lead to significant reputational damage for us and our therapeutic candidates going forward and other issues, including delays in our other programs, the need for re-design of our clinical trials and the need for significant additional financial resources.

In addition, in the event one of our COVID-19 therapeutic candidates is approved for marketing we may also need to further expand our sales and marketing activities in the U.S. and outside the U.S. and increase or maintain personnel to accommodate sales. In this case, we may need to devote significant additional resources to this program, which would require diversion of additional resources from our other programs.

Since the beginning of 2020, we have entered into several collaborations with leading manufacturers, including with U.S.-based partners, to expand manufacturing capacity of opaganib for COVID-19 in preparation for potential emergency use applications and to gradually meet subsequent large-scale demand and distribution that could follow potential emergency use authorization and/or full marketing approval, if at all. We cannot guarantee that our ongoing efforts in relation to the drug candidates or their manufacturing, including the scale-up of manufacturing will be successful or that we will be able to supply the potential high demand for opaganib for COVID-19 that could follow potential emergency use authorization and/or full marketing approval, if at all. The exercise of march-in rights by the U.S. government may also adversely affect our ability to supply sufficient quantities of opaganib. See " *– The development of opaganib has been supported by government-funded programs and thus may be subject to federal regulations such as "march-in" rights and certain reporting requirements, and compliance with such regulations may limit our exclusive rights and our ability to contract with manufacturers*" below.

The development of opaganib has been supported by government-funded programs and thus may be subject to federal regulations such as "march-in" rights and certain reporting requirements, and compliance with such regulations may limit our exclusive rights and our ability to contract with manufacturers.

Our intellectual property rights to opaganib, which we in-licensed from Apogee Biotechnology Corporation, have been generated through the use of U.S. federal and state government funding and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in opaganib pursuant to the Bayh-Dole Act of 1980, or the Bayh-Dole Act. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require the licensor to grant exclusive, partially exclusive or non-exclusive licenses to any of these inventions to a third party if it determines that (i) adequate steps have not been taken to commercialize the invention, (ii) government action is necessary to meet public health or safety needs or (iii) government action is necessary to meet requirements for public use under federal regulations (also collectively referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if the licensor fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. These rights of the government may affect us even though the U.S. government has not previously contacted us with respect to these intellectual property rights. Any exercise by the government of such rights could harm our competitive position, business, financial condition, results of operations and prospects. Intellectual property generated under a government-funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources.

In addition, the U.S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the U.S. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the U.S. or that under the circumstances domestic manufacture is not commercially feasible. This preference for having products covered by such intellectual property be substantially manufactured in the U.S. may limit our ability to contract with non-U.S. product manufacturers or even U.S. product manufacturers whose manufacturing capacity is offshore.

The ongoing COVID-19 pandemic may adversely affect our business, revenues, results of operations and financial condition.

Outbreaks of epidemic, pandemic or contagious diseases, such as COVID-19, may adversely affect our business, revenues, financial condition and results of operations. The various precautionary measures taken by many governmental authorities around the world in order to limit the spread of SARS-CoV-2 have and may continue to have an adverse effect on the global markets and its economy and demand for pharmaceutical products, including on the availability and pricing of employees, resources, materials, manufacturing and delivery efforts and other aspects of the global economy. The spread

of this pandemic has caused significant volatility and uncertainty in U.S. and international markets and has resulted in increased risks to our operations.

Specifically, we are monitoring a number of risks that have or may affect our business related to this pandemic, including the following:

- Commercial Operations: An extended pandemic could have a material adverse effect on sales of our commercial products. We have experienced and continue to experience decreased commercial activities, which have affected the sales of some of our commercial products due to slower initiation of some promotional activities associated with a significant decrease in in-clinic patient visits, tests and treatments and the impact on our sales force's ability to engage with healthcare providers in an in-person setting, cancellation of events such as industry conferences and limited local and international travel. In addition, there may be a negative impact on our business as a result of COVID-19 within our commercial organization, including reductions in our sales force. The ability to successfully commercialize Movantik® Aemcolo ® and Talicia ® depends on in-clinic patient visits and the availability of diagnostics, both of which have been negatively affected by the pandemic, especially with respect to Aemcolo® and Talicia®, which we launched shortly before or at the time of the COVID-19 outbreak. In addition, the significant decrease in travel has significantly reduced the demand and sales of Aemcolo® for travelers' diarrhea. We expect the decreased level of demand and sales of Aemcolo® to continue over the coming quarters due to the effects of the pandemic. The COVID-19 pandemic may also adversely affect our ability to attract commercial partners, our relationships with commercial partners and our ability to sell our commercial products outside the U.S., including sales of Talicia® in the UAE.

- Supply Chain: To date, there have been no significant disruptions to our supply chain, and we currently have sufficient supply of commercial products on hand to meet U.S. commercial demand. However, an extended duration of this pandemic could result in broad supply disruptions and difficulty in finding alternative sources in the future which may adversely affect our ability to distribute certain of our commercial products for commercial supply and our therapeutic candidates for clinical supply. For example, quarantines, shelter-in-place and similar government orders, travel restrictions and health impacts of the COVID-19 pandemic could impact the availability or productivity of personnel at third-party manufacturers, distributors, freight carriers and other necessary components of our supply chain. In addition, there may be unfavorable changes in the availability or cost of raw materials, intermediates and other materials necessary for production, which may result in disruptions in our supply chain and could significantly and adversely affect our business if one or more of our manufacturers or suppliers are impacted by any interruption at a particular location or in relation to a particular material. To the extent the disruptions in the global supply chain (especially those connected to COVID-19-related supply and logistics issues) continue, our business could be adversely affected.

- Clinical Trials: The pandemic has adversely affected and may continue to adversely affect our clinical and preclinical trials, including our ability to initiate and complete our clinical and preclinical trials within the anticipated timelines, and delays or difficulties in enrolling patients in our clinical trials and recruiting clinical site investigators and clinical site staff. Interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by government officials or entities, employers and others or interruption of clinical trial patient visits and study procedures (particularly any procedures that may be deemed non-essential), may impact the completeness of clinical trial data and clinical study endpoints. The current pressure on medical systems and the prioritization of healthcare resources toward the COVID-19 pandemic have also resulted in interruptions in data collection and submissions for certain clinical trials and delayed starts for certain planned studies. As a result, our previously anticipated filing and marketing timelines may be adversely impacted. For example, the enrollment of patients for our Phase 3 study with RHB-204 in first-line pulmonary nontuberculous mycobacteria (NTM) infections have been slow, which have slowed the progress of the study.

  – In addition, we may be unable to meet the timelines and milestones established for the contemplated postmarketing studies we are required to conduct for Aemcolo®, in which case we could be subject to

FDA enforcement actions and civil monetary penalties, among others, unless the FDA agrees to an extension of the timelines and milestones.

Our clinical trials can also be adversely affected by the reduction or diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trial. Any delays or interruption of our clinical trials could have an adverse effect on our development efforts of our therapeutic candidates, and failure to fulfill any postmarketing commitments could subject us to FDA enforcement actions or result in our breach of certain license agreements and cause us to lose our rights thereunder.

- Regulatory Reviews: The operations of the FDA or other regulatory agencies may be adversely affected. We may also experience delays in necessary interactions with regulatory authorities around the world, including with respect to any anticipated filings.

Additionally, because our corporate headquarters are in Israel while our commercial office is in the U.S., there is additional risk in our ability as a company to control the activities occurring in the U.S., due to the geographic separation within our company.

Assessment of the complete extent of the impact of COVID-19 on our results will depend on future developments, which are highly uncertain and cannot be predicted, including new information that may emerge concerning the severity of COVID-19 and the actions to contain COVID-19 or treat its impact, among others. The continuation of the COVID-19 pandemic could materially disrupt our business and operations and have an adverse effect on the global markets and global economy generally, including on the availability and cost of employees, resources, materials, manufacturing and delivery efforts, and other aspects of the economy. The continuation of the COVID-19 pandemic could also in particular materially affect the sales of our commercial products, making it more difficult for us to meet our financial obligations.

Supply chain and shipping disruptions may result in shipping delays, a significant increase in shipping costs, and could increase product costs and result in lost sales and reputational damage, which may have a material adverse effect on our business, operating results and financial condition.

Our third-party manufacturers and suppliers have experienced, and expect to continue to experience, supply chain disruption and shipping disruptions, including disruptions or delays in loading container cargo in ports of origin or off-loading cargo at ports of destination, as a result of the COVID-19 pandemic, congestion in port terminal facilities, labor supply and shipping container shortages, inadequate equipment and persons to load, dock and offload container vessels and for other reasons. These disruptions may impact our ability to receive APIs and other materials and products from our manufacturers and suppliers, to distribute our products to our customers in a cost-effective and timely manner and to meet customer demand, all of which could have an adverse effect on our financial condition and results of operations. There can be no assurance that further unforeseen events impacting the supply chain will not have a material adverse effect on us in the future. Additionally, the impacts that supply chain disruptions have on our third-party manufacturers and suppliers are not within our control. It is not currently possible to predict how long it will take for these supply chain disruptions to cease or ease. Prolonged supply chain disruption that may impact us or our manufacturers and suppliers could interrupt product manufacturing, increase raw material and product lead times, increase raw material and product costs, impact our ability to meet customer demand and result in lost sales and reputational damage, all of which could have a material adverse effect on our business, financial condition and results of operations.

Risks Related to Our Business

We have a history of operating losses. We may continue to incur significant losses in the coming years.

From our incorporation in 2009 until establishment of our commercial presence in the U.S., we focused primarily on the development and acquisition of late-stage clinical therapeutic candidates, and since we established our commercial presence in the U.S., we have focused primarily on the acquisition and commercialization or promotion of products in the U.S. We only started to record meaningful revenues since the end of 2020, and there is no assurance that we will be able to generate substantial positive cash flow or be profitable in the future.

We plan to further fund our future operations through commercialization and out-licensing of our therapeutic candidates, commercialization of in-licensed or acquired products and raising additional capital through equity or debt financing or through non-dilutive financing. Our current cash resources are not sufficient to complete the research and development of all of our therapeutic candidates and to fully support our commercial operations until generation of sustainable positive cash flows. We expect that we will incur additional losses as we continue to focus our resources on advancing the development of our therapeutic candidates, as well as advancing our commercial operations, based on a prioritized plan that may result in negative cash flows from operating activities.

Most of our therapeutic candidates are in late-stage clinical development. All of our therapeutic candidates will likely require successful additional clinical trials before we can obtain the regulatory approvals in order to initiate commercial sales of them, if at all. We have incurred losses since inception, principally as a result of research and development, selling, marketing, and business development, and general and administrative expenses in support of our operations. We experienced net losses of approximately $97.7 million in 2021, $76.2 million in 2020, and $42.3 million in 2019. As of December 31, 2021, we had an accumulated deficit of approximately $367.9 million. Our ability to generate sufficient revenues to sustain our business operations in accordance with our plan and to achieve profitability depends mainly upon our ability, alone or with others, to successfully commercialize or promote our current commercial products and products that we may acquire or for which we may acquire commercialization rights in the future, develop our therapeutic candidates, obtain the required regulatory approvals in various territories. We may be unable to achieve any or all of these goals with regard to our current commercial products, our therapeutic candidates or products we may commercialize or promote in the future. As a result, we may never achieve sufficient revenues to sustain our business operations in accordance with our plan or be profitable.

Our limited operating history, especially under current COVID-19 pandemic conditions, makes it difficult to evaluate our business and prospects.

We have limited operating history, and our operations to date have been limited primarily to certain commercialization and promotion of products in the U.S., acquiring and in-licensing therapeutic candidates and rights to commercialize or promote products in the U.S., research and development, raising capital and recruiting scientific, commercial and management personnel, and third-party partners. Talicia® is our first and only product that was developed internally and approved for marketing by the FDA. We have limited experience achieving regulatory approval or out-licensing our therapeutic candidates. Consequently, any predictions about our future performance may not be accurate, and we may not be able to fully assess our ability to commercialize our current commercial products or ones we may acquire or develop in the future, complete the development or obtain regulatory approval for our current and future therapeutic candidates or obtain regulatory approvals, reimbursement by third-party payors, achieve market acceptance or competitive pricing of our current commercial products or products that we may commercialize or promote in the future.

Our current working capital is not sufficient to commercialize our current commercial products or to complete the research and development with respect to any or all of our therapeutic candidates. We may need to raise additional capital to achieve our strategic objectives and to execute our business plans, and our failure to raise sufficient capital or on favorable terms would significantly impair our ability to fund the commercialization of our current commercial products, therapeutic candidates, or the products we may commercialize or promote in the future, attract development or commercial partners or retain key personnel, and to fund operations and develop our therapeutic candidates.

As of December 31, 2021, we had cash, cash equivalents, short-term investments and restricted cash of approximately $54.2 million, and as of December 31, 2020, we had cash, cash equivalents and short-term investments of approximately $46.0 million. Our restricted cash as of December 31, 2021, was $16 million as required by our credit agreement with HCR Collateral Management, LLC ("HCRM"). We have funded our operations primarily through public and private offerings of our securities, through strategic investments and our credit agreement with HCRM (see "– *Our term loan facility imposes significant operating and financial restrictions on us, which may prevent us from capitalizing on business opportunities and may restrict our operational flexibility, and our failure to comply with the restrictive covenants in our term loan facility could have a material adverse effect on our business*."). We will need to raise additional capital to achieve our strategic objectives of commercializing our current commercial products and other products that we may commercialize or promote in the future and acquiring, in-licensing and developing therapeutic candidates. We plan to fund our future operations through commercialization of Movantik®, Talicia® and Aemcolo®, out-licensing of our therapeutic

candidates and commercialization of in-licensed or acquired products, and we will also need to raise additional capital through equity or debt financing or non-dilutive financing. We are not yet certain of the financial impact of our commercialization activities, and the amounts we raise may not be sufficient to complete the research and development of all of our therapeutic candidates.

We only started to record meaningful net revenues since the end of 2020, and our business is not yet profitable. As we plan to continue expending funds to commercialize Movantik®, Talicia® and Aemcolo®, out-license Talicia®, Movantik® and our therapeutic candidates and acquire additional products and therapeutic candidates and expand our efforts in research and development, we will need to raise additional capital in the future through equity or debt financing, non-dilutive financing or pursuant to development or commercialization agreements with third parties with respect to particular therapeutic candidates and commercial products approved for sale in the U.S. However, we cannot be certain that we will be able to raise capital on commercially reasonable terms or at all, or that our actual cash requirements will not be greater than anticipated. We may have difficulty raising needed capital or securing development or commercialization partners in the future as a result of, among other factors, unsuccessful commercialization of Movantik®, Talicia®, Aemcolo® or products that we may commercialize or promote in the future, as well as the inherent business risks associated with our Company, our current commercial products, products that we may commercialize or promote in the future, our therapeutic candidates, and present and future market conditions. Any financing may also involve significant dilution to our shareholders. To the extent we are able to generate meaningful revenues from our current and future commercial products, we may still need to raise capital because the revenues from our current and future commercial products may not be sufficient to cover all of our operating expenses and may not be sufficient to cover our commercial operations expenses. In addition, global and local economic conditions may make it more difficult for us to raise needed capital or secure a development or commercialization partner in the future and may impact our liquidity. If we are unable to obtain sufficient future financing, we may be forced to delay, reduce the scope of, or eliminate one or more of our commercialization programs for our current commercial products and products that we may commercialize or promote in the future, or research and development programs for our therapeutic candidates, any of which may have an adverse effect on our reputation, business, financial condition or results of operations. Moreover, to the extent we are able to raise capital through the issuance of debt or equity securities, it could result in substantial dilution to existing shareholders.

Our long-term capital requirements are subject to numerous risks.

Our long-term capital requirements are expected to depend on many potential factors, including but not limited to:

- the progress, success, and cost of our clinical trials and research and development programs, including manufacturing;
- the number and type of commercial products we commercialize or are in the process of launching;
- our ability to successfully commercialize our current commercial products and products that we may commercialize or promote in the future, including through securing commercialization agreements with third parties and favorable pricing and market share or through our own commercialization capabilities;
- the existence and entrance of generics into the market, including entrances into the market as a result of adverse outcomes in Abbreviated New Drug Application ("ANDA") litigation, that could compete with our products and erode the profitability of our commercial products or products that we may commercialize or promote in the future;
- the number and type of therapeutic candidates in development;
- our ability to successfully complete our clinical trials and research and development programs, including recruitment and completion of relevant pediatric and oncology studies, since the pediatric population and the very advanced disease state and poor prognosis of the oncology patients in our oncology studies make it particularly difficult to recruit and successfully treat the patients, and to successfully complete the studies;
- the identification and acquisition of additional therapeutic candidates and commercial products;
- the costs, timing, and outcome of regulatory review and obtaining regulatory clarity and approval of our therapeutic candidates and addressing regulatory and other issues that may arise post-approval;
- the costs of enforcing our issued patents and defending intellectual property-related claims;
- the costs of manufacturing, developing and maintaining sales, marketing, and distribution channels for our commercial products;

- our consumption of available resources, especially at a more rapid consumption than currently anticipated, resulting in the need for additional funding sooner than anticipated;
- our ability to satisfy our obligations under our credit agreement with HCRM, our license agreement with AstraZeneca and our arrangement with Daiichi Sankyo, Inc.; and
- the amount and frequency of any milestone or royalty payments for which we are responsible.

If we are unable to maintain and train an effective commercial infrastructure, including sales and marketing infrastructure, or maintain compliant and adequate commercial capabilities, we will not be able to successfully commercialize and grow our current commercial products and any products we may commercialize or promote in the future.

We and our employees, as well as our contractors, must comply with applicable regulatory requirements and restrictions relating to marketing and advertising. If we are unable to maintain compliant and adequate sales and marketing capabilities, including training our new sales personnel (including sales contractors) regarding applicable regulatory requirements and restrictions, we may not be able to increase our product revenue, may generate increased expenses, and may be subject to regulatory investigations and enforcement actions.

Our commercial efforts, including our sales and marketing efforts, must comply with various laws and regulations. Under applicable FDA marketing regulations, prescription drug promotions must be consistent with and not contrary to labeling, present "fair balance" between risks and benefits, be truthful and not false or misleading, be adequately substantiated (when required), and include adequate directions for use. Additionally, our marketing activities may be subject to enforcement by the Federal Trade Commission, state attorneys general, and consumer class-action liability if we engage in any practices that appear misleading or deceptive to the applicable agencies or consumers.

In addition to the requirements applicable to approved drug products, we may also be subject to enforcement action in connection with any promotion of an investigational new drug. A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, may not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the therapeutic candidate.

If the FDA investigates our marketing and promotional materials or other communications and finds that any of our current or future commercial products are being marketed or promoted in violation of the applicable regulatory restrictions, we could be subject to FDA enforcement action. Any enforcement action (or related lawsuit, which could follow such action) brought against us in connection with alleged violations of applicable drug promotion requirements, or prohibitions, could have an adverse effect on our reputation, business, financial condition or results of operations, as well as the reputation of any approved drug products we may commercialize or promote in the future. In addition, we may also be reliant on third parties' compliance with such regulations. For example, the initial marketing and promotional materials we previously used to commercialize Movantik® were developed by the sub licensor without any input from us.

Moreover, laws and regulations covering commercialization activities in the pharmaceutical industry are constantly changing, and we will need to continually update and adjust our policies and sales and marketing and commercialization activities to meet legal and regulatory requirements. Our ability to comply with legal and regulatory requirements at any time in time does not guarantee we will continue to be able to comply in the future.

In addition to complying with applicable laws and regulations covering commercialization activities in the pharmaceutical industry, we must also comply with various contractual terms governing our use of third-party intellectual property in our commercialization materials.

In order to maintain and increase our commercialization capabilities in the U.S. and outside the U.S., we may need to further expand, among others, our development, regulatory, manufacturing, sales and marketing capabilities, and to increase or maintain our personnel to accommodate sales. We may experience difficulties in managing this growth and integrating new personnel.

To maintain and increase our own commercialization capabilities in the U.S. and outside the U.S. we may need to expand, among others, our development, regulatory, manufacturing, sales and marketing capabilities, and to increase or maintain

our personnel to accommodate sales. We may not be able to secure or retain personnel, organizations or vendors that are adequate in number or expertise to successfully and lawfully market and sell our products in the U.S. or outside the U.S. If we are unable to expand our sales and marketing capabilities, train our sales force or contractors effectively or provide any other capabilities necessary to commercialize products, we may need to contract with third parties to market and sell our products which could have an adverse effect on our financial condition and our results of operations.

We may also have difficulty in integrating into our existing U.S. operations sales and other commercial personnel or contractors that we may hire or engage to support the commercialization of Movantik®, Talicia® and Aemcolo®. Sales personnel or contractors' productivity may decrease as we hire new, less experienced sales personnel or contractors who are not yet familiar with our commercial products. In addition, we may be exposed to greater regulatory and compliance risks with our expanded sales force and activities.

Future growth may impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees or contractors. Our U.S. subsidiary, RedHill U.S., has recently experienced high turnover rates due to the overall tightening and increasingly competitive labor market in the U.S. employment market in response to the COVID-19 pandemic. See "– *Our business could suffer if we are unable to attract and retain key personnel*" below. In addition, management may have to divert a disproportionate amount of its attention away from running our day-to-day activities and devote a substantial amount of time to managing these growth activities.

We may not successfully continue the commercialization of Movantik®, Talicia® or Aemcolo®.

We may not successfully continue the commercialization of Movantik®, Talicia® or Aemcolo® and our products may not be, or continue to be, commercially successful for various reasons, including but not limited to:

- difficulty in large-scale manufacturing, including yield and quality, and in shipping product internationally;
- low market acceptance by physicians, healthcare payors, patients and the medical community as a result of lower demonstrated clinical safety or efficacy compared to products, prevalence, and severity of adverse side effects, or other potential disadvantages relative to alternative treatment methods;
- changes to the underlying dynamics of the markets for these products, including significant extended decrease in U.S. international travel that will affect the market for Aemcolo®;
- infringement on proprietary rights of others for which we or third parties involved in the development or commercialization of our products or potential future therapeutic candidates have not received licenses;
- incompatibility with other marketed products;
- other potential advantages of alternative treatment methods and competitive forces or advancements that may make it more difficult for us to penetrate a particular market segment, if at all;
- ineffective marketing, sales, and distribution activities and support;
- lack of significant competitive advantages over other products on the market;
- lack of cost-effectiveness or unfavorable pricing compared to other alternatives available on the market;
- inability to generate sufficient revenues to sustain our business operations in accordance with our plan from the sale or marketing of a product;
- changes to product labels, indications or other relevant information that may trigger additional regulatory requirements that may have a direct or indirect impact on the commercialization of our products;
- our inability or unwillingness, for cost or other reasons, to commercialize Movantik®, Talicia® and Aemcolo® to the extent any are approved for commercialization at the time of any such collaboration issues;
- timing of market introduction of competitive products, including from generic competitors; and
- changes in any laws, regulations, or other relevant policies related to drug pricing or other marketing conditions and requirements that may directly or indirectly limit, restrict, or otherwise negatively impact our ability or success in marketing or commercializing.

With respect to Aemcolo®, due to the significant decrease in travel as a result of the COVID-19 pandemic, the travelers' diarrhea market has been significantly impacted, and we have generated very limited revenues from the sale of Aemcolo®. If U.S. international travel does not return or partially return to pre-COVID-19 pandemic levels, we cannot assure that we

will generate meaningful revenues from sales of Aemcolo®, and the likelihood of our ability to successfully market Aemcolo® is doubtful.

Physicians, various other healthcare providers, patients, payors or the medical community, in general, may be unwilling to accept, utilize or recommend Movantik®, Talicia® or Aemcolo ®. If we are unable, either on our own or through third parties, to manufacture, commercialize or market Talicia®, or to commercialize or market Movantik® or Aemcolo®, we may not achieve or continue to achieve market acceptance or continue to generate meaningful revenues from Movantik® or generate meaningful revenues from Talicia® and Aemcolo®. In addition, in order to support our growing development product portfolio, we will need to achieve revenues from sales of Movantik® and Talicia® consistent with our business expectations, which may prove more difficult than currently expected. Our reputation, business, financial condition and results of operations may be materially adversely affected by any failure to meet such expectations.

Although Aemcolo® was approved by the FDA before we acquired rights to it, such approval is contingent upon the completion of two additional postmarketing studies in specified pediatric populations.

The Pediatric Research Equity Act (PREA) amended the federal Food, Drug, and Cosmetic Act (FDCA) by authorizing the FDA to require that NDA submissions must each contain an assessment of the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations that supports dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, in some cases, grant deferrals for submission of some or all pediatric data until after the product's approval for use in adults (in addition to full and partial waivers).

Aemcolo® received FDA approval on November 16, 2018, for the treatment of travelers' diarrhea caused by non-invasive strains of *Escherichia coli* in adults, subject to the completion of the deferred pediatric studies required by PREA as mandatory postmarketing studies. In acquiring the ownership rights to Aemcolo®, we assumed responsibility for completing any postmarketing requirements or commitments that may be required to retain approval. Accordingly, we must conduct two randomized, placebo-controlled studies to evaluate the safety, tolerability, and efficacy of Aemcolo® for the treatment of travelers' diarrhea in (i) children from 6 to 11 years of age and (ii) children from 12 to 17 years of age, respectively.

In conducting the required pediatric postmarketing studies for Aemcolo®, we must comply with various regulatory requirements set forth in, or pursuant to, PREA (in addition to other FDA regulations to which clinical trials are subject, more generally). For example, pediatric study sponsors must submit periodic reports to the FDA on the status of each study and other relevant information, such as (among other things) whether any difficulties have been encountered, as well as annual reports regarding clinical safety. Such sponsors are also required to submit to the FDA a timetable for completion in connection with each pediatric postmarketing study, along with a set of milestone dates (which typically include dates for final protocol submission, clinical study completion, and final report submission) by which the FDA will measure the study's progress and compliance with applicable requirements. After submitted to and approved by the FDA, pediatric study sponsors must adhere to the agreed-upon timetables and milestones in conducting each study. Any failure to meet the deadlines established by the applicable timetable or milestone dates for a given pediatric study constitutes a violation of the FDCA (per PREA).

The timelines and milestones established for the contemplated postmarketing Aemcolo® studies, in relevant part, require that we complete the study in children from 6 to 11 years of age by June 2022 and the study in children from 12 to 17 years of age by December 2022, with submission of the final study reports by December 2022 and 2023, respectively. Due to the impact of COVID-19 and travel restrictions, we submitted a proposal to the FDA to extend the deadlines for study completion to June 2025 for our study in 6-11 year-old children and to January 2025 for our study in 12-17 year-old children and to extend the corresponding final report submission deadlines to December 2025 and June 2025, respectively. We submitted such proposal on January 2, 2022 and are awaiting the FDA's response. Upon completion of the Aemcolo® studies, if achieved, we will submit the required reports containing the safety and efficacy results of each study as supplements to the approved NDA for Aemcolo®, along with the proposed labeling changes (incorporating the relevant dosage and administration information for the studied pediatric populations) that we believe to be warranted based on the data derived from such studies. We cannot be certain that the safety and efficacy results of the pediatric postmarketing studies for Aemcolo® will be favorable, and it is possible that such study results could ultimately cause the FDA to require

certain pediatric-specific labeling for Aemcolo® that may negatively affect its reputation, competitive advantages, and/or profitability.

If we fail to complete the required pediatric postmarketing studies for Aemcolo® in accordance with PREA, we may be subject to the traditional FDA enforcement actions authorized under most other contexts, such as warning letters, seizure, injunction, and withdrawal or suspension of the marketing approval for Aemcolo®, among others, any of which may have a material adverse effect on our reputation, business, financial condition or results of operations. In addition, the FDA is required to issue PREA-Non-Compliance Letters to any sponsors who fail to meet specified PREA requirements and to publicly post each such Non-Compliance Letter on the designated FDA webpage. The postmarket pediatric obligations we assumed upon acquiring Aemcolo® could subject us to any of the above-described actions, as well as more substantial consequences beyond the scope of the FDA's traditional enforcement authority. In particular, non-compliance with PREA's postmarketing pediatric requirements could give rise to civil monetary penalties of up to $250,000 per violation and up to a total of $10 million for all violations adjudicated in a single proceeding. In addition, failure to fulfill any postmarketing commitments that we agreed to assume could also result in our breach of the license agreement with Cosmo Pharmaceuticals N.V. ("Cosmo") and cause us to lose our rights thereunder.

Any collaborative arrangements that we have established or may establish may not be successful, or we may otherwise not realize the anticipated benefits from these collaborations, including commercialization of our current commercial products. We do not control third parties with whom we have or may have collaborative arrangements, and we rely on such third parties to achieve results which may be significant to us. In addition, any current or future collaborative arrangements may place the commercialization of our current commercial products or products that we may commercialize or promote in the future or the development of our therapeutic candidates outside our control and may require us to relinquish important rights or may otherwise be on terms unfavorable to us.

Each of our collaborative arrangements requires us to rely on external consultants, advisors, and experts for assistance in several key functions, including clinical development, manufacturing, regulatory, market research, intellectual property, and commercialization. We do not control these third parties, but we rely on such third parties to achieve results, which may be significant to us. With respect to Aemcolo®, we rely on Cosmo, the party responsible for, among others, the manufacture, supply, and other operating responsibilities. With respect to Talicia®, we rely on Recipharm Strängnäs AB ("Recipharm") and other contracting parties for the manufacture of Talicia® and its components and we rely on Gaelan Medical Trade LLC ("Gaelan Medical") to obtain necessary approvals and commercialize Talicia® in the UAE. With respect to Movantik ®, we rely on AstraZeneca to, among other things, manufacture, supply and provide other operating services. With respect to opaganib, we rely on Kukbo Co. Ltd. ("Kukbo") to obtain necessary regulatory approvals and commercialize opaganib in South Korea.

Relying upon collaborative arrangements to commercialize our current commercial products and other products that we may commercialize or promote in the future and to develop our therapeutic candidates, subjects us to a number of risks, including but not limited to the following:

- we will be responsible for making certain milestones, royalty or other payments under our various in-licenses even if our operating costs exceed the revenues generated from the relevant products;
- our collaborators may default on their obligations to us and we may be forced to either terminate, litigate or renegotiate such arrangements;
- our collaborators may have claims that we breached our obligations to them which may result in termination, renegotiation, litigation or delays in performance of such arrangements;
- we may not be able to control the amount and timing of resources that our collaborators may devote to our current commercial products, products that we may commercialize or promote in the future or our therapeutic candidates;
- our collaborators may fail to comply with applicable laws, rules, or regulations when performing services for us, and we could be held liable for such violations;
- our collaborators may experience financial difficulties, making it difficult for them to fulfill their obligations to us, including payment obligations, or they may experience changes in business focus;
- our collaborators' partners may fail to secure adequate commercial supplies for our current commercial products or products that we may commercialize or promote;
- our collaborators' partners may have a shortage of qualified personnel;

- we may be required to relinquish important rights, such as marketing and distribution rights;
- business combinations or significant changes in a collaborator's business or business strategy may adversely affect a collaborator's willingness or ability to complete its obligations under any arrangement;
- under certain circumstances, a collaborator could move forward with a competing therapeutic candidate or commercial product developed either independently or in collaboration with others, including our competitors;
- collaborative arrangements are often terminated or allowed to expire, which may limit or terminate our rights to commercialize our current commercial products or products we may commercialize or promote in the future, or could delay the development and may increase the cost of developing our therapeutic candidates;
- our collaborators may not wish to extend the terms of our agreements related to our commercial products or therapeutic candidates beyond the existing terms, in which case, we will not have access to existing rights upon the expiration and will therefore not be able to develop such therapeutic candidates or commercialize or promote such products following the initial terms of our agreements; and
- our collaborators may wish to terminate the collaborative arrangements due to any disagreements or conflicts with us, a change in their assessment that the arrangement is no longer valuable, a change in control or in management or in strategy, changes in product development or business strategies of our collaborators.

In addition, our reliance upon our partners in connection with commercial activities subjects us to a number of additional risks, including but not limited to, the following:

- we do not generally control our partners' communications with the FDA or other foreign regulatory authorities, and the FDA or other foreign regulatory authorities may determine elect not to approve or to withdraw the products from the market due to various factors including any action or inaction taken by our partners (see "Item 3. Key Information – Our current commercial products or products which we may commercialize or promote in the future may be subject to recalls or market withdrawal that could have an adverse effect on our reputation, business, financial condition or results of operations.");
- in many instances, we rely on our partners to take enforcement action to protect the IP and regulatory protections, if any, of some of our commercial products. Their failure to diligently protect these products could materially affect our commercial success;
- we rely on our partners to be responsible for the manufacture of some of our current commercial products, including through third-party manufacturers with the requisite quality and manufacturing standards as required under applicable laws and regulations, and we also rely on those same partners to supply their respective products and APIs, which may result in us having those respective products and APIs in insufficient quantities or not delivered in as timely a manner as is necessary to achieve adequate or successful promotion and sale of their respective products;
- our partners relating to our commercial products may significantly create or change reimbursement agreements or increase or decrease the price of their respective products to a level that could adversely affect our sales or revenues;
- our partners may make decisions related to the product and take critical actions to support the product, including with respect to promotion, sales and marketing, medical affairs and pharmacovigilance, and any action or inaction taken by those same partners may adversely affect the sales of their respective commercial products;
- our partners may terminate their agreements with us after an agreed-upon period for reasons set forth in those same partners' respective agreements with us;
- our partners for future commercial products may change or create new agreements with wholesalers, Pharmacy Benefit Managers or other important stakeholders, which may significantly impact our ability to achieve commercial success, or they may fail to negotiate reimbursement agreements with payors which could also negatively affect our commercial success;
- our partners may change the price of their respective commercial products to a level that could adversely affect our sales or revenues; and
- our partners may not be successful in maintaining or expanding reimbursement from government or third-party payors, such as insurance companies, health maintenance organizations and other health plan administrators, which may adversely affect the sales of their respective products

If any of these or other scenarios materialize, they could have an adverse effect on our reputation, business, financial condition or results of operations.

If we acquire products, technologies, companies or businesses that own rights to, or otherwise acquire commercialization and related rights to, products, such transactions could result in additional costs, integration or operating difficulties, dilution and other adverse consequences. Such acquired products, technologies or businesses that own rights to products may not achieve commercial success or further establish our marketing and commercialization capabilities.

Part of our strategy is to identify and acquire rights to products that have been cleared or approved for marketing in the U.S. or elsewhere, and in particular, those with a therapeutic focus on GI or with therapeutic activities which are overlapping or complementary to our existing commercial activities (for example, Movantik®). Management has evaluated, and expects to continue to evaluate, a wide array of potential strategic acquisitions. From time to time, management may engage in discussions regarding potential acquisitions or licensing of rights to certain products that management believes are important to our business. Any one of these transactions could have a material effect on our reputation, business financial condition or results of operations. In connection with these acquisitions or licensing transactions, we may:

- issue equity securities that may substantially dilute our shareholders' percentage of ownership;
- be obligated to make upfront milestones, royalty or other contingent or non-contingent payments;
- incur debt or non-recurring and other charges, or assume liabilities; and
- incur amortization expenses related to intangible assets or incur large and immediate write-offs of assets or goodwill or impairment charges.

For example, to fund our growing operations and our in-license for Movantik®, we entered into a credit agreement with HCRM (see "Item 3. Risk Factors – *Our term loan facility imposes significant operating and financial restrictions on us, which may prevent us from capitalizing on business opportunities and may restrict our operational flexibility, and our failure to comply with the restrictive covenants in our term loan facility could have a material adverse effect on our business.*").

In addition, the process of integrating an acquired product, technology, company or business may create operating difficulties and expenditures and pose numerous additional risks to our operations, including:

- difficulty and expense in integrating the acquired product, technology, company or business, and personnel in accordance with our business strategy and existing operations, including the failure to achieve the expected benefits and synergies;
- obligations to further develop and commercialize the acquired product, technology, company or business, in particular in jurisdictions outside of those in which we have experience operating;
- higher than anticipated acquisition costs and expenses;
- failure to manufacture or supply, or procure manufacturers or suppliers for, the acquired product, technology, company or business economically or successfully commercialize or achieve market acceptance of the acquired product;
- exposure to liabilities of the acquired product, technology, company or business, including contract terms and conditions that are less favorable to us than our standard contractual terms, known or unknown risks relating to the validity or enforceability of patents, expiration of patents or exclusivity rights, generic competition, product defects or product liability claims, patent and other litigation and clinical, development or other liabilities;
- disruption of our business and diversion of our management's and technical personnel's time and attention from their day-to-day responsibilities;
- adverse effects on our reputation, business, financial condition or results of operations, including due to expenditures or acquisition-related costs, costs of commercialization or amortization or impairment costs for acquired goodwill and other intangible assets;

- impairment of relationships with key suppliers and manufacturers due to changes in management and ownership and difficulty in maintaining existing agreements, licenses and other arrangements or rights on substantially similar terms as existed prior to the acquisition;
- regulatory changes and market dynamics after the acquisition; and
- potential loss of key employees, particularly those of the acquired entity.

If any of the above events (or more) occur, or if we cannot effectively manage or respond to such events following one or more acquisitions, they may have a material adverse effect on our reputation, business, results of operations or financial condition.

Moreover, there can be no assurance that we will accurately or consistently identify products approved or cleared for marketing that will achieve commercial success, that we will be able to successfully acquire or commercialize such products or that such acquisitions would further establish our marketing and commercialization capabilities. In addition, pursuant to the credit agreement with HCRM, we will need lender consent in order to complete future in-licenses or acquisitions of additional therapeutic candidates or products, which may limit us from executing our business strategy.

If we are unable to successfully continue the commercialization of Movantik® and Talicia®, our business and results of operations will suffer.

In recent years, we have undertaken efforts to expand our product portfolio, including the acquisition of certain rights to promote Movantik® and the launch of Talicia®, as a result of which our commercial portfolio is significantly larger than it was previously. A significant portion of the revenues generated in the twelve-month period ended December 31, 2021, was attributable to revenues from Movantik®, and we expect our future success will significantly depend upon our ability to successfully commercialize Movantik® and Talicia®. In addition, there can be no guarantee that we will be able to establish our own manufacturing capabilities, including through third parties, in order to continue the successful commercialization of Movantik® and Talicia®. Our success depends on obtaining reimbursement to patients for our products and there is no guarantee we will be able to secure commercial or government coverage for any of our products. There is significant pressure within the U.S. healthcare reimbursement system to reduce costs of prescription drugs which could adversely affect us. In addition, in the case of Movantik®, we face competitive pressures from other drugs in the peripherally-acting mu-opioid receptor antagonist (PAMORA) class as well as non-PAMORA alternatives. Our management team could face further challenges in effectively and collaboratively working with AstraZeneca (as well as Nektar Therapeutics, the originator of Movantik®, in accordance with the terms of the AstraZeneca License Agreement). In order to support our growing development product portfolio, we will need to achieve revenues from sales of Movantik® and Talicia® consistent with our business expectations, which may prove more difficult than currently expected. Our reputation, business, financial condition and results of operations may be materially adversely affected by any failure to meet such expectations.

We may not be able to enforce claims relating to a breach of the representations and warranties that our counterparties provided under their respective agreements.

In connection with the various agreements and arrangements we have entered into or may enter into in order to, among other things, acquire, license, manufacture, supply, promote or commercialize our current products or any future products, our counterparties have given certain representations and warranties and undertaken certain indemnification obligations as applicable. Nonetheless, we may not be able to enforce any claims against such other parties relating to breaches of these representations and warranties or obligations. Moreover, even if we are able to eventually recover any losses resulting from a breach of these representations and warranties or obligations, we may temporarily be required to bear these losses ourselves.

Maintaining and potentially expanding our commercial infrastructure in the U.S., and potentially expanding to outside the U.S., is a significant undertaking that requires substantial financial and managerial resources, and we may encounter setbacks or may not be successful in our efforts.

Maintaining and potentially expanding the necessary commercial capabilities is competitive and time-consuming, and the commercialization of Movantik®, Talicia® and Aemcolo® requires a significant expenditure of operating, financial and

management resources. Even with those investments, we may not be able to effectively commercialize our current commercial products, or we may incur more expenditures than anticipated in order to maximize our sales. We cannot guarantee that we will be able to maintain or expand our sales, marketing, distribution, and market access capabilities and enter into and maintain any agreements necessary for commercialization with payors and third-party providers on acceptable terms, if at all. If we are unable to maintain or expand such capabilities, either on our own or by entering into agreements with others, or are unable to do so in an efficient manner or on a timely basis, we will not be able to maximize the commercialization of our current commercial products or products that we may commercialize or promote in the future, which would adversely affect our reputation, business, financial condition or results of operations.

Even if the commercialization of our current and future commercial products is successful, we may fail to further our business strategy as anticipated or to achieve anticipated benefits and success. We may incur higher than expected costs in connection with the commercialization of our current commercial products, and we may encounter general economic or business conditions that adversely affect these products.

In addition, if we incur higher than expected costs in connection with the commercialization of our current and future commercial products, we may need to reduce or terminate our commercial activities, which may have a material adverse effect on our reputation, business, financial condition or results of operations.

We have a limited history of independently commercializing products that we developed and for which we obtained regulatory approval, such as Talicia®, and a limited history of commercializing products in the U.S. Due to our limited experience, we may have difficulty commercializing current commercial products, including Movantik®, Talicia® and Aemcolo ®, or promoting or commercializing any products for which we may obtain FDA approval or to which we may acquire commercialization or promotion rights in the future.

Compared to competitors in the industry, we have relatively limited experience marketing and selling products in the U.S. In particular, we have limited experience in commercializing products that we developed and for which we obtained regulatory approval, such as Talicia®, which may materially increase our marketing and sales expenses or cause us to be ineffective in these efforts. Talicia® is the first product that we are commercializing that we developed and for which we obtained regulatory approval. Our prior experience promoting and commercializing several other commercial products in the U.S. that we no longer commercialize or promote was limited and brief. There can be no assurance we will successfully commercialize our current commercial products or any products we may commercialize or promote in the future.

In addition, many companies, both public and private, including well-known pharmaceutical companies and smaller niche-focused companies, are currently selling, marketing and distributing drug products that directly compete with our current commercial products and therapeutic candidates that we may seek to commercialize in the future. Many of these companies have significantly greater financial capabilities, marketing, and sales experience and resources than us. As a result, our competitors may be more successful than we are in commercializing products, and we may not be able to generate sufficient revenue to achieve or sustain profitability.

Our failure to accurately forecast demand for our commercial products, or to quickly adjust to forecast changes, could adversely affect our business and financial results.

Market uncertainty and COVID-19 pandemic conditions make it difficult for us to accurately forecast future commercial product demand. We will be setting target levels for the manufacture of our commercial products in advance of purchases based upon our forecasts of commercial product sales.

If our forecasts exceed demand, we could experience excess inventory of active pharmaceutical ingredients (“APIs”) or of our commercial products, which can increase our inventory costs and result in obsolete inventory. Alternatively, if demand exceeds our forecasts, this may cause a shortage of commercial products, or the APIs used in our products, which could result in an inability to satisfy demand for our commercial products and a resulting material loss of market share and potential revenue. A failure to accurately predict the level of demand for our commercial products could adversely affect our revenues and net income. Moreover, the supply agreement that we have entered into in connection with our in-license for Movantik® limits the extent to which we can deviate from our forecasts.

In addition, some of our suppliers may require extensive advance notice of our requirements in order to produce APIs or commercial products in the quantities we desire. Long lead times may require us to place orders far in advance of the time when the commercial products will be offered for sale, and limitations on our flexibility to change such orders may not only make it difficult for us to accurately forecast demand for our commercial products, but also expose us to risks relating to shifts in consumer demand and trends and adversely affecting our operating results.

We rely on data from third parties in connection with the sale of our commercial products and our assessment of product acquisition opportunities. Inaccuracies in such data may affect the revenues of our commercial products and our allocation of resources, and as a result, may adversely affect our reputation, business, financial condition or results of operations.

We rely on data from third parties, including data providers, in connection with our commercial business. Revenues for the commercialization of some of our commercial products, as well as our assessment of opportunities to acquire rights to products, are dependent on the volume of sales of commercial products, which is calculated based on information obtained from third parties. Although we take steps to verify this data, the information we receive may be inaccurate or incomplete. In the event the information we receive is inaccurate or incomplete, this may affect our reported revenue for a reporting period or our decisions of whether to acquire rights to certain products.

If third parties do not manufacture or sell our current commercial products, our therapeutic candidates, upon approval, if any, or products we may commercialize or promote in the future in sufficient quantities, within the required timeframes, at an acceptable cost and in accordance with applicable quality standards and other regulatory requirements, the commercialization of our current commercial products or products we may commercialize or promote in the future may be adversely affected, or clinical development of our therapeutic candidates.

We do not currently own or operate manufacturing facilities. We rely on, and expect to continue to rely on, third parties to manufacture commercial quantities of our current commercial products and products that we may commercialize or promote in the future and clinical quantities of our therapeutic candidates. We rely on the manufacturer of Talicia® to provide sufficient quantities of Talicia® in the required timeframe. We rely on Cosmo to provide sufficient quantities of Aemcolo® in the required timeframe. In addition, we rely on AstraZeneca to provide sufficient quantities of both Movantik® and the API used in connection therewith for a set transition period. In addition, we are in the process of transitioning the manufacture of Movantik® from AstraZeneca to other third parties. This transition will need to be completed in a successful and timely manner for our supply requirements to be met. During the transition and thereafter, we will rely on various third parties to satisfy our supply requirements and there is no guarantee they will be able to do so successfully or in a timely manner. Our reliance on third parties includes our reliance on them for quality assurance related to regulatory compliance. Our current and anticipated future reliance upon others for the manufacture of our therapeutic candidates and any products that we may commercialize or promote may adversely affect our future operations and our ability to commercialize our current commercial products and any products that we may commercialize or promote on a timely and competitive basis, and to develop therapeutic candidates.

We may not be able to maintain our existing or future third-party manufacturing arrangements on acceptable terms, if at all. If for some reason our manufacturers or our development or commercialization partners' manufacturers do not perform as agreed or expected or terminate or fail to renew the agreements for any reason, we or our partners may be required to replace them, in which event we may incur added costs and delays in identifying, engaging, qualifying under applicable regulatory requirements and training any such replacements and entering into agreements with such replacements on acceptable terms. In addition, our ability to enter into such alternative arrangements within a reasonable period of time, if at all, may be contractually limited by the terms of our manufacturing agreements existing at that time. Obtaining the necessary FDA or other regulatory approvals or other qualifications required for changes in manufacturing sites, methods or processes under applicable regulatory requirements could result in a significant interruption of supply. In the case of the manufacturers of Movantik® and Talicia®, in particular, the delay in identifying, engaging, qualifying and training its replacement may be extended, leading to a significant interruption of supply. Any such additional costs and delays may adversely impact our ability to obtain regulatory clearances and approvals for our therapeutic candidates or any product we may commercialize or promote or make such commercialization or marketing economically unfeasible.

We rely on third parties to manufacture and supply us with high-quality APIs and their starting materials in the quantities and quality we require on a timely basis.

We currently do not manufacture any APIs ourselves. Instead, we rely on third-party vendors for the development, manufacture, and supply of our APIs that are used to formulate our current commercial products and products we may commercialize or promote in the future and our therapeutic candidates. If these suppliers are incapable or unwilling to meet our current or future needs on acceptable terms or at all, we could experience delays in supplying product to market or commercial supply shortages that would adversely affect our sales of products we currently or may commercialize or promote in the future, or delays in obtaining regulatory clearances or approvals for our therapeutic candidates.

While there may be several alternative suppliers of APIs on the market, for most of our products we have yet to conclude extensive investigations into the quality or availability of their APIs. Changing API suppliers or finding and qualifying new API suppliers can be costly and take a significant amount of time. Many APIs require significant lead-time to manufacture. There can also be challenges in maintaining similar quality or technical standards from one manufacturing batch to the next. In connection with our in-license for Movantik®, we rely on AstraZeneca to provide the necessary API during a set transition period. Upon the expiration of such transition period, we will be responsible for finding a new API supplier as we do not expect to manufacture the necessary API ourselves.

If we are not able to find stable, affordable, high quality, or reliable supplies of our APIs, we may not be able to produce enough supplies of our current commercial products or products we may commercialize or promote in the future, or of our therapeutic candidates, which could have a material adverse effect on our reputation, business, financial condition or results of operations.

In addition, while to date there have been no significant disruptions to our supply chain, including to the manufacture of our APIs or their starting materials, there may be unfavorable changes in the availability or cost of raw materials, intermediates, and other materials necessary for production, which may result in disruptions in our supply chain. See " – *The ongoing COVID-19 pandemic may adversely affect our business, revenues, results of operations and financial condition*."

We anticipate continued reliance on third-party manufacturers for our current commercial products, and we expect to rely on third-party manufacturers if we are successful in obtaining marketing approval from the FDA and other regulatory agencies for any of our therapeutic candidates.

We rely on, and we expect to continue to rely on, third-party manufacturers to produce commercial quantities of our current commercial products. In addition, we expect to rely on third-party manufacturers to produce products that we may commercialize or promote in the future. To date, other than Talicia®, which the FDA has approved for marketing in the U.S., our therapeutic candidates have been manufactured in relatively small quantities for preclinical testing and clinical trials, as well as for other regulatory purposes by third-party manufacturers. If the FDA or other regulatory agencies approve any of our current or future therapeutic candidates for commercial sale, we expect that we would rely, at least initially, on third-party manufacturers to produce commercial quantities of our approved therapeutic candidates. These manufacturers may not be able to successfully increase or maintain the manufacturing capacity for our current commercial products or any product we may commercialize or promote in the future or any of our therapeutic candidates that may be approved in the future, in a timely or economic manner, or at all. The significant scale-up of manufacturing may require additional validation studies, which the FDA must review and approve. Foreign regulatory agencies may also require the approval of additional validation studies for scaling up the manufacturing process of any of our therapeutic candidates or current or future commercial products. If the third-party manufacturers are unable to successfully increase or maintain the manufacturing capacity for a therapeutic candidate, current commercial products or for products that we may commercialize or promote in the future, or if we are unable to secure replacement third-party manufacturers or unable to establish our own manufacturing capabilities, the commercial launch of any approved products may be delayed or there may be a shortage in supply. With respect to Movantik®, until we are able to establish long-term manufacturing capabilities (including through third-party manufacturers), which will not be earlier than the expiration of the set transition period, our ability to arrange for an alternative manufacturer is contractually limited in the event that AstraZeneca is unable to increase or maintain the manufacturing capacity to satisfy our needs. A supply disruption from any of our third-party manufacturers could have a material adverse effect on our reputation, business, financial condition or results of operations.

Reliance on third-party manufacturers entails risks, including, but not limited to:

- manufacturing delays if our third-party manufacturers give greater priority to the supply of other products over our current or future commercial products, including Movantik®, Talicia® and Aemcolo ®, or any future therapeutic candidates, if approved, or otherwise do not satisfactorily perform according to the terms of their agreements with us;
- the possible termination or nonrenewal of manufacturing agreements by the third-party manufacturers at a time that is costly or inconvenient for us;
- the possible breach of manufacturing agreements by third-party manufacturers;
- delays in obtaining regulatory approval for any future therapeutic candidates, if our third-party manufacturers fail to satisfy FDA inspection requirements in connection with pre-approval inspections or otherwise fail to comply with regulatory requirements; and
- product loss or serious adverse events due to contamination, equipment failure, or improper installation or operation of equipment or operator error.

If we are unable to establish collaborations for our therapeutic candidates or products we may commercialize or promote, or otherwise not be able to raise substantial additional capital, we will likely need to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our approved products or our therapeutic candidates and products that we may commercialize or promote in the future will require additional cash to fund expenses. As such, our strategy includes either selectively partnering or collaborating with multiple pharmaceutical and biotechnology companies to assist us in furthering the development or potential commercialization of our approved products and therapeutic candidates, if approved, promoting or commercializing products, in whole or in part, in some or all jurisdictions or through our own commercialization capabilities, such as our commercial partnership with Gaelan Medical and commercial partnership with Kukbo. With respect to potential new third-party partners for the development or commercialization of our approved products and therapeutic candidates, if approved, and development or commercialization of products that we may commercialize or promote in the future, we may not be successful in entering into collaborations with third parties on acceptable terms, or at all. In addition, if we fail to negotiate and maintain suitable development, commercialization or promotion agreements or otherwise raise substantial additional capital to secure our own commercialization capabilities, we may have to limit the size or scope of our activities or we may have to delay or terminate one or more of our development or commercialization programs. Any failure to enter into development or commercialization agreements with respect to the development, marketing and commercialization of any therapeutic candidates or products we may commercialize or promote or failure to develop, market and commercialize such commercial products or therapeutic candidates or products we may commercialize or promote independently may have an adverse effect on our reputation, business, financial condition or results of operations.

We may depend on our ability to identify, consummate and integrate in-licenses or acquire additional therapeutic candidates to achieve commercial success, including products approved or cleared for marketing in the U.S. or elsewhere.

Movantik®, Talicia®, Aemcolo® and our six clinical-stage development therapeutic candidates were all acquired or licensed by us from third parties and we may in the future pursue in-licenses or acquisitions of additional therapeutic candidates or products and seek to integrate them into our operations as well. We evaluate internally and with external consultants each therapeutic candidate we in-license or acquire. However, there can be no assurance as to our ability to accurately or consistently identify therapeutic candidates or products that have been approved or cleared for marketing in the U.S. or elsewhere that are likely to achieve commercial success. In addition, even if we identify additional therapeutic candidates or products that have been approved or cleared for marketing in the U.S. or elsewhere that are likely to achieve commercial success, there can be no assurance as to our ability to in-license or acquire such therapeutic candidates or products under favorable terms or at all. In-licenses and acquisitions of therapeutic candidates and products involve risks that could adversely affect our future results of operations.

We compete with other entities for some in-license or acquisition opportunities.

As part of our overall strategy, we pursue opportunities to in-license or acquire therapeutic candidates and products that have been approved or cleared for marketing in the U.S. We may compete for in-license and acquisition opportunities with other companies, including established and well-capitalized companies. As a result, we may be unable to in-license or acquire additional therapeutic candidates or products that have been approved or cleared for marketing in the U.S. at all or on favorable terms. Our failure to further in-license or acquire therapeutic candidates or products that have been approved or cleared for marketing in the U.S. in the future may materially hinder our ability to grow and could materially harm our reputation, business, financial condition or results of operations.

If we or a licensor or a partner of ours cannot meet our or their respective obligations under our acquisition, in-license or other development or commercialization agreements or renegotiate the obligations under such agreements, or if other events occur that are not within our control, such as bankruptcy of a licensor or a partner, we could lose the rights to our therapeutic candidates or products we may commercialize or promote, experience delays in developing or commercializing our therapeutic candidates or products we may commercialize or promote or incur additional costs, which could have a material adverse effect on our reputation, business, financial condition or results of operations.

We acquired our rights to Talicia® and two of our other therapeutic candidates, RHB-104, and RHB-106, from a third party pursuant to an asset purchase agreement. In addition, we in-licensed our rights to three other therapeutic candidates, RHB-102 (Bekinda®), opaganib, and RHB-107 (upamostat), pursuant to license agreements in which we received exclusive perpetual licenses to certain patent rights and know-how related to these therapeutic candidates. We have also obtained the exclusive U.S. rights to commercialize Aemcolo® and we obtained the global rights (excluding Europe, and Canada) to commercialize Movantik®, each pursuant to a license agreement. These agreements require us to make payments and satisfy various performance obligations in order to maintain our rights and licenses with respect to these marketed products and therapeutic candidates. If we or our collaborators do not meet our or their respective obligations under these or future agreements, or if other events occur that are not within our control, such as the bankruptcy of a licensor, we could lose the rights to commercialize our current and future commercial products or to our therapeutic candidates, experience delays in developing our therapeutic candidates or incur additional costs. For example, AstraZeneca divested its rights in Movantik® in Europe, Canada and Israel in 2016 to other third-party sublicensees. In connection with our in-license for Movantik®, if our sub licensor or such third-party sublicensees do not meet their respective obligations under their respective agreements, we may lose the ability to commercialize Movantik®. The loss of such rights could have a material adverse effect on our reputation, business, financial condition or results of operations.

In addition, we are responsible for the cost of filing and prosecuting certain patent applications and maintaining certain issued patents licensed to us. If we do not meet our obligations under these agreements in a timely manner or if other events occur that are not within our control, such as the bankruptcy of a licensor, which impact our ability to prosecute certain patent applications and maintain certain issued patents licensed to us, we could lose the rights to our current and future commercial products or our therapeutic candidates which could have a material adverse effect on our reputation, business, financial condition or results of operations. We manage a large portfolio of patents and may decide to discontinue maintaining certain patents in certain territories for various reasons, including costs, such as a current belief that the commercial market for the therapeutic candidate will not be large or that there is a near-term patent expiration that may reduce the value of the therapeutic candidate. In the event we discontinue maintaining such patents, we may not be able to enforce rights for our therapeutic candidates or protect our therapeutic candidates from competition in those territories.

Disputes may arise between us and third parties from whom we have acquired assets or commercialization rights or with which we have license agreements. Any conflict, dispute or disagreement with such third parties may result in disruptions to our business relationships, require us to pay damages and incur costs, adversely affect our results of operations and may lead to loss of rights that are important to our business or costly litigation.

Our existing agreements impose, and we expect that future acquisition, commercialization or license agreements will impose, various diligence, milestone payments, royalty or other obligations on us. Such agreements require, or may in the future require, us to remit upfront and royalty payments or performance milestone payments, for commercial products that we in-license and to supply and delivery of know-how for products that we out-license. Any failure on our part to perform our obligations could lead to us losing rights under our licenses and could thereby adversely affect our business. If there

is any conflict, dispute, disagreement or issue of non-performance between us and our third-party partners regarding our rights or obligations under the acquisition, commercialization or license agreements, including any such conflict, dispute or disagreement arising from our failure to satisfy payment obligations under any such agreement or to perform certain activities or to adhere to any contractual obligation, we may be liable to pay damages and incur costs, and it could lead to delays in the research, development, collaboration, and commercialization of our commercial products, products we may promote or commercialize in the future or our therapeutic candidates. The resolution of such disputes could require or result in litigation or arbitration, which could be time-consuming and expensive. Such third-party partner may have a right to terminate the affected license subject to a dispute. If our existing agreements are terminated, it would have a material adverse effect on our reputation, business, financial condition or results of operations.

Our business could suffer if we are unable to attract and retain key personnel and additional highly qualified personnel.

The loss of the services of members of senior management or other key personnel could delay or otherwise adversely impact the successful completion of our planned clinical trials or the commercialization of our current commercial products and therapeutic candidates, if approved, and any product we may commercialize or promote in the future, or otherwise affect our ability to manage our company effectively and to carry out our business plan. These key personnel are Dror Ben-Asher, our Chief Executive Officer, Reza Fathi, Ph.D., our Senior Vice President for Research and Development, Gilead Raday, our Chief Operating Officer, Adi Frish, our Chief Corporate and Business Development Officer, Guy Goldberg, our Chief Business Officer, Micha Ben Chorin, our Chief Financial Officer, Rick D. Scruggs, our Chief Commercial Officer, Dr. June Almenoff, our Chief Medical Officer, Dr. Mark Levitt, our Chief Scientific Officer and Rob Jackson, our Senior VP, Sales & Marketing. We do not maintain key-man life insurance. Although we have entered into employment or consultancy agreements with all of the members of our senior management team, members of our senior management team may resign at any time. High demand exists for senior management and other key personnel in the pharmaceutical industry. There can be no assurance that we will be able to continue to retain and attract such personnel.

Our growth and success also depend on our ability to attract and retain additional highly qualified scientific, technical, business development, marketing, sales, managerial and finance personnel. We experience intense competition for qualified personnel, and the existence of non-competition agreements between prospective employees and their former employers may prevent us from hiring those individuals or subject us to liability from their former employers An overall tightening and increasingly competitive labor market in the U.S. employment market generally, especially in response to the COVID-19 pandemic, has been recently observed in the U.S. Our U.S. subsidiary, RedHill U.S., has recently experienced high turnover rates. A sustained labor shortage or increased turnover rates within our employee base, caused by the COVID-19 pandemic or as a result of general macroeconomic factors, could lead to increased costs, such as increased overtime to meet demand and increased wage rates to attract and retain employees, and could negatively affect our ability to efficiently operate our manufacturing and distribution facilities and overall business. If we are unable to hire and retain employees capable of performing at a high-level, or if mitigation measures we may take to respond to a decrease in labor availability, such as overtime and third-party outsourcing, have unintended negative effects, our business could be adversely affected. An overall labor shortage, lack of skilled labor, increased turnover or labor inflation, caused by the COVID-19 pandemic or as a result of general macroeconomic factors, could have a material adverse impact on our operations, results of operations, liquidity or cash flows.

In addition, as part of our plan to promote our current commercial products and potential products we may develop, we may need to expand and maintain our marketing and sales capabilities. While we attempt to provide competitive compensation packages to attract and retain key personnel, many of our competitors are likely to have greater resources and more experience than we have, making it difficult for us to compete successfully for key personnel. If we cannot attract and retain sufficiently qualified suitable employees on acceptable terms, we may not be able to develop and commercialize our commercialized products and competitive therapeutic candidates. Further, any failure to effectively integrate new personnel could materially prevent us from successfully growing our company.

We face several risks associated with international business.

We operate our business in multiple international jurisdictions. Such operations could be materially affected by changes in foreign exchange rates, capital and exchange controls, expropriation and other restrictive government actions, changes in intellectual property legal protections and remedies, changes in data privacy laws, trade regulations and procedures and

actions affecting approval, production, pricing, and marketing of, reimbursement for and access to, our current commercial products and products we may commercialize or promote, or our therapeutic candidates, as well as by political unrest, unstable governments and legal systems, and inter-governmental disputes. For example, though we have an exclusive license agreement with Gaelan Medical for Talicia® in the UAE and an exclusive license agreement with Kukbo for opaganib in South Korea, we may not be able to obtain regulatory approval in the UAE or South Korea, may experience a termination of the agreement, or may be unable to sell the product or sell the product in sufficient quantities to generate meaningful revenues. In addition, we are subject to global events beyond our control, including war, public health crises, such as pandemics and epidemics (as described above), trade disputes and other international events. In the UAE, for example, threats to the stability of the Abraham Accords between the UAE, the U.S. and Israel may disrupt our ability to supply Talicia® to our first non-U.S. territory. Any of these changes could have a material adverse effect on our reputation, business, financial condition or results of operations. In addition, the current armed conflict in Ukraine and the subsequent economic sanctions imposed by some countries on Russia and certain territories in Ukraine may negatively impact the supply chain for our commercial products, our R&D activities and our business development activities.

Risks Related to Regulatory Matters

If we or our current or future development or commercialization partners are unable to obtain or maintain the FDA or other foreign regulatory clearance and approval for our commercial products or therapeutic candidates, we or our commercialization partners will be unable to commercialize our current commercial products, products we may commercialize or promote in the future or our therapeutic candidates, upon approval, if any.

Our current commercial products must maintain, and the products we may commercialize or promote in the future may be required to obtain and maintain, FDA and other foreign regulatory clearance and approval.

Aemcolo® was approved by the FDA in 2018 for the treatment of travelers' diarrhea caused by non-invasive strains of *E. coli* in adults, and Movantik® was approved for marketing in the U.S. for the treatment of OIC in adult patients with chronic, non-cancer pain. In addition, Talicia® was approved for marketing in the U.S. for the treatment of *H. pylori* infection in adults in November 2019. Under our license agreement with Gaelan Medical, Gaelan Medical is expected to submit Talicia® to the regulatory authorities in the UAE for approval, which approval may not be obtained. However, future regulatory developments may lead to a loss of the right to commercialize Movantik®, Talicia® or Aemcolo® or any product we may commercialize or promote in the future.

We currently have six therapeutic candidates in development, most of which are in late-clinical stage development, and for which we currently intend to develop with the goal of eventually seeking FDA or other foreign regulatory approvals. Our commercial products and therapeutic candidates are subject to extensive governmental laws, regulations, and guidelines relating to the development, clinical trials, manufacturing, marketing, promotion, and commercialization of pre- and post-approval prescription drugs. We may not be able to submit for or obtain marketing approval for any of our therapeutic candidates in a timely manner or at all.

Any material delay in obtaining or maintaining, or the failure to obtain or maintain, required regulatory clearances and approvals will increase our costs and may materially adversely affect our ability to continue to generate meaningful revenues and could adversely impact our reputation, business, financial condition, results of operations or ability to attain or sustain revenues from other markets. We also are, and will be, subject to numerous regulatory requirements from both the FDA and other foreign regulatory authorities that govern the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. Moreover, clearance or approval by one regulatory authority does not ensure clearance or approval by other regulatory authorities in separate jurisdictions. Each jurisdiction may have different approval processes and requirements and may impose additional testing, development and manufacturing requirements for our current commercial products and products that we may commercialize or promote in the future and for or our therapeutic candidates.

Additionally, the FDA or other foreign regulatory authorities may require, or companies may pursue, additional clinical trials after a product is approved for marketing. Such postmarketing studies may be mandated by the FDA or other foreign regulatory authorities as conditions for initial or continued approval for marketing. The FDA or other foreign regulatory authorities have expressed statutory authority to require holders of NDAs to conduct postmarketing trials to specifically

address safety and other issues identified by the regulatory authority. For example, in connection with our in-license for Movantik®, we will assume the costs of and responsibility for a postmarketing observational clinical trial on major adverse cardiovascular events (MACE) and for the PREA post-marketing requirements of Aemcolo®.

Certain changes related to an approved drug, including changes to the product labeling, manufacturing process, indications and other certain specifications set forth within the product's NDA, may not be made until a new NDA or NDA supplement reflecting the applicable changes is submitted to and approved by the FDA. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, including relevant pediatric data, and the FDA typically uses the same procedures and standards in reviewing NDA supplements as it does in reviewing NDAs.

Even if a therapeutic candidate receives regulatory marketing approval, such approval will be limited to a specific disease state(s) and might contain significant limitations on use in the form of warnings, precautions or contraindications, or in the form of onerous risk management plans, restrictions on distribution, among other possible restrictions. Further, even after regulatory approval is obtained, later discovery of previously unknown information, such as safety risks, problems with a product or such information, the extent or severity of which were previously unknown, may result in restrictions on the product's ability to be marketed as initially approved or even complete withdrawal of the product's NDA approval and, in effect, its removal from the market.

Additionally, the FDA or other foreign regulatory authorities may change their clearance or approval policies or adopt new laws, regulations or guidelines that materially delay or impair our ability to commercialize our current commercial products and products that we may commercialize or promote in the future, or our ability to obtain the necessary regulatory clearances or approvals for any of our current or future therapeutic candidates.

Although Movantik® has already been approved by the FDA, such approval is contingent upon the completion of an additional postmarketing safety study. If the study results are unfavorable, such that they reflect a negative benefit-risk profile for Movantik®, this could lead to label changes or possibly market withdrawal.

Movantik® first received FDA approval on September 16, 2014, for the treatment of OIC in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g. weekly) opioid dosage escalation. We have agreed to assume responsibility for completing any postmarketing requirements or commitments that may be required to assess possible serious cardiovascular risks associated with the drug . Accordingly, we will be required to continue the postmarketing observational epidemiological study to evaluate the MACE of Movantik®.

The timelines and milestones established for the MACE study require that we complete the study accrual by December 2021, with submission of the final study report to the FDA by December 2023.The study has been accrued and final supplementary data (e.g. MACE charts reviews, National Death Index follow-up) are being collected for inclusion in the final report. Upon completion of the MACE study, we will submit the required report containing the results of this safety study as a supplement to the approved NDA for Movantik®, along with any proposed labeling changes (incorporating the relevant dosage and administration information for the studied populations) if we believe it warranted based on study outcomes. We cannot be certain that the results of the MACE study for Movantik® will be favorable, and it is possible that such study results could ultimately cause the FDA to require certain labeling for Movantik® that may negatively affect its reputation, competitive advantages or profitability.

If we fail to complete the required MACE study for Movantik®, we may be subject to the traditional FDA enforcement actions authorized under most other contexts, such as warning letters, seizure, injunction, and withdrawal or suspension of the marketing approval for Movantik®, among others, any of which may have a material adverse effect on our reputation, business, financial condition or results of operations. The postmarketing obligations we have agreed to assume upon acquiring Movantik® could subject us to any of the above-described actions, as well as more substantial consequences beyond the scope of the FDA's traditional enforcement authority. In addition, failure to fulfill any postmarketing commitments that we have agreed to assume could also result in our breach of the license agreement with AstraZeneca AB (the "AstraZeneca License Agreement") and cause us to lose our rights thereunder.

Our current commercial products or products which we may commercialize or promote in the future may be subject to recalls or market withdrawal that could have an adverse effect on our reputation, business, financial condition or results of operations.

The FDA and similar foreign governmental authorities have the authority to require the recall of regulated products in the event of material deficiencies or defects in design or manufacture. In the case of the FDA, the authority to require a recall must be based on a FDA finding that there is a reasonable probability that the product would cause serious injury or death. In addition, foreign governmental bodies have the authority to require the recall of our products in the event of material deficiencies or defects in design or manufacture.

Product manufacturers or owners, as applicable, may, on their own initiative, recall a product if any material deficiency in a product is found. A government-mandated or voluntary recall by us or one of our collaborators, as applicable, could occur as a result of manufacturing errors, design or labeling defects or other deficiencies and issues. Recalls of any of our products would divert managerial and financial resources and will have an adverse effect on our reputation, business, financial condition or results of operations. The FDA requires that certain classifications of recalls be reported to the FDA within 10 working days after the recall is initiated. Companies are required to maintain certain records of recalls even if they are not reportable to the FDA. We may initiate voluntary recalls involving our products in the future that we determine do not require notification of the FDA. If the FDA disagrees with our determinations, they could require us to report those actions as recalls. A future recall announcement could harm our reputation with customers and negatively affect our sales. In addition, the FDA could take enforcement action for failing to report the recalls when they were conducted.

Regulatory authorities in other jurisdictions may have similar procedures that may subject any product we may commercialize or promote to limitations or withdrawal requests. In addition, the FDA or other foreign regulatory authorities may determine that the chemistry, manufacturing and controls ("CMC") of marketed products that we develop, acquire or to which we acquire commercialization rights, such as our current commercial products, is unsatisfactory due to the manufacturing standards of the products. If either of these or any regulatory action is taken, our current commercial products or any product we commercialize or promote in the future could be withdrawn from the market at any time. In addition, we may suffer from delays in further commercialization of any product we commercialize or promote.

We and our third-party manufacturers or our partners' manufacturers are, and will be, subject to regulations of the FDA and other foreign regulatory authorities, such as applicable current good manufacturing practices and other quality-based regulations.

We and our third-party manufacturers or our partners' manufacturers are, and will be, required to adhere to laws, regulations, and guidelines of the FDA and other foreign regulatory authorities setting forth current good manufacturing practices ("cGMP"). These laws, regulations, and guidelines cover all aspects of the manufacturing, testing, quality control and recordkeeping relating to our current commercial products and any products we may commercialize or promote, and our therapeutic candidates with varying cGMP rigors depending on what phase each of our respective therapeutic candidates is in with respect to its drug development process. We and our third-party manufacturers and our partners' manufacturers may not be able to comply with applicable laws, regulations, and guidelines. We and our third-party manufacturers and our partners' manufacturers are, and will be, subject to unannounced inspections by the FDA, state regulators and similar foreign regulatory authorities outside the U.S. Our failure, or the failure of our third-party manufacturers or our partners' manufacturers, to comply with applicable laws, regulations and guidelines could result in the imposition of sanctions on us, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our therapeutic candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of our current and future commercial products and therapeutic candidates, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect regulatory approval and supplies of our current and future commercial products and therapeutic candidates, and materially and adversely affect our reputation, business, financial condition or results of operations.

Furthermore, changes in the manufacturing process or procedure, including a change in the location where the product is manufactured or a change of a third-party manufacturer, will require prior FDA or other regulatory review or approval of the manufacturing process and procedures in accordance with the FDA's regulations or comparable foreign requirements. This review may be costly and time-consuming and could delay or prevent the launch or commercial production of a

product. The new facility will also be subject to pre-approval inspection. In addition, we will have to demonstrate that the product made at the new facility is equivalent to the product made at the former facility by physical and chemical methods, which are costly and time-consuming. It is also possible that the FDA may require clinical testing as a way to prove equivalency, which would result in additional costs and delay, and may also result in delays in approval or commercialization of a product or render it unfeasible.

Our current commercial products, and any product we may commercialize or promote in the future, even if all regulatory clearances and approvals are obtained, will be subject to ongoing regulatory review. If we fail to comply with continuing U.S. and applicable foreign laws, regulations, and guidelines, we could lose those clearances and approvals, and our reputation, business, financial condition or results of operations may be materially and adversely affected.

We or our commercialization partners, as applicable, are and will be subject to ongoing reporting obligations with respect to our current commercial products and any cleared or approved product that we may commercialize or promote in the future, including pharmacovigilance, and with respect to our therapeutic candidates, even if they receive regulatory clearance or approval. In addition, the manufacturing of our current commercial products, and any other product we may commercialize or promote, whether currently or in the future, and our therapeutic candidates, will be subject to continuing regulatory review, including inspections by the FDA and other foreign regulatory authorities. Furthermore, according to our in-license for Movantik®, we are responsible for managing the product's global safety database, which may result in increased inspection from foreign regulatory authorities with which we do not have experience interacting. The results of any ongoing review may result in withdrawal from the market of one of our current commercial products or products we may commercialize or promote in the future, interruption of manufacturing operations or imposition of labeling or marketing limitations for such commercial product or therapeutic candidate, or other potentially significant enforcement actions. Since many more patients are exposed to drugs following their marketing clearance or approval, serious adverse reactions that were not observed in clinical trials may occur during the commercial marketing of our current commercial products or any product we may commercialize or promote in the future, including therapeutic candidates.

If a product receives regulatory approval, the approval is limited to the specific indications for use identified in the approved marketing application and by any additional requirements, restrictions, and limitations identified at the time of the product's approval or thereafter, which could restrict the commercial value of the product. As a condition of approval or after approval (if the FDA becomes aware of new safety information), the FDA may require us to implement a Risk Evaluation and Mitigation Strategy (REMS), which may include distribution or use restrictions to manage a known or potential serious risk associated with the product. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use (ETASU). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of a given drug. Once adopted, REMS are subject to periodic assessment and modification. Additionally, the FDA may require post-approval, "Phase 4" clinical trials (for example, the MACE study with respect to Movantik®) to generate additional information on safety or efficacy. The results of such postmarketing studies may be negative and could cause the FDA to, among other things, further limit marketing efforts or a product's approved uses.

If we or our current or future commercialization partners, as applicable, are required to conduct additional clinical trials or other testing of our current commercial products, or any other product we may commercialize or promote, or of our therapeutic candidates, we may face substantial additional expenses, be delayed in obtaining marketing clearance or approval, if required by the FDA, or may never obtain marketing clearance or approval for such product we may commercialize or promote or therapeutic candidate.

Third-party manufacturers and the manufacturing facilities that we and our development or commercialization partners use to manufacture any of our current commercial products and any other products that we may commercialize or promote, and therapeutic candidate, will be subject to periodic review and inspection by the FDA and may be subject to similar review by other regulatory authorities. Later discovery of previously unknown problems with any of our current commercial products and product we may commercialize or promote, or any therapeutic candidate, manufacturer or

manufacturing process, or failure to comply with rules and regulatory requirements, may result in actions, including but not limited to the following:

- restrictions on such therapeutic candidate, marketed product, manufacturer or manufacturing process;
- warning letters from the FDA or other foreign regulatory authorities;
- withdrawal of the marketed product from the market;
- withdrawal of the therapeutic candidate from use in a clinical trial;
- suspension or withdrawal of regulatory approvals;
- refusal to approve pending applications or supplements to approved applications that we or our development or commercialization partners submit;
- voluntary or mandatory recall;
- fines;
- refusal to permit the import or export of our current commercial products or products that we may commercialize or promote in the future or our therapeutic candidates;
- product seizure or detentions;
- injunctions or the imposition of civil or criminal penalties; and
- adverse publicity.

If we or our current or future commercialization partners, suppliers, third-party contractors or clinical investigators are slow to adapt, or are unable to adapt, to changes in existing regulatory requirements or the adoption of new regulatory requirements or policies, we and our development or commercialization partners may lose marketing clearance or approval for any products already cleared or approved for marketing in any jurisdiction, resulting in decreased or lost revenue from such products and could also result in other civil or criminal sanctions, including fines and penalties, and we may lose marketing clearance or approval of any of our therapeutic candidates, if any of our therapeutic candidates are approved for marketing.

We may encounter delays in receipt of FDA approval, if any, for our therapeutic candidates due to CMC, clinical, efficacy, safety, or regulatory or other issues.

We may encounter significant delays in receipt of FDA approval, if any, for our therapeutic candidates. For example, the FDA may determine that the CMC of one of our therapeutic candidates is not satisfactory due to the manufacturing standards of the products or that additional CMC work, information or quality assurances are needed. The FDA may also consider the clinical studies conducted with a therapeutic candidate and the additional information provided to be inadequate, or insufficient, or require us to provide additional information, which may require us to conduct additional studies or otherwise significantly delay potential FDA approval of the potential NDA for a therapeutic candidate, if at all. In addition, we cannot guarantee that potential future manufacturers or other vendors related to manufacturing will be able to perform as required, will not terminate their agreements with us, or otherwise will not perform satisfactorily. The potential delay in identifying, engaging, qualifying and training an alternative manufacturer may be extended, leading to a significant delay. Furthermore, the FDA may also change its clearance or approval policies or adopt new laws, regulations or guidelines in a manner that materially delays or impairs our ability to obtain approval of the potential NDA for a therapeutic candidate, if any.

If any of these or other issues occur, we may face substantial additional expenses and otherwise experience delays in obtaining FDA approval of the NDAs we may file in the future for our therapeutic candidates, including RHB-104 for Crohn's disease, or may never obtain the FDA approval for such NDAs.

Clinical trials and related non-clinical studies may involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. We or our development or commercialization partners may not be able to obtain regulatory approvals for our therapeutic candidates or commercialize products we may commercialize or promote without completing such trials in accordance with the applicable regulatory standards, even products that may have already been cleared or approved for marketing.

We have limited experience in conducting and managing the clinical trials that are required to obtain or maintain regulatory approvals and commence or continue commercial sales. We have agreed to manage and complete the postmarketing major adverse cardiovascular events (MACE) trial for Movantik® and will be reliant on third parties in connection therewith as well. Clinical trials and related non-clinical studies are expensive, complex, can take many years and have uncertain outcomes. We cannot predict whether we, independently or through third parties, will encounter problems with any of the completed, ongoing or planned clinical trials that will cause delays, including suspension of a clinical trial, delay of data analysis or release of the final report. The clinical trials of our therapeutic candidates may take significantly longer to complete than estimated. Failure can occur at any stage of the testing, and we may experience numerous unforeseen events during, or as a result of, the clinical trial process that could materially delay or prevent the obtainment of a regulatory approval of current or future therapeutic candidates and delay or prevent their commercialization.

In connection with the clinical trials for our therapeutic candidates and other therapeutic candidates that we may seek to develop in the future, either on our own or through licensing or partnering agreements, we face various risks and uncertainties, including but not limited to:

- delays or failure in securing clinical investigators or trial sites for the clinical trials;
- delays or failure in receiving import or other government approvals to ensure appropriate drug supply;
- delays or failure in obtaining institutional review board (IRB) and other regulatory approvals to commence or continue a clinical trial;
- expiration of clinical trial material before or during our trials as a result of delays, including suspension of a clinical trial, degradation of, or other damage to, the clinical trial material;
- negative or inconclusive results or results that are not sufficiently positive from clinical trials;
- the FDA or other foreign regulatory authorities may disagree with the number, design, size, conduct or implementation of our clinical studies;
- the FDA or other foreign regulatory authorities may require us to conduct additional clinical trials or studies in connection with therapeutic candidates in development, as well as for products that have already been cleared and approved for marketing;
- inability to monitor patients adequately during or after treatment;
- inability to retain patients;
- lack of technology to support clinical trials results;
- problems with investigator or patient compliance with the trial protocols;
- a therapeutic candidate may not prove safe or efficacious; there may be unexpected or even serious adverse events and side effects from the use of a therapeutic candidate;
- the results with respect to any therapeutic candidate may not confirm the positive results from earlier preclinical studies or clinical trials;
- the results may not meet the level of statistical significance required by the FDA or other foreign regulatory authorities;
- the results may justify only limited or restrictive uses, including the inclusion of warnings and contraindications, which could significantly limit the marketability and profitability of a therapeutic candidate;
- the clinical trials may be delayed or not completed due to the failure to recruit suitable candidates or if there is a lower rate of suitable candidates than anticipated or if there is a delay in recruiting suitable candidates; and
- changes to the current regulatory requirements related to clinical trials, which can delay, hinder or lead to unexpected costs in connection with our receiving the applicable regulatory clearances or approvals.

A number of companies in the pharmaceutical and biotechnology industries, including those with greater resources and experience than us, have suffered significant setbacks in advanced clinical trials, even after seeing promising results in earlier clinical trials. As such, despite the results reported in earlier clinical trials of our therapeutic candidates, we do not

know if we will be able to complete the clinical trials we conduct or if such clinical trials will demonstrate adequate safety and efficacy sufficient to request and obtain regulatory approval to market our therapeutic candidates. If any of the clinical trials of any of our current or future therapeutic candidates do not produce favorable results or are found to have been conducted in violation of the FDA's or other regulatory body's standards governing such studies, our ability to request and obtain regulatory approval for the therapeutic candidate may be adversely impacted, which could have a material adverse effect on our reputation, business, financial condition or results of operations.

If we are unable to develop a diagnostic test for MAP, this may adversely impact our ability to develop or obtain approval for RHB-104.

We are expecting to continue to advance the development program for a companion diagnostic for the detection of MAP bacteria in Crohn's disease patients in collaboration with several U.S. universities and laboratories. However, we do not know if and when a diagnostic test for MAP will become available. If we are unable to develop a diagnostic test for MAP, this may adversely impact our ability to develop or obtain regulatory approval to market RHB-104.

We rely on third parties to conduct our clinical trials and related non-clinical studies and those third parties may not perform satisfactorily, including but not limited to failing to meet established deadlines and compliance with applicable laws and regulations for the completion of such clinical trials.

We currently do not have the ability to independently conduct clinical trials and related non-clinical studies for our therapeutic candidates, and we rely on third parties, such as contract research organizations, medical institutions, contract laboratories, development and commercialization partners, clinical investigators and independent study monitors to perform these functions. We have agreed to manage and complete the postmarketing major adverse cardiovascular events ("MACE") trial for Movantik®. Our reliance on these third parties for research and development activities reduces our control over these activities. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. Although we have, in the ordinary course of business, entered into agreements with such third parties, we continue to be responsible for confirming that each of our clinical trials and related non-clinical studies is conducted in accordance with its general investigational plan and protocol, as well as all applicable laws and regulations. For example, the FDA requires us to comply with regulations and standards, commonly referred to as good clinical practices ("GCP"), for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the trial participants are adequately protected, and regulatory authorities in other jurisdictions may have similar responsibilities and requirements. Our reliance on third parties does not relieve us of these responsibilities and requirements. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be required to replace them or perform such functions independently. Although we believe that there are a number of other third-party contractors we could engage to continue these activities, it may result in a delay of the affected trial and additional costs. Accordingly, we may be materially delayed in obtaining regulatory approvals, if any, for our therapeutic candidates and may be materially delayed in our commercialization efforts for the targeted indications.

In addition, our ability to bring our therapeutic candidates to market depends on the quality and integrity of data that we present to regulatory authorities in order to obtain marketing authorizations. Although we attempt to audit and control the quality of third-party data, we cannot guarantee the authenticity or accuracy of such data, nor can we be certain that such data has not been fraudulently generated. Furthermore, the FDA may consider clinical studies inadequate where steps have not been taken in the design, conduct, reporting, and analysis of the studies to minimize bias. For example, one potential source of bias in clinical studies is a clinical investigator with a financial stake in the outcome of the study. Accordingly, we (or the applicant of the IND or Biologics License Application, as applicable) must submit for all applicable clinical investigators either: (i) a completed Form FDA 3454 attesting to the absence of financial interests and arrangements described in the regulations, dated and signed by the chief financial officer or another responsible corporate official; or (ii) for any investigators for whom a Form FDA 3454 is not submitted, a Form FDA 3455 disclosing completely and accurately the following:

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of a covered clinical trial, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

- any significant payments of other sorts from the sponsor of the covered study, such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- any proprietary interest in the tested product held by any clinical investigator involved in a study;
- any significant equity interest in the sponsor of the covered study held by any clinical investigator involved in any study; and
- any steps taken to minimize the potential for bias resulting from any of the disclosed arrangements, interests, or payments.

The FDA may refuse to accept a filing of an NDA that does not contain the required certifications and disclosures or attestations by the applicant that the applicant has acted with due diligence to obtain the information but was unable to do so and stating the reason. Additionally, FDA refusal of an NDA on potential bias grounds may have a material adverse effect on our reputation, business, financial condition or results of operations and the credibility of our other commercial products or therapeutic candidates.

We rely on contract research organizations for the management of clinical data generated from our studies, and such contract research organizations may not perform satisfactorily.

We rely on contract research organizations to provide monitors for and to manage data for our studies. Our reliance on these contract research organizations for data management reduces our control over clinical data management. While we have agreements governing their activities, we have limited influence over their actual performance. If these contract research organizations do not successfully carry out their contractual duties or obligations or meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or for other reasons, we may be required to replace them, or our clinical studies may be extended, delayed or terminated. In addition, such failure of our contract research organizations would pose risks to the accuracy and usability of clinical data from our clinical studies. Replacing a contract research organization may result in a delay in our clinical studies and generation of data from such studies. In addition, we face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by contract research organizations, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology.

We may fail to receive or maintain the benefits from the orphan drug and QIDP designations granted by the FDA for our applicable products or therapeutic candidates, as applicable.

In the U.S., under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biologic intended to treat a rare disease or condition, which is defined as one occurring in a patient population of fewer than 200,000 in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug or biologic will be recovered from sales in the U.S. In 2011, the FDA granted RHB-104 orphan drug designation for the treatment of Crohn's disease in the pediatric population; in 2017, the FDA granted opaganib orphan drug designation for the treatment of cholangiocarcinoma and granted RHB-107 (upamostat, formerly Mesupron) orphan drug designation for the treatment of pancreatic cancer, and in 2020 the FDA granted orphan drug designation to RHB-204 for the treatment of NTM infections.

In the U.S., the orphan drug designation entitles a party to financial incentives, such as opportunities for grant funding toward clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has the orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including an NDA, to market the same drug or biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the original manufacturer is unable to assure sufficient product quantity.

Exclusive marketing rights from a given orphan drug designation may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective, or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the orphan-designated disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties

may receive and be approved for the same condition, and only the first applicant to receive approval will receive the benefits of marketing exclusivity. Even after an orphan-designated product is approved, the FDA can subsequently approve a later drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

In addition, in 2017, we announced that RHB-204 had been granted QIDP designation by the FDA for the treatment of pulmonary NTM infections. Like orphan drugs, QIDPs may take advantage of market exclusivity, which in the case of QIDPs is five years (total period of twelve years together with the orphan drug designation). However, the five-year exclusivity extension does not apply to a supplement to an application under Section 505(b) of the FDCA for any QIDP for which an extension is in effect or has expired; a subsequent application submitted with respect to a product approved by the FDA for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength; or a product that does not meet the definition of a QIDP under Section 505(g) based upon its approved uses.

Modifications to our current commercial products or to any product that we may commercialize or promote in the future, or our therapeutic candidates, may require new regulatory clearances or approvals or may require us or our development or commercialization partners, as applicable, to recall or cease marketing any of our approved products, or delay further studies of our therapeutic candidates in human subjects until clearances or approvals are obtained.

Modifications to our current commercial products and any products we may commercialize or promote, or to our therapeutic candidates, after they have been cleared or approved for marketing, if at all, may require new regulatory clearance or approvals, in particular, if we seek or are required to expand our operations to jurisdictions outside of the U.S., and, if necessitated by a problem with a marketed product, may result in the recall or suspension of marketing of the previously approved and marketed product until clearances or approvals of the modified product are obtained. The FDA and other regulatory authorities require pharmaceutical product and device manufacturers to initially make and document a determination of whether or not a modification requires a new approval, supplement or clearance. A manufacturer may determine in conformity with applicable laws, regulations, and guidelines that a modification may be implemented without pre-clearance by the FDA or other regulatory authorities. However, the FDA or other regulatory authorities can review a manufacturer's decision and may disagree. The FDA or other regulatory authorities may also, on their own initiative, determine that a new clearance or approval is required. If the FDA or other regulatory authorities require new clearances or approvals of any pharmaceutical product for which we or our partners, including development or commercialization partners, previously received marketing approval, we or our partners, including development or commercialization partners, may be required to recall and stop marketing such marketed product, which could require us or our partners, including development or commercialization partners, to redesign the marketed product and may cause a material adverse effect on our reputation, business, financial condition or results of operations.

Risks Related to Our Indebtedness

Our term loan facility imposes significant operating and financial restrictions on us, which may prevent us from capitalizing on business opportunities and may restrict our operational flexibility, and our failure to comply with the restrictive covenants in our term loan facility could have a material adverse effect on our business.

On February 23, 2020, we, through our wholly-owned U.S. subsidiary, RedHill U.S., entered into a credit agreement and certain security documents with HCR Collateral Management, LLC ("HCRM") for up to $115 million in a non-dilutive, six-year term loan facility. Under the terms of the term loan facility, RedHill U.S. borrowed $30 million to support our commercial operations and borrowed an additional $50 million under the term loan facility to fund the acquisition of rights to Movantik® from AstraZeneca AB ("AstraZeneca") . The borrowings under the term loan facility are secured by a first priority lien on substantially all of the current and future assets of our wholly-owned U.S. subsidiary, RedHill U.S., all of our assets related in any material respect to Talicia®, and all of the equity interests of RedHill U.S.

Our term loan facility contains a number of restrictive covenants that impose financial and operating restrictions on us, including our ability to:

- create liens;
- make certain investments;
- incur, assume or guarantee indebtedness;
- make restricted payments, including paying dividends and making certain acquisitions;
- merge, consolidate, sell or otherwise dispose of substantially all our assets;
- enter into transactions with affiliates and insiders;
- enter into sale and leaseback transactions;
- enter into agreements that restrict the ability of any persons to make payments to us or RedHill U.S.;
- prepay other indebtedness;
- dispose of assets;
- terminate, or alter the responsibilities of, certain executive officers; and
- permit net sales to drop below a certain threshold.

Our term loan facility also contains a number of other covenants regarding our commercial operations, including covenants that require us to maintain a minimum cash balance of $16 million at all times, a covenant requiring us to maintain minimum net sales of $90 million for each 4-quarter period beginning on June 30, 2021 and to operate our business with respect to Talicia® in a manner agreed upon with HCRM, including maintaining a number of 119 sale representatives.

Our ability to comply with the various covenants under the term loan facility may be affected by events beyond our control, and we may not be able to continue to meet the covenants. Failure to comply with such covenants could result in an event of default that, as the term loan facility provides us with limited or no opportunity to cure certain such failures, if not waived, could result in the acceleration of all our indebtedness under our term loan facility. Our term loan facility also includes various cross-default provisions with respect to our other indebtedness and our commercial agreements. If HCRM accelerates the indebtedness under the terms of the term loan facility, we may not have sufficient funds to repay our existing debt. If we are unable to repay those amounts, HCRM could proceed against the collateral granted to it to secure such indebtedness, which could have a material adverse effect on our reputation, business, financial condition or results of operations.

Our term loan facility and the restrictive covenants contained in our term loan facility could also have important consequences on our financial position and results of operations, including increasing our vulnerability to increases in interest rates because the debt under our loan agreement bears interest at variable rates. In addition, our term loan facility indebtedness uses LIBOR as a benchmark for establishing the interest rate.

The most popular LIBOR indices will be phased out by the end of June 2023. It is unclear whether new methods of calculating LIBOR will be established or if alternative benchmark reference rates will be adopted. The replacement of LIBOR with an alternative benchmark reference rate may adversely affect interest rates and result in higher borrowing costs for us under current or future credit agreements. This could adversely affect our liquidity and financial condition, results of operations, and ability to acquire debt financing. We cannot predict the effect of the elimination of LIBOR or the establishment and use of alternative benchmark reference rates and the corresponding effects of our cost of capital.

We may be unable to generate sufficient cash flow to make the required payments under the term loan facility.

Making the required payments under our loan term facility will require a significant amount of cash. Our ability to generate sufficient cash depends on numerous factors beyond our control, and our business may not generate sufficient cash flow from the sale of our commercial products. Our ability to make the required payments under our term loan facility will depend on our ability to generate cash in the future. To some extent, this is subject to general economic, market, financial, competitive, regulatory and other factors that are beyond our control. See " - The ongoing COVID-19 pandemic may adversely affect our business, revenues, results of operations and financial condition."

If our cash flow and capital resources are insufficient to make the required payments under our term loan facility, we may be forced to reduce or delay the incurrence of expenses, sell assets, seek additional capital or restructure or refinance our term loan facility. These alternative measures may not be successful and may not permit us to meet our scheduled payment obligations. Our ability to restructure or refinance our debt will depend on the market conditions and our financial position at such time. Any refinancing of our debt could be at higher interest rates and may require us to comply with more onerous covenants, which could further restrict our business operations. If we are unable to restructure or refinance our indebtedness, HCRM may accelerate the indebtedness, and if we are unable to repay those amounts, HCRM could proceed against the collateral granted to it to secure such indebtedness, which would have a material adverse effect on our reputation, business, financial condition or results of operations.

The indebtedness under our term loan facility is secured by substantially all of the current and future assets of RedHill U.S., all of our assets related in any material respect to Talicia®, and all of the equity interests of RedHill U.S. As a result of these security interests, such assets would only be available to satisfy claims of our general creditors or to holders of our equity securities if we were to become insolvent to the extent the value of such assets exceeded the amount of our indebtedness and other obligations. In addition, the existence of these security interests may adversely affect our financial flexibility.

Indebtedness under our term loan facility is secured by substantially all of the current and future assets RedHill U.S., all of our assets related in any material respect to Talicia®, and all of the equity interests of RedHill U.S. Accordingly, if an event of default were to occur under our term loan facility, HCRM could foreclose on its security interests and liquidate some or all of these assets and would have a prior right to these assets, to the exclusion of our general creditors in the event of our bankruptcy, insolvency, liquidation or reorganization. In that event, our assets would first be used to repay in full all indebtedness and other obligations secured by such assets, resulting in a substantial portion of our assets being unavailable to satisfy the claims of our unsecured indebtedness. Only after satisfying the claims of our unsecured creditors would any amount be available for our equity holders. The pledge of these assets may limit our flexibility in raising capital for other purposes. Because these assets are pledged under the term loan facility, and because of the limitations on incurring debt and granting liens in the term loan facility, our ability to incur additional secured indebtedness or to sell or dispose of assets to raise capital may be impaired, which could have an adverse effect on our financial flexibility.

If certain individuals no longer serve as chief executive officer of RedHill or chief commercial officer of RedHill U.S. or their titles, duties or authorities are diminished, we may be obligated to pay all outstanding obligations under our term loan facility.

Our term loan facility provides that, if (i) we terminate Dror Ben-Asher or Rick Scruggs from their employment as the full-time, active chief executive officer of RedHill and full-time, active chief commercial officer of RedHill U.S., respectively, or diminish their respective titles, duties or authorities as of the date we entered into our term loan facility or (ii) we permit any of the foregoing to occur and, in the case of each of clause (i) and (ii), we do not find replacements within 90 days for such individuals who are approved in writing by HCRM after its good faith consideration of potential replacements proposed by us, this constitutes an event of default and all outstanding obligations under the term loan facility can become immediately due and payable. Whether Mr. Ben-Asher and Mr. Scruggs remain as chief executive officer of RedHill and chief commercial officer of RedHill U.S., respectively, is not entirely under our control. Although we intend to find an appropriate replacement satisfactory to HCRM if either Mr. Ben-Asher or Mr. Scruggs leaves their current position, we cannot assure you that we will be able find such a replacement within the time period permitted under our term loan facility, if at all, or that such replacement will be satisfactory to HCRM. We cannot assure you that we will be able to repay all outstanding obligations payable under the term loan facility in such event or that we will be able to find alternative financing. Even if alternative financing is available, it may be on unfavorable terms, and the interest rate charged on any new borrowings could be substantially higher than the interest rate under our term loan facility, thus adversely affecting our reputation, business, financial condition or results of operations.

Risks Related to Our Industry

The market for our current commercial products, for any product we may commercialize or promote in the future and for our therapeutic candidates is rapidly changing and competitive, and new drug delivery mechanisms, drug delivery technologies, new drugs, generic products, treatments and products which may be developed by others could impair our ability to maintain and grow our business and remain competitive.

The pharmaceutical and biotechnology industry is highly competitive, and we face significant competition from many pharmaceutical, biopharmaceutical and biotechnology companies that are researching, developing and marketing products designed to address the indications for which we are currently developing therapeutic candidates or may develop therapeutic candidates in the future or for which we may commercialize or promote products. There are various other companies that currently market, are in the process of developing or may develop in the future products that address all of the indications or diseases treated by our current commercial products, products that we may commercialize or promote in the future, and our therapeutic candidates.

New drug delivery mechanisms, drug delivery technologies, new drugs and new treatments that have been developed or that are in the process of being developed or will be developed by others may render our current commercial products, products we may commercialize or promote in the future and our therapeutic candidates noncompetitive or obsolete, or we may be unable to keep pace with technological developments or other market factors. Some of these technologies may have an entirely different approach or means of accomplishing similar therapeutic effects compared to our current commercial products, products we may commercialize or promote in the future and our therapeutic candidates. In addition, our current commercial products and products we may commercialize or promote in the future may compete with products of third parties for market share, and generic drugs or products that treat the same indications as our current commercial products or products we may commercialize or promote in the future, which can have an adverse effect on our revenues by reducing our market share or requiring us to reduce the price of the products we market.

Movantik® primarily competes with other approved PAMORA drugs, several other branded prescription therapies already approved and used extensively to treat OIC, as well as with OTC products.

Talicia® primarily competes with several branded and generic therapies already approved and used extensively to treat *H. pylori*. Additionally, Phathom Pharmaceuticals, Inc. is developing a Vonoprazan-based combination treatment, for the treatment of gastroesophageal reflux disease and *H. pylori* infection. Vonoprazan is an oral small molecule potassium acid blocker.

Aemcolo® primarily competes with several competing drugs marketed in the U.S. intended for the treatment of travelers' diarrhea, including Xifaxan® (marketed by Salix Pharmaceuticals). Aemcolo® also competes with generic antibiotics such as fluoroquinolones and azithromycin. Aemcolo® also competes with prescription and OTC anti-diarrheal medications such as loperamide and bismuth subsalicylate, as well as probiotics and medical foods which may offer symptomatic relief. We may also be exposed to potentially competitive products, which may be under development to treat or prevent travelers' diarrhea, including new antibiotics, anti-diarrheals, and vaccines.

Technological competition from, and commercial capabilities of, pharmaceutical and biotechnology companies, universities, governmental entities, and others is intense and is expected to increase. Many of these entities have significantly greater research and development capabilities, human resources, and budgets than we do, as well as substantially more marketing, manufacturing, financial and managerial resources. These entities represent significant competition for us. Acquisitions of, or investments in, competing pharmaceutical or biotechnology companies by large corporations could increase such competitors' financial, marketing, manufacturing, and other resources.

The potential widespread acceptance of therapies that are alternatives to ours may limit market acceptance of our formulations, current commercial products or products we may commercialize or promote in the future, even if commercialized and therapeutic candidates. Many of our targeted diseases and conditions can also be treated by other medications or drug delivery technologies. These treatments may be widely accepted in medical communities and have a longer history of use, among other possible advantages. The established use of these competitive drugs may limit the potential for widespread acceptance of our current commercial products and products we may commercialize or promote

in the future and may limit the potential for our commercial products and therapeutic candidates to receive widespread acceptance, if commercialized.

Talicia® or any product for which we may obtain regulatory approval or acquire commercialization rights may not become or continue to be commercially viable products.

Other than Talicia®, none of our therapeutic candidates have been cleared or approved for marketing, and none of our therapeutic candidates are currently being marketed or commercialized in any jurisdiction. Even if any of our therapeutic candidates or any product we may commercialize or promote receives regulatory clearance or approval, such as Talicia®, or do not require regulatory clearance or approval, it may not become a commercially viable product. For example, even if we or our development or commercialization partners receive regulatory clearance or approval to market a therapeutic candidate or receive regulatory clearance or approval to commercialize or promote any product, the clearance or approval may be subject to limitations on the indicated uses or subject to labeling or marketing restrictions, which could materially and adversely affect their marketability and profitability. In addition, a new therapeutic candidate may appear promising at an early stage of development or after clinical trials but never reach the market, or it may reach the market but not result in sufficient product sales, if any. A therapeutic candidate or any product that we may commercialize or promote, may not result in commercial success for various reasons, including but not limited to:

- difficulty in large-scale manufacturing, including yield and quality;
- low market acceptance by physicians, healthcare payors, patients and the medical community as a result of lower demonstrated clinical safety or efficacy compared to products, prevalence, and severity of adverse side effects, or other potential disadvantages relative to alternative treatment methods;
- insufficient or unfavorable levels of reimbursement from government or third-party payors, such as insurance companies, health maintenance organizations and other health plan administrators;
- infringement on proprietary rights of others for which we or our development or commercialization partners have not received licenses;
- incompatibility with other therapeutic candidates or marketed products;
- other potential advantages of alternative treatment methods and competitive forces that may make it more difficult for us to penetrate a particular market segment, if at all;
- ineffective marketing, sales, and distribution activities and support;
- lack of significant competitive advantages over existing products on the market;
- lack of cost-effectiveness or unfavorable pricing compared to other alternatives available on the market;
- inability to generate sufficient revenues to sustain our business operations in accordance with our plan from the sale or marketing of a product in view of the economic arrangements that we have with commercialization or other partners;
- changes to labels, indications or other regulatory requirements as they relate to the commercialization of our products;
- inability to establish collaborations with third-party development or commercialization partners on acceptable terms, or at all, and our inability or unwillingness for cost or other reasons to commercialize the therapeutic candidates or any product we may commercialize or promote on our own; and
- timing of market introduction of competitive products.

Physicians, various other healthcare providers, patients, payors or the medical community, in general, may be unwilling to accept, utilize or recommend Talicia® and any product we may commercialize or promote. If we are unable, either on our own or through third parties, to manufacture, commercialize or market Talicia®, our proposed formulations, therapeutic candidates or any product we may commercialize or promote when planned, or to develop them commercially, we may not achieve any market acceptance or generate meaningful revenue.

Unexpected product safety or efficacy concerns may arise and cause any product we may commercialize or promote to fail to gain or lose market acceptance.

Unexpected safety or efficacy concerns can arise with respect to any product we may commercialize or promote, whether or not scientifically justified, potentially resulting in product recalls, withdrawals or declining sales, as well as product

liability, consumer fraud or other claims. The market perception and reputation of any product we commercialize or may commercialize or promote in the future, and their safety and efficacy are important to our business and the continued acceptance of any such product. Any negative publicity about any of our current or future commercial products, such as the pricing of any product, discovery of safety issues, adverse events, or even public rumors about such events, could have a material adverse effect on our reputation, business, financial condition or results of operations. In addition, the discovery of one or more significant problems with a product similar to any of our current commercial products or products we may commercialize or promote in the future that implicate (or are perceived to implicate) an entire class of products or the withdrawal or recall of such similar products could have an adverse effect on the current or future commercialization of any product we may commercialize or promote. New data about any of our current commercial products or products that we may commercialize or promote in the future, or products similar to any of our current commercial products or those we may commercialize or promote in the future, could cause us reputational harm and could negatively impact demand for such products due to real or perceived side effects or uncertainty regarding safety or efficacy and, in some cases, could result in product withdrawal. Any of the foregoing could have a material adverse effect on our reputation, business, financial condition or results of operations.

Heightened attention on the problems associated with the abuse of opioids could adversely affect our ability to commercialize certain of our current or future products, which would adversely affect our reputation, business, financial condition and results of operations.

In recent years, there has been increased public attention on the public health issue of opioid abuse in the U.S. Public inquiries and governmental investigations into opioid use and litigation and heightened regulatory activity regarding the sales, marketing, distribution or storage of opioid products, among other things, could cause additional unfavorable publicity regarding the use and misuse of opioids and products related to opioids (such as Movantik®), which could have a material adverse effect on our reputation as a manufacturer of an opioid-related product and our potential ability to successfully commercialize such product.

Such negative publicity could reduce the potential size of the market for Movantik® and decrease the revenues we may be able to generate from its sale, which in turn would adversely affect our business and results of operations. Additionally, such increased scrutiny of opioids generally, whether focused on Movantik® or otherwise, could have the effect of negatively impacting relationships with healthcare providers and other members of the healthcare community, reducing the overall market for opioid-related products or reducing the prescribing and use of Movantik®.

We could be adversely affected if healthcare reform measures substantially change the market for medical care or healthcare coverage in the U.S.

On March 23, 2010, President Obama signed the "Patient Protection and Affordable Care Act" (P.L. 111-148) (the "ACA") and on March 30, 2010, he signed the "Health Care and Education Reconciliation Act" (P.L. 111-152), collectively commonly referred to as the "Healthcare Reform Law." The Healthcare Reform Law included a number of new rules regarding health insurance, the provision of healthcare, conditions to reimbursement for healthcare services provided to Medicare and Medicaid patients, and other healthcare policy reforms. Through the law-making process, substantial changes have been and continue to be made to the current system for paying for healthcare in the U.S., including changes made to extend medical benefits to certain Americans who lacked insurance coverage and to contain or reduce healthcare costs (such as by reducing or conditioning reimbursement amounts for healthcare services and drugs, and imposing additional taxes, fees, and rebate obligations on pharmaceutical and medical device companies). This legislation was one of the most comprehensive and significant reforms ever experienced by the U.S. in the healthcare industry and has significantly changed the way healthcare is financed by both governmental and private insurers. This legislation has impacted the scope of healthcare insurance and incentives for consumers and insurance companies, among others. Additionally, the Healthcare Reform Law's provisions were designed to encourage providers to find cost savings in their clinical operations. Pharmaceuticals represent a significant portion of the cost of providing care. This environment has caused changes in the purchasing habits of consumers and providers and resulted in specific attention to the pricing negotiation, product selection and utilization review surrounding pharmaceuticals. This attention may result in our current commercial products, products we may commercialize or promote in the future, and our therapeutic candidates, being chosen less frequently or the pricing being substantially lowered. At this stage, it is difficult to estimate the full extent of the direct or indirect impact of the Healthcare Reform Law on us.

These structural changes could entail further modifications to the existing system of private payors and government programs (such as Medicare, Medicaid, and the State Children's Health Insurance Program), creation of government-sponsored healthcare insurance sources, or some combination of both, as well as other changes. Restructuring the coverage of medical care in the U.S. could impact the reimbursement for prescribed drugs and pharmaceuticals, including our current commercial products, those we and our development or commercialization partners are currently developing or those that we may commercialize or promote in the future. If reimbursement for the products we currently commercialize or promote, any product we may commercialize or promote, or approved therapeutic candidates is substantially reduced or otherwise adversely affected in the future, or rebate obligations associated with them are substantially increased, it could have a material adverse effect on our reputation, business, financial condition or results of operations.

Extending medical benefits to those who currently lack coverage will likely result in substantial costs to the U.S. federal government, which may force significant additional changes to the healthcare system in the U.S. Much of the funding for expanded healthcare coverage may be sought through cost savings. While some of these savings may come from realizing greater efficiencies in delivering care, improving the effectiveness of preventive care and enhancing the overall quality of care, much of the cost savings may come from reducing the cost of care and increased enforcement activities. Cost of care could be reduced further by decreasing the level of reimbursement for medical services or products (including our current commercial products, our development or commercialization partners or any product we may commercialize or promote, or those therapeutic candidates currently being developed by us), or by restricting coverage (and, thereby, utilization) of medical services or products. In either case, a reduction in the utilization of, or reimbursement for our current commercial products, any product we may commercialize or promote, or any therapeutic candidate, or for which we receive marketing approval in the future, could have a material adverse effect on our reputation, business, financial condition or results of operations.

Several states and private entities initially mounted legal challenges to the Healthcare Reform Law, in particular, the ACA, and they continue to litigate various aspects of the legislation. On July 26, 2012, the U.S. Supreme Court generally upheld the provisions of the ACA at issue as constitutional. However, the U.S. Supreme Court held that the legislation improperly required the states to expand their Medicaid programs to cover more individuals. As a result, states have a choice as to whether they will expand the number of individuals covered by their respective state Medicaid programs. Some states have not expanded their Medicaid programs and have chosen to develop other cost-saving and coverage measures to provide care to currently uninsured individuals. Many of these efforts to date have included the institution of Medicaid-managed care programs. The manner in which these cost-saving and coverage measures are implemented could have a material adverse effect on our reputation, business, financial condition or results of operations.

Further, the healthcare regulatory environment has seen significant changes in recent years and is still in flux. Legislative initiatives to modify, limit, replace, or repeal the ACA and judicial challenges have continued. We cannot predict the impact on our business of future legislative and legal challenges to the ACA or other aspects of the Healthcare Reform Law or other changes to the current laws and regulations. The financial impact of U.S. healthcare reform legislation over the next few years will depend on a number of factors, including the policies reflected in implementing regulations and guidance and changes in sales volumes for therapeutics affected by the legislation. From time to time, legislation is drafted, introduced and passed in the U.S. Congress that could significantly change the statutory provisions governing coverage, reimbursement, and marketing of pharmaceutical products. In addition, third-party payor coverage and reimbursement policies are often revised or interpreted in ways that may significantly affect our business and our products.

During his time in office, former President Trump supported the repeal of all or portions of the ACA. President Trump also issued an executive order in which he stated that it is his administration's policy to seek the prompt repeal of the ACA and in which he directed executive departments and federal agencies to waive, defer, grant exemptions from, or delay the implementation of the provisions of the ACA to the maximum extent permitted by law. Congress has enacted legislation that repeals certain portions of the ACA, including but not limited to the Tax Cuts and Jobs Act, passed in December 2017, which included a provision that eliminates the penalty under the ACA's individual mandate, effective January 1, 2019, as well as the Bipartisan Budget Act of 2018, passed in February 2018, which, among other things, repealed the Independent Payment Advisory Board (which was established by the ACA and was intended to reduce the rate of growth in Medicare spending).

Additionally, in December 2018, a district court in Texas held that the individual mandate is unconstitutional and that the rest of the ACA is, therefore, invalid. On appeal, the Fifth Circuit Court of Appeals affirmed the holding on the individual mandate but remanded the case back to the lower court to reassess whether and how such holding affects the validity of the rest of the ACA. The Fifth Circuit's decision on the individual mandate was appealed to the U.S. Supreme Court. On June 17, 2021, the Supreme Court held that the plaintiffs (comprised of the state of Texas, as well as numerous other states and certain individuals) did not have standing to challenge the constitutionality of the ACA's individual mandate and, accordingly, vacated the Fifth Circuit's decision and instructed the district court to dismiss the case. As a result, the ACA will remain in-effect in its current form for the foreseeable future; however, we cannot predict what additional challenges may arise in the future, the outcome thereof, or the impact any such actions may have on our business.

The Biden administration also introduced various measures in 2021 focusing on healthcare and drug pricing, in particular. For example, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021, and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. On the legislative front, the American Rescue Plan Act of 2021 was signed into law on March 11, 2021, which, in relevant part, eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source drugs and innovator multiple source drugs, beginning January 1, 2024. And, in July 2021, the Biden administration released an executive order entitled, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response, on September 9, 2021, HHS released a "Comprehensive Plan for Addressing High Drug Prices" that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. And, in November 2021, President Biden announced the "Prescription Drug Pricing Plan" as part of the Build Back Better Act (H.R. 5376) passed by the House of Representatives on November 19, 2021, which aims to lower prescription drug pricing by, among other things, allowing Medicare to negotiate prices for certain high-cost prescription drugs covered under Medicare Part D and Part B after the drugs have been on the market for a certain number of years and imposing tax penalties on drug manufacturers that refuse to negotiate pricing with Medicare or increase drug prices "faster than inflation." If enacted, this bill could have a substantial impact on our business. In the coming years, additional legislative and regulatory changes could be made to governmental health programs that could significantly impact pharmaceutical companies and the success of our product candidates. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

There is uncertainty as to what healthcare programs and regulations may be implemented or changed at the federal and/or state level in the U.S. or the effect of any future legislation or regulation. Furthermore, we cannot predict what actions the Biden administration will implement in connection with the Health Reform Law. However, it is possible that such initiatives could have an adverse effect on our ability to obtain approval and/or successfully commercialize products in the U.S. in the future. For example, any changes that reduce, or impede the ability to obtain, reimbursement for the type of products we currently, or intend to, commercialize in the U.S. or that reduce medical procedure volumes could adversely affect our operations and/or future business plans.

Third-party payors may not adequately reimburse customers for any of our products that we may commercialize or promote, including our current commercial products, and may impose coverage restrictions or limitations such as prior authorizations and step edits that affect their use.

Our revenues and profits depend heavily upon the availability of adequate reimbursement for the use of our current commercial products, and any products that we may commercialize or promote, from governmental or other third-party payors, both in the U.S. and in foreign markets. Reimbursement by a third-party payor may depend upon a number of

factors, including, but not limited to, the third-party payor's determination that the use of an approved or cleared therapeutic candidate or product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining reimbursement approval for a product that we may commercialize or promote, including our current commercial products, from any government, commercial or other third-party payor is a time-consuming and costly process that could require us or our development or commercialization partners to provide supporting scientific, clinical and cost-effectiveness data for the use of our products that we currently, or may, commercialize or promote to each payor. Even when a payor determines that a product that we currently or may commercialize or promote is eligible for reimbursement under its criteria, the payor may impose coverage limitations that preclude payment for some uses that are approved by the FDA or other foreign regulatory authorities, or may impose restrictions, such as prior authorization requirements, or may simply deny coverage altogether. Reimbursement rates may vary according to the use of the product that we commercialize or may commercialize or promote in the future and the clinical setting in which it is used, may be based on payments allowed for lower-cost products that are already reimbursed, may be incorporated into existing payments for products or services, and may reflect budgetary constraints or imperfections in Medicare, Medicaid or other data used to calculate these rates. In particular, reimbursement for our products may not be available from Medicare or Medicaid, and reimbursement from other third-party payors may be limited, reduced or revoked. Overall, our ability to get reimbursement coverage for our commercial products has historically been limited. Successful commercialization of our commercial products requires a conducive reimbursement environment. If our products do not receive adequate reimbursement coverage, or if reimbursement coverage is reduced or otherwise adversely affected, then their respective commercial prospects could be severely limited. Although certain payors may currently provide some form of coverage for our commercial products, payors may suspend or discontinue reimbursement at any time, may require or increase co-payments from patients, may impose restrictions or limitations on coverage, or may reduce reimbursement rates for our products. If we fail to establish broad adoption of and reimbursement for our commercial products, or if we are unable to maintain any existing reimbursement from payors, our ability to generate revenue could be harmed and this could have a material adverse effect on our reputation, business, financial condition or results of operations. In addition to our existing commercial products, any new product we may commercialize or promote in the future may require that we expend substantial time and resources in order to obtain and retain reimbursement, and any of these efforts may not be successful.

In the U.S., there have been, and we expect that there will continue to be, federal and state proposals to constrain expenditures for medical products and services, which may affect payments for any product that we currently or may commercialize or promote in the U.S. In addition, there is a growing emphasis on comparative effectiveness research, both by private payors and by government agencies. To the extent other drugs or therapies are found to be more effective than our products, payors may elect to cover such therapies in lieu of our products or reimburse our products at a lower rate. Legislation that reduces reimbursement for our current or future commercial products could adversely impact how much or under what circumstances healthcare providers will prescribe or administer those products. This could materially and adversely impact our reputation, business, financial condition or results of operations by reducing our ability to continue to generate meaningful revenue, raise capital, obtain additional collaborators and market share. At this stage, we are unable to estimate the extent of the direct or indirect impact of any such federal and state proposals.

Furthermore, the Centers for Medicare and Medicaid Services frequently change product descriptors, coverage policies, product and service codes, payment methodologies and reimbursement values. Third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, and both the Centers for Medicare and Medicaid Services and other third-party payors may have sufficient market power to demand significant price reductions. Price reductions or other significant coverage policies or payment limitations could materially and adversely affect our reputation, business, financial condition or results of operations.

We are subject to U.S. federal and state healthcare laws and regulations relating to our business, and our failure to comply with such laws could have a material adverse effect on our reputation, business, financial condition or results of operations.

We are subject to additional healthcare regulation and enforcement by the U.S. federal government and the states in which we conduct or will conduct our business. Healthcare providers, physicians, and third-party payors play a primary role in the recommendation and prescription of our current commercial products or any products we may commercialize or promote in the future. Our arrangements with third-party payors, customers, employees, or others may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our products. The laws that may affect our ability to operate include, but are not limited to, the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under government healthcare programs such as the Medicare and Medicaid programs;
- the federal Anti-Inducement Law (also known as the Civil Monetary Penalties Law), which prohibits a person from offering or transferring remuneration to a Medicare or State healthcare program beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular provider, practitioner or supplier of any item or service for which payment may be made, in whole or in part, by Medicare or a State healthcare program;
- the Ethics in Patient Referrals Act of 1989, commonly referred to as the Stark Law, which prohibits physicians from referring Medicare or Medicaid patients for certain designated health services where that physician or family member has a financial relationship with the entity providing the designated health service, unless an exception applies;
- federal false claims laws that prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other government healthcare programs that are false or fraudulent;
- the so-called federal "Sunshine Act", which requires certain pharmaceutical and medical device companies to monitor and report certain financial relationships with physicians and other healthcare providers to the Centers for Medicare and Medicaid Services for disclosure to the public;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") and its implementing regulations, which impose obligations on certain covered entities and their business associates with respect to safeguarding the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals, regulatory authorities, and potentially the media of certain breaches of security of individually identifiable health information;
- HIPAA's fraud and abuse provision, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the FDCA, which among other things, strictly regulates drug product and medical device marketing, prohibits manufacturers from marketing such products for off-label use and regulates the distribution of samples;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers.

Compliance efforts may involve substantial costs, and if our operations or business arrangements with third parties are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, monetary damages, the curtailment or restructuring of our operations, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely affect our financial results. Although effective compliance programs can help mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any violation of these

laws, or any action against us for violation of these laws, even if we successfully defend against it, could result in a material adverse effect on our reputation, business, financial condition or results of operations.

The Healthcare Reform Law also imposes reporting requirements on certain medical device and pharmaceutical manufacturers, among others, to make annual public disclosures of certain payments and other transfers of value to physicians and teaching hospitals and ownership or investment interests held by physicians or their immediate family members. Failure to submit required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not reported. In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians for marketing, medical directorships, and other purposes. Some states impose a legal obligation on companies to adhere to voluntary industry codes of behavior (e.g., the PhRMA Code and the AdvaMed Code of Ethics), which apply to pharmaceutical and medical device companies' interactions with healthcare providers; some mandate implementation of corporate compliance programs, along with the tracking and reporting of gifts, compensation and other remuneration to physicians, and some states limit or prohibit such gifts.

Most recently, there has been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, which has resulted in the enactment (or proposal) of federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, several states have passed or introduced bills designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. The U.S. Congress has also introduced bills targeting the same concerns surrounding drug pricing and related considerations. For example, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. In addition, Congress is considering additional health reform measures as part of the budget reconciliation process. These laws and any other such implementation of legislation requiring publication of drug costs could materially and adversely impact our reputation, business, financial condition or results of operations by promoting a reduction in drug prices. As such, patients may choose to use other low-cost, established drugs or therapies.

The scope and enforcement of these laws are uncertain and subject to change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and guidance. We cannot predict the impact that new legislation or any changes in existing legislation will have on our reputation, business, financial condition, or results of operations. Federal or state regulatory authorities may challenge our current or future activities under these laws. Any such challenge could have a material adverse effect on our reputation, business, financial condition or results of operations. Any state or federal regulatory review of us, regardless of the outcome, would be costly and time-consuming and could negatively and adversely affect our business or results of operations.

Our marketing, promotional and business practices, including with respect to pricing, as well as the manner in which sales forces interact with purchasers, prescribers and patients, are subject to extensive regulation, including but not limited to, state and federal anti-kickback laws and any material failure to comply could result in significant sanctions against us.

The marketing, promotional, and business practices, including with respect to pricing, of pharmaceutical companies, as well as the manner in which companies' in-house or third-party sales forces interact with purchasers, prescribers, and patients, are subject to extensive regulation, the enforcement of which may result in the imposition of civil or criminal penalties, injunctions, or limitations on marketing practices for some of our products or pricing restrictions or mandated price reductions for some of our products. Many companies have been the subject of claims related to these practices asserted by state or federal authorities. These claims have resulted in fines and other consequences, such as entering into corporate integrity agreements with the U.S. government. Companies may not promote drugs for "off-label" use, that is, uses that are not described in the product's labeling and that differ from those approved by the FDA or other applicable regulatory agencies. A company that is found to have improperly promoted drug products for off-label use may be subject to significant liability, including civil and administrative remedies, as well as criminal sanctions. In addition, enforcement

action against us could cause management's attention to be diverted from our business operations and damage our reputation.

We could be exposed to significant drug product liability claims which could be time-consuming and costly to defend, divert management attention and adversely impact our ability to obtain and maintain insurance coverage.

The clinical trials that we conduct and the testing, manufacturing, marketing, and commercial sale and use or misuse of our therapeutic candidates and any products we may commercialize or promote, involve and will involve an inherent risk that significant liability claims may be asserted against us or our development or commercial partners. Product liability claims, or other claims related to our therapeutic candidates and any products we may commercialize or promote, regardless of merit or their outcome, could require us to spend significant time and money in litigation or to pay significant settlement amounts or judgments. A product liability claim could also significantly harm our reputation and the market price of our shares and decrease demand for any of our current commercial products, products that we commercialize or promote, and delay market acceptance of our therapeutic candidates or products we may commercialize or promote. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for approved products;
- impairment of our business reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- litigation costs;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- loss of revenues; and
- the inability to receive regulatory approval for and commercialize our therapeutic candidates, upon approval, if any, in the future.

We currently have a product-liability policy that includes coverage for our clinical trials and our commercial operations. However, our insurance may prove inadequate to cover claims or litigation costs, especially in the case of wrongful death claims. Any successful product liability or other claim may prevent us from obtaining adequate liability insurance in the future on commercially desirable or reasonable terms. An inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of our current commercial products or products we may commercialize or promote in the future, or the development of our therapeutic candidates.

Our clinical trials may indicate unexpected serious adverse events or other adverse events or undesirable side effects that may harm our reputation, business, financial condition or results of operations. Serious adverse events identified during one of our Expanded Access Programs (EAPs) may present additional risks that may adversely affect our development of the therapeutic candidates involved in the applicable EAP.

As is the case with pharmaceuticals generally, certain side effects and adverse events may emerge as safety risks associated with the use of our therapeutic candidates. Similarly, serious adverse events have occurred and may occur in the future in connection with our clinical trials. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our therapeutic candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may have a material adverse effect on our reputation, business, financial condition or results of operations.

Patients who receive access to investigational new drugs that have not yet received regulatory marketing approval through expanded access programs may be suffering from life-threatening illnesses and poor prognosis and may have exhausted

all other available therapies. The risk for serious adverse events in this patient population is high, which could have a negative impact on the prospects of our therapeutic candidates that are provided under the EAP.

Serious adverse events or other undesirable side effects in connection with the use of our therapeutic candidates provided under the EAP could cause significant delays or an inability to successfully develop or commercialize such therapeutic candidates, which could materially harm our business. In particular, any such serious adverse events or other undesirable side effects could cause us or regulatory authorities to interrupt, delay or halt non-clinical studies and clinical trials, or could make it more difficult for us to enroll patients in our clinical trials. If serious adverse events or other undesirable side effects, or unexpected characteristics of our investigational new drugs that have not yet received regulatory marketing approval are observed in patients who were granted expanded access to our investigational new drugs under the EAP, further clinical development of such therapeutic candidate may be delayed or we may not be able to continue development of such therapeutic candidates at all, and the occurrence of these events could have a material adverse effect on our business. Undesirable side effects caused by our therapeutic candidates could also result in the delay or denial of regulatory approval by the FDA or other regulatory authorities or in a more restrictive label than we expect and could cause us to incur additional costs.

Global economic conditions may make it more difficult for us to commercialize our current commercial products and any products that we may commercialize or promote in the future and develop our therapeutic candidates.

The pharmaceutical industry, like other industries and businesses, continues to face the effects of the challenging economic environment. Patients experiencing the effects of the challenging economic environment, including high unemployment levels and increases in co-pays, may switch to generic products, delay treatments, skip doses or use other less effective treatments to reduce their costs. Challenging economic conditions in the U.S. include the demands by payors for substantial rebates and formulary restrictions limiting access to brand-name drugs. In addition, in Europe and in a number of emerging markets there are government-mandated reductions in prices for certain pharmaceutical products, as well as government-imposed access restrictions in certain countries. All of the aforesaid may make it more difficult for us to commercialize our current commercial products, any products that we may commercialize or promote, and our therapeutic candidates, upon approval, if any.

Our business involves risks related to handling regulated substances, which could severely affect our ability to commercialize our current commercial products and any products that we may commercialize or promote in the future and to conduct research and development of our therapeutic candidates.

In connection with our or our development or commercialization partners' research and development activities, as well as the manufacture of commercial products, materials, and therapeutic candidates and any products that we may commercialize or promote in the future, we and our development or commercialization partners are subject to federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens and waste. We and our research and development or commercialization partners may be required to incur significant costs to comply with environmental and health and safety regulations in the future. Our research and development, as well as the activities of our commercial and clinical manufacturing and commercialization partners, both now and in the future, may involve the controlled use of hazardous materials, including, but not limited to, certain hazardous chemicals. We cannot completely eliminate the risk of accidental contamination or injury from these materials. In the event of such an occurrence, we could be held liable for any damages that could result and any such liability could exceed our resources.

Security breaches, loss of data, and other disruptions could compromise sensitive information and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we may collect and store sensitive data, including intellectual property, compliance-related data, research data, our proprietary business information and that of our suppliers and business partners, technical information about our products, clinical trial plans as well as personally identifiable information of patients, clinical trial participants and employees. We also have outsourced elements of our information technology structure, and as a result, we are managing independent vendor relationships with third parties who may or could have access to our confidential information. Similarly, our business partners and other third-party providers possess certain of our sensitive data and

confidential information. The secure maintenance of this information is critical to our operations and business strategy. Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, malware, ransomware, cyber-fraud, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber-intrusion, including by computer hackers, foreign governments, and cyber-terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased.

We, our partners, vendors, and other third-party providers could be susceptible to attacks on our and their information security systems, which attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including criminal groups. Any such breach could compromise our and their networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, inappropriate disclosure of confidential or proprietary information or other loss of information, including our data being breached at third-party providers, could result in legal claims or proceedings, liability or financial loss under laws that protect the privacy of personal information, disrupt our operations, or our product development programs and damage our reputation, any of which could adversely affect our business. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

We are highly dependent on information technology networks and systems, including the Internet, to securely process, transmit and store this critical information. Security breaches of this infrastructure, including physical or electronic break-ins, computer viruses, attacks by hackers and similar breaches, can create system disruptions, shutdowns or unauthorized disclosure or modification of confidential information. The secure processing, storage, maintenance and transmission of this critical information is vital to our operations and business strategy, and we devote significant resources to protecting such information. Although we take measures to protect sensitive information from unauthorized access or disclosure, our information technology and infrastructure may be vulnerable to attacks by hackers or viruses or breached due to employee error, malfeasance or other disruptions.

A security breach or privacy violation that leads to disclosure or modification of or prevents access to consumer information (including personally identifiable information or protected health information) could harm our reputation, compel us to comply with disparate state breach notification laws, require us to verify the correctness of database contents and otherwise subject us to liability under laws that protect personal data, resulting in increased costs or loss of revenue. If we are unable to prevent such security breaches or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer a loss of reputation, financial loss, and other regulatory penalties because of lost or misappropriated information, including sensitive consumer data. In addition, these breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above.

Any such breach or interruption could compromise our networks, and the information stored there could be inaccessible or could be accessed by unauthorized parties, publicly disclosed, lost or stolen. Any such interruption in access, improper access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, such as HIPAA and the General Data Protection Regulation (GDPR) in connection with our required maintenance of the global safety database for Movantik®, and regulatory penalties. Unauthorized access, loss or dissemination could also disrupt our operations, including our ability to perform tests, provide test results, bill facilities or patients, process claims and appeals, provide customer assistance services, conduct research and development activities, collect, process and prepare Company financial information, provide information about our current and future solutions and other patient and clinician education and outreach efforts through our websites, and manage the administrative aspects of our business and damage our reputation, any of which could adversely affect our reputation, business, financial condition or results of operations. Any such breach could also result in the compromise of our trade secrets and other proprietary information, which could adversely affect our competitive position.

In addition, the interpretation and application of consumer, health-related, privacy and data protection laws in the U.S. and elsewhere are often uncertain, contradictory, and in flux. It is possible that these laws may be interpreted and applied in a

manner that is inconsistent with our practices. If so, this could result in government-imposed fines or orders requiring that we change our practices, which could adversely affect our reputation, business, financial condition or results of operations. Complying with these various laws could cause us to incur substantial costs or require us to change our business practices and compliance procedures in a manner adverse to our business.

Risks Related to Intellectual Property

We may be unable to adequately protect or enforce our rights to intellectual property, causing us to lose valuable rights. Loss of patent rights may lead us to lose market share and anticipated profits.

Our success depends, in part, on our ability, and the ability of our commercialization or development partners to obtain patent protection for our therapeutic candidates and any products that we may commercialize or promote, maintain the confidentiality of our trade secrets and know-how, operate without infringing or violating on the proprietary rights of others and prevent others from infringing or violating on our proprietary rights.

We try to protect our proprietary position by, among other things, filing U.S., European, and other patent applications related to our therapeutic candidates, inventions and improvements that may be important to the continuing development of our commercial products and therapeutic candidates, and we plan to try to do the same with products we may acquire, commercialize or promote in the future, where this is possible.

Because the patent position of pharmaceutical companies involves complex legal and factual questions, we cannot predict the scope, validity or enforceability of patents with certainty. Our issued patents and the issued patents of our commercialization or development partners may not provide us with any competitive advantages, may be held invalid or unenforceable as a result of legal challenges by third parties or could be circumvented. Ownership of the patent rights we in-license from our commercialization or development partners or the patent rights to the products already approved for marketing that we develop, acquire or for which we acquire commercialization rights may be challenged, and as a result, the rights we in-license and the rights to products we acquire may turn out not to be exclusive or we may not actually have rights under the patents despite receiving representations from a commercialization or development partner. Our competitors may also independently develop drug delivery technologies or products similar to ours or design around or otherwise circumvent patents issued to, or licensed by, us. Thus, any patents that we own or license from others may not provide any protection against competitors. Our pending patent applications, those we may file in the future or those we may license from third parties may not result in patents being issued. If these patents are issued, they may not provide us with proprietary protection or competitive advantages. The degree of future protection to be afforded by our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage.

In the U.S., Europe, and other jurisdictions, patent applications are typically not published until 18 months after filing. In addition, many companies and universities do not publish their discoveries until after patent filings are made. This makes it difficult to be certain that we were the first to file for protection of the inventions or the first to invent the inventions. As a result, we may not be able to obtain or maintain protection for certain inventions. Therefore, the enforceability and scope of our patents and patent applications in the U.S., Europe, and other jurisdictions are uncertain and unpredictable. Any patents that we own may not provide sufficient protection against competitors and may be of insufficient scope to achieve our business objectives. Additionally, the patent filings of others might act as an impediment to our ability to commercialize our current or future commercial products.

Patent rights are territorial; thus, the patent protection we do have will only extend to those countries in which we have issued patents. Even so, the laws of certain countries do not protect our intellectual property rights to the same extent as do the laws of the U.S. and the European Union. Competitors may successfully challenge our patents, produce similar drugs or products that do not infringe our patents or produce drugs in countries where we have not applied for patent protection or that do not respect our patents. Furthermore, it is not possible to know the scope of claims that will be allowed in published applications, and it is also not possible to know which claims of granted patents, if any, will be deemed enforceable in a court of law.

In some cases, litigation may be necessary to enforce our patent rights. If we choose to take an infringing third party to court, the third party may challenge the validity or enforceability of our patent rights or may assert that their activities do not infringe our patents. Litigation is expensive and unpredictable, and we may not have the proper resources to pursue such litigation or to protect our patent rights. Moreover, there is the risk that the court will find that our patents are not valid or enforceable, or that the third party does not infringe our rights in these patents. Adverse results in any such litigation could materially impair our patent rights and our ability to prevent generic and other competition for our products. Such results might also materially affect our economics and our ability to require third parties to enter a license with us or to pay us a reasonable royalty for using our technology.

In connection with the closing of our in-license for Movantik®, we assumed control of ANDA litigation related to U.S. Patent No. 9,012,469, which covers the commercial, oxalate salt, form of naloxegol (naloxegol oxalate) that is due to expire in April 2032. In September 2021, we announced that all pending patent litigation brought pursuant to the Drug Price Competition and Patent Term Restoration Act (the Hatch-Waxman Act) had been settled regarding Movantik®. The earliest licensed entry date of any generic naloxegol in the U.S. is October 1, 2030.

After the completion of the development and registration of our patents, third parties may still manufacture or market products in infringement of our patent-protected rights. Such manufacture or market of products in infringement of our patent-protected rights is likely to cause us damage and lead to a reduction in the prices of our current commercial products, any product we may commercialize or promote, or any of our therapeutic candidates, thereby reducing our potential profits.

In addition, due to the extensive time needed to develop, test and obtain regulatory approval for our therapeutic candidates or any product we may commercialize or promote, any patents that protect our therapeutic candidate or any product we may commercialize or promote may expire early during commercialization. This may reduce or eliminate any market advantages that such patents may give us. Following patent expiration, we may face increased competition through the entry of generic products into the market and a subsequent decline in market share and profits.

In addition, in some cases, we may rely on our licensors to conduct patent and trademark prosecution, patent and trademark maintenance or patent and trademark defense on our behalf. Therefore, our ability to ensure that these patents and trademarks are properly prosecuted, maintained, or defended may be limited, which may adversely affect our rights in the commercialization of our commercial products, development of our therapeutic candidates, and potential approval for marketing of our therapeutic products. Any failure by our licensors or commercialization or development partners to properly conduct patent and trademark prosecution, patent and trademark maintenance, patent and trademark enforcement, or patent defense could materially harm our ability to obtain suitable patent protection covering our commercial products or therapeutic candidates or ensure freedom to commercialize the products in view of third-party patent rights, thereby materially reducing our potential profits.

If we are unable to protect the confidentiality of our trade secrets or know-how, such proprietary information may be used by others to compete against us.

In addition to filing patents, we generally try to protect our trade secrets, know-how, and technology by entering into confidentiality or non-disclosure agreements with parties that have access to them, such as our development or commercialization partners, employees, contractors, and consultants. We also enter into agreements that purport to require the disclosure and assignment to us of the rights to the ideas, developments, discoveries and inventions of our employees, advisors, research collaborators, contractors and consultants while we employ or engage them. However, these agreements can be difficult and costly to enforce or may not provide adequate remedies. Any of these parties may breach the confidentiality agreements and willfully or unintentionally disclose our confidential information, or our competitors might learn of the information in some other way. The disclosure to, or independent development by, a competitor of any trade secret, know-how or other technology not protected by a patent could materially adversely affect any competitive advantage we may have over any such competitor.

To the extent that any of our employees, advisors, research collaborators, contractors or consultants independently develop, or use independently developed, intellectual property in connection with any of our projects, disputes may arise as to the proprietary rights to this type of information. If a dispute arises with respect to any proprietary right, enforcement of our rights can be costly and unpredictable, and a court may determine that the right belongs to a third party.

Legal proceedings or third-party claims of intellectual property infringement and other challenges may require us to spend substantial time and money and could prevent us from developing or commercializing any of our commercial products and our therapeutic candidates.

The development, manufacture, use, offer for sale, sale or importation of any of our commercial products or any of our therapeutic candidates may infringe on the claims of third-party patents or other intellectual property rights. Patentability, invalidity, freedom-to-operate or other opinions may be required to determine the scope and validity of third-party proprietary rights. The nature of claims contained in unpublished patent filings around the world is unknown to us and it is not possible to know which countries patent holders may choose for an extension of their filings under the Patent Cooperation Treaty or other mechanisms. We may also be subject to claims based on the actions of employees and consultants with respect to the usage or disclosure of intellectual property learned at other employers. The cost to us of any intellectual property litigation or other infringement proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation or defense of intellectual property litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Intellectual property litigation and other proceedings may also absorb significant management time. Consequently, we are unable to guarantee that we will be able to manufacture, use, offer for sale, sell or import any of our commercial products or of our therapeutic candidates in the event of an infringement action.

In the event of patent infringement claims, or to avoid potential claims, we may choose or be required to seek a license from a third party and would most likely be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we were able to obtain a license, the rights may be non-exclusive, which could potentially limit our competitive advantage. Ultimately, we could be prevented from commercializing a therapeutic candidate and any products that we may commercialize or promote or be forced to cease some aspect of our business operations if, as a result of actual or threatened patent infringement or other claims, we are unable to enter into licenses on acceptable terms. This inability to enter into licenses or the ability to exclude others using proprietary rights could have a material adverse effect on our reputation, business, financial condition or results of operations.

On February 22, 2021, Aether Therapeutics Inc., filed a complaint against us in the United States District Court for the District of Delaware, alleging that our marketing of the Movantik® product infringes certain patents held by Aether Therapeutics Inc. See "Item 8. Financial Information A. Consolidated Statements and Other Financial Information - Legal Proceedings regarding the Aether Litigation." Given the stage of the Aether litigation, we are unable to predict the likelihood of success of the claims of Aether Therapeutics Inc. against us or to quantify any risk of loss. The Aether litigation could last for an extended period of time and require us to dedicate significant financial resources and management resources to our defense. An adverse ruling against us could materially and adversely affect our business, financial position, results of operations or cash flows and could also result in reputational harm. Even if we are successful in defending against these claims, the Aether litigation could result in delays in future product developments, reputational harm or other collateral consequences.

The license agreements we maintain, including our license agreement with Cosmo, may be amended or terminated. If we or the other parties to our license agreements amend or terminate the license agreements, the development, testing, manufacture, production and sale of our products or product candidates may be delayed or terminated, and our business may be adversely affected.

We are parties to commercialization or license agreements, which may be terminated, subject to conditions set forth in such agreements. On October 17, 2019, we entered into a strategic collaboration with Cosmo, which included a license agreement (the "Cosmo License Agreement") with a wholly-owned subsidiary of Cosmo pursuant to which we were granted exclusive rights to commercialize Aemcolo® in the U.S. The Cosmo License Agreement provides that, beginning in October 2022, both parties have the right to terminate the Cosmo License Agreement unilaterally, subject to certain conditions. Cosmo recently expressed an interest in regaining its rights to Aemcolo® from us prior to October 2022 and in December 2021, the parties signed an amendment to the Cosmo License Agreement providing that either party may terminate the Cosmo License Agreement upon advance notice at any time. Subject to and following the termination of the Cosmo License Agreement, we would no longer be able to commercialize Aemcolo® and may never recover the costs we incurred during the term of the Cosmo License Agreement.

We may be subject to other patent-related litigation or proceedings that could be costly to defend and uncertain in their outcome.

In addition to infringement claims against us, we may become a party to other patent litigation or proceedings before regulatory agencies, including post-grant review, inter parties review, interference or re-examination proceedings filed with the U.S. Patent and Trademark Office or opposition proceedings in other foreign patent offices regarding intellectual property rights with respect to our therapeutic candidates or any products that we may commercialize or promote, as well as other disputes regarding intellectual property rights with development or commercialization partners, or others with whom we have contractual or other business relationships. Post-issuance proceedings challenging patent claims validity are not uncommon, and we or our development or commercialization partners will be required to defend these procedures as a matter of course. Such procedures may be costly, and there is a risk that we may not prevail, which could harm our business significantly.

Our status as a sublicensee under our in-license for Movantik® may increase the likelihood we will lose valuable rights to Movantik®.

Rather than obtaining direct licenses from Nektar Therapeutics, the originator of Movantik® ("Nektar"), for certain intellectual property covering the manufacture and use of Movantik®, we obtained sublicenses to such rights from AstraZeneca pursuant to AstraZeneca's agreement with Nektar. Therefore, our success depends, in part, on AstraZeneca exercising its rights and fulfilling its obligations under its agreement with Nektar. AstraZeneca's failure to exercise its rights and fulfill its obligations under its agreement with Nektar could cause us to lose our rights covering the manufacture and use of Movantik®.

In addition, AstraZeneca has previously sublicensed its rights under its agreement with Nektar to other sublicensees in Canada and Europe. Therefore, our success also depends, in part, on such other sublicensees complying with the terms and conditions of their respective agreements with AstraZeneca.

Risks Related to our ADSs

U.S. holders of ADSs may suffer adverse tax consequences if we were characterized as a passive foreign investment company.

Based on the current composition of our gross income and assets and on reasonable assumptions and projections, we believe we will not be treated as a passive foreign investment company (a "PFIC") for U.S. federal income tax purposes for 2021. However, there can be no assurance that this will be the case in future taxable years. If we were characterized as a PFIC, U.S. holders of the ADSs may suffer adverse tax consequences such as (i) having gains realized on the sale of the ADSs treated as ordinary income rather than capital gain, the preferential rate otherwise applicable to dividends received in respect of the ADSs by individuals who are U.S. holders, and (ii) having interest charges apply to certain distributions by us and sales of the ADSs.

There has been a limited market for our ADSs. We cannot ensure investors that an active market will continue or be sustained for our ADSs on the Nasdaq and this may limit the ability of our investors to sell our ADSs.

In the past, there was limited trading in our ADSs, and there is no assurance that an active trading market of our ADSs will continue or will be sustained. Limited or minimal trading in our ADSs has in the past, and may in the future, lead to dramatic fluctuations in market price and investors may not be able to liquidate their investment at all or at a price that reflects the value of the business.

While our ADSs began trading on the Nasdaq Capital Market in December 2012 and on the Nasdaq Global Market in July 2018, we cannot assure you that we will maintain compliance with all of the requirements for our ADSs to remain listed. Additionally, there can be no assurance that trading of our ADSs will be sustained or desirable.

As a foreign private issuer, we are permitted to follow certain home country corporate governance practices instead of applicable SEC and Nasdaq Stock Market requirements, which may result in less protection than is accorded to investors under rules applicable to domestic issuers.

As a foreign private issuer, we are permitted to follow certain home country corporate governance practices instead of those otherwise required under the Nasdaq Listing Rules for domestic issuers. For instance, we follow the home country practice in Israel with regard to, among other things, director nomination procedures and quorum at shareholders' meetings. In addition, we follow our home country law, instead of the Nasdaq Listing Rules, which require that we obtain shareholder approval for certain dilutive events, such as for the establishment or amendment of certain equity-based compensation plans, an issuance that will result in a change in control, certain transactions other than a public offering involving issuances of a 20% or more interest in us and certain acquisitions of the stock or assets of another company. Following our home country governance practices as opposed to the requirements that would otherwise apply to a U.S. domestic issuer listed on the Nasdaq Stock Market may provide less protection than is accorded to investors under the Nasdaq Listing Rules applicable to domestic issuers.

In addition, as a foreign private issuer, we are exempt from the rules and regulations under the Exchange Act related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file annual, quarterly and current reports and financial statements with the SEC as frequently or as promptly as domestic companies whose securities are registered under the Exchange Act.

We currently do not anticipate paying cash dividends, and accordingly, investors must rely on the appreciation in our ADSs for any return on their investment.

We currently anticipate that we will retain future earnings, if any, for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, the terms of our term loan facility prohibit us from paying dividends. Therefore, the success of an investment in our ADSs will depend upon any future appreciation in their value. There is no guarantee that our ADSs will appreciate in value or even maintain the price at which our investors have purchased their securities.

Investors in our ADSs may not receive the same distributions or dividends as those we make to the holders of our ordinary shares, par value NIS 0.01 per share ("Ordinary Shares"), and, in some limited circumstances, investors in our ADSs may not receive dividends or other distributions on our Ordinary Shares and may not receive any value for them, if it is illegal or impractical to make them available to investors in our ADSs.

The depositary for the ADSs has agreed to pay to investors in our ADSs the cash dividends or other distributions it or the custodian receives on Ordinary Shares or other deposited securities underlying the ADSs, after deducting its fees and expenses. Investors in our ADSs will receive these distributions in proportion to the number of Ordinary Shares such ADSs represent. However, the depositary is not responsible if it decides that it is unlawful or impractical to make a distribution available to any holders of ADSs. For example, it would be unlawful to make a distribution to a holder of ADSs if it consists of securities that require registration under the Securities Act of 1933, as amended, but that is not properly registered or distributed under an applicable exemption from registration. In these cases, the depositary may determine not to distribute such property and hold it as "deposited securities" or may seek to effect a substitute dividend or distribution, including net cash proceeds from the sale of the dividends that the depositary deems an equitable and practicable substitute. We have no obligation to register under U.S. securities laws any ADSs, Ordinary Shares, rights or other securities received through such distributions. We also have no obligation to take any other action to permit the distribution of ADSs, Ordinary Shares, rights or anything else to holders of ADSs. In addition, the depositary may deduct from such dividends or distributions its fees and may withhold amounts on account of taxes or other governmental charges to the extent the depositary believes it is required to make such withholding. This means that investors in our ADSs may not receive the same distributions or dividends as those we make to the holders of our Ordinary Shares, and, in some limited circumstances, investors in our ADSs may not receive any value for such distributions or dividends if it is illegal or impractical for us to make them available to investors in our ADSs. These restrictions may cause a material decline in the value of the ADSs.

Holders of ADSs must act through the depositary to exercise their rights.

Holders of our ADSs do not have the same rights as our holders of Ordinary Shares and may only exercise the voting rights with respect to the underlying Ordinary Shares in accordance with the provisions of the deposit agreement for the ADSs. Under Israeli law, the minimum notice period required to convene a shareholders' meeting is no less than 35 or 21 calendar days, depending on the proposals on the agenda for the shareholders' meeting. When a shareholders' meeting is convened, holders of our ADSs may not receive sufficient advance notice of a shareholders' meeting to permit them to cancel the ADSs and withdraw their Ordinary Shares to allow them to cast their vote with respect to any specific matter. In addition, the depositary and its agents may not be able to send voting instructions to holders of our ADSs or carry out their voting instructions in a timely manner. We will make all reasonable efforts to cause the depositary to extend voting rights to holders of our ADSs in a timely manner, but we cannot assure holders that they will receive the voting materials in time to ensure that they can instruct the depositary to vote their ADSs. Furthermore, the depositary and its agents are not responsible for any failure to carry out any instructions to vote, for the manner in which any vote is cast or for the effect of any such vote. As a result, holders of our ADSs may not be able to exercise their right to vote and they may lack recourse if their ADSs are not voted as they requested. In addition, in the capacity as an ADS holder, they are not able to call a shareholders' meeting.

The depositary for our ADSs gives us a discretionary proxy to vote our Ordinary Shares underlying ADSs if a holder of our ADSs does not give voting instructions, except in limited circumstances.

Under the deposit agreement for the ADSs, the depositary gives us a discretionary proxy to vote our Ordinary Shares underlying ADSs at shareholders' meetings if a holder of our ADSs does not give voting instructions, unless:

- we have instructed the depositary that we do not wish a discretionary proxy to be given;
- we have informed the depositary that there is substantial opposition as to a matter to be voted on at the meeting; or
- we have informed the depositary that a matter to be voted on at the meeting would have a material adverse impact on shareholders.

The effect of this discretionary proxy is that a holder of our ADSs cannot prevent our Ordinary Shares underlying such ADSs from being voted by us at our discretion, absent the situations described above. Holders of our Ordinary Shares are not subject to this discretionary proxy.

Risks Related to our Operations in Israel

We conduct our operations in Israel and therefore our results may be adversely affected by political, economic and military instability in Israel and the region.

We are incorporated under the laws of the State of Israel, and our principal offices are located in central Israel. Accordingly, political, economic and military conditions in Israel and the surrounding region may directly affect our business. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its Arab neighbors, including Hezbollah in Lebanon (and Syria) and Hamas in the Gaza Strip, both of which involved missile strikes in various parts of Israel causing the disruption of economic activities. Our principal offices are located within the range of rockets that could be fired from Lebanon, Syria or the Gaza Strip into Israel. In addition, Israel faces many threats from more distant neighbors, in particular, Iran. Parties with whom we do business have sometimes declined to travel to Israel during periods of heightened unrest or tension, forcing us to make alternative arrangements when necessary. In addition, the political and security situation in Israel may result in parties with whom we have agreements involving performance in Israel claiming that they are not obligated to perform their commitments under those agreements pursuant to force majeure provisions in such agreements. Any hostilities involving Israel or the interruption or curtailment of trade within Israel or between Israel and its trading partners could adversely affect our operations or results of operations and could make it more difficult for us to raise capital.

Our commercial insurance does not cover losses that may occur as a result of events associated with the security situation in the Middle East. Although the Israeli government is currently committed to cover the reinstatement value of direct

damages that are caused by terrorist attacks or acts of war, there is no assurance that this government coverage will be maintained, or if maintained, will be sufficient to compensate us fully for damages incurred. Any losses or damages incurred by us could have a material adverse effect on our business.

Several countries, principally in the Middle East, restrict doing business with Israel and Israeli companies, and additional countries may impose restrictions on doing business with Israel and Israeli companies. In addition, there have been increased efforts by activists to cause companies and consumers to boycott Israeli goods based on Israeli government policies. Such business restrictions and boycotts, particularly if they become more widespread, may materially and adversely impact our business.

Because a certain portion of our expenses is incurred in currencies other than the U.S. dollar, our results of operations may be harmed by currency fluctuations and inflation.

Our reporting and functional currency is the U.S. dollar. Most of our revenues and royalty payments from our agreements with our development or commercialization partners are in U.S. dollars, and we expect our revenues from future licensing and co-promotion agreements to be denominated mainly in U.S. dollars or in Euros. We pay a substantial portion of our expenses in U.S. dollars; however, a portion of our expenses, including salaries of our employees in Israel and payment to part of our service providers in Israel and other territories, are paid in NIS and in other currencies. In addition, a portion of our financial assets is held in NIS and in other currencies. As a result, we are exposed to currency fluctuation risks. For example, if the NIS strengthens against the U.S. dollar, our reported expenses in U.S. dollars may be higher. In addition, if the NIS weakens against the U.S. dollar, the U.S. dollar value of our financial assets held in NIS will decline.

Provisions of the RedHill Biopharma Ltd. Award Plan, Israeli law, our articles of association and our change in control retention plan may delay, prevent or otherwise impede a merger with, or an acquisition of, our Company, or an acquisition of a significant portion of our shares, which could prevent a change in control, even when the terms of such a transaction are favorable to us and our shareholders.

Our Award Plan provides that all options granted by us will be fully accelerated upon a "hostile takeover" of us. A "hostile takeover" is defined in our Award Plan as an event in which any person, entity or group that was not an "interested party", as defined in the Israeli Securities Law – 1968, on the date of the initial public offering of our Ordinary Shares on the TASE, will become a "controlling shareholder" as defined in the Israel Securities Law, 1968, or a "holder," as defined in the Israeli Securities Law – 1968, of 25% or more of our voting rights or any merger or consolidation involving us, in each case without a resolution by our board of directors supporting the transaction. In addition, if a "Significant Event" occurs and following which the employment of a grantee with us or a related company is terminated by us or a related company other than for "Cause", and unless the applicable agreement provides otherwise, all the outstanding options held by or for the benefit of any such grantee will be accelerated and immediately vested and exercisable. A "Significant Event" is defined in our Award Plan as a consolidation or merger with or into another corporation approved by our board of directors in which we are the continuing or surviving corporation or in which the continuing or surviving corporation assumes the option or substitutes it with an appropriate option in the surviving corporation.

The Israeli Companies Law, 1999, or the Israeli Companies Law, regulates mergers, requires tender offers for acquisitions of shares or voting rights above specified thresholds, requires special approvals for transactions involving directors, officers or significant shareholders and regulates other matters that may be relevant to these types of transactions. For example, a merger may not be consummated unless at least 50 days have passed from the date that a merger proposal was filed by each merging company with the Israel Registrar of Companies and at least 30 days from the date that the shareholders of both merging companies approved the merger. In addition, a majority of each class of securities of the target company must approve a merger. Moreover, the Israeli Companies Law provides that certain purchases of securities of a public company are subject to tender offer rules. As a general rule, the Israeli Companies Law prohibits any acquisition of shares or voting power in a public company that would result in the purchaser holding 25% or more, or more than 45% of the voting power in the company, if there is no other person holding 25% or more, or more than 45% of the voting power in a company, respectively, without conducting a special tender offer. The Israeli Companies Law further provides that a purchase of shares or voting power of a public company or a class of shares of a public company which will result in the purchaser's holding 90% or more of the company's shares, class of shares or voting rights, is prohibited unless the purchaser conducts a full tender offer for all of the company's shares or class of shares. The purchaser will be allowed to

purchase all of the company's shares or class of shares (including those shares held by shareholders who did not respond to the offer), if either (i) the shareholders who do not accept the offer hold less than 5% of the issued and outstanding share capital of the company or of the applicable class, and more than half of the shareholders who do not have a personal interest in the offer accept the offer, or (ii) the shareholders who do not accept the offer hold less than 2% of the issued and outstanding share capital of the company or of the applicable class. The shareholders, including those who indicated their acceptance of the tender offer (except if otherwise detailed in the tender offer document), may, at any time within six months following the completion of the tender offer, petition the court to alter the consideration for the acquisition. At the request of an offeree of a full tender offer which was accepted, the court may determine that the consideration for the shares purchased under the tender offer was lower than their fair value and compel the offeror to pay to the offerees the fair value of the shares. Such an application to the court may be filed as a class action.

In addition, the Israeli Companies Law provides for certain limitations on a shareholder that holds more than 90% of the company's shares, or class of shares.

Pursuant to our articles of association, the size of our board of directors may be no less than five persons and no more than eleven, including any external directors whose appointment is required under the law. The directors who are not external directors are divided into three classes, as nearly equal in number as possible. At each annual general meeting, the term of one class of directors expires, and the directors of such class are re-nominated to serve an additional three-year term that expires at the annual general meeting held in the third year following such election (other than any director nominated for election by Cosmo pursuant to the Company's subscription agreement with Cosmo, whose term of office may expire earlier depending on the beneficial ownership by the Cosmo investor of the Cosmo shares). This process continues indefinitely. Such provisions of our articles of association make it more difficult for a third party to effect a change in control or takeover attempt that our management and board of directors oppose.

In addition, we have adopted a change in control employee retention plan and entered into employment agreements providing for compensation to Company officers and employees in the event of a change in control (as defined by the plan and employment agreements), subject to the satisfaction of various conditions. See "Item 6 B. – Compensation – Change in Control Retention Plan."

Furthermore, Israeli tax considerations may, in certain circumstances, make potential transactions unappealing to us or to some of our shareholders. For example, Israeli tax law does not recognize tax-free share exchanges to the same extent as U.S. tax law. With respect to mergers, Israeli tax law allows for tax deferral in certain circumstances but makes the deferral contingent on the fulfillment of numerous conditions, including a holding period of two years from the date of the transaction during which sales and dispositions of shares of the participating companies are restricted. Moreover, with respect to certain share swap transactions, the tax deferral is limited in time, and when such time expires, the tax becomes payable even if no actual disposition of the shares has occurred.

These and other similar provisions could delay, prevent or impede an acquisition of us or our merger with another company, or an acquisition of a significant portion of our shares, even if such an acquisition or merger would be beneficial to us or to our shareholders.

It may be difficult to enforce a U.S. judgment against us and our directors and officers in Israel or the U.S. or to serve process on our directors and officers.

We are incorporated in Israel. Most of our directors and executive officers reside outside of the U.S., and most of the assets of our directors and executive officers may be located outside of the U.S. Therefore, a judgment obtained against us or most of our executive officers and our directors in the U.S., including one based on the civil liability provisions of the U.S. federal securities laws, may not be collectible in the U.S. and may not be enforced by a U.S. or Israeli court. It may also be difficult to effect service of process on these persons in the U.S. or to assert U.S. securities law claims in original actions instituted in Israel.

The obligations and responsibilities of our shareholders are governed by Israeli law, which may differ in some respects from the obligations and responsibilities of shareholders of U.S. companies. Israeli law may impose obligations and responsibilities on a shareholder of an Israeli company that are not imposed upon shareholders of corporations in the U.S.

We are incorporated under Israeli law. The obligations and responsibilities of the shareholders are governed by our articles of association and Israeli law. These obligations and responsibilities differ in some respects from the obligations and responsibilities of shareholders in typical U.S.-based corporations. In particular, a shareholder of an Israeli company has a duty to act in good faith toward the company and other shareholders and to refrain from abusing its power in the company, including, among other things, in voting at the general meeting of shareholders on matters such as amendments to a company's articles of association, increases in a company's authorized share capital, mergers and acquisitions and interested party transactions requiring shareholder approval. In addition, a shareholder who knows that it possesses the power to determine the outcome of a shareholder vote or to appoint or prevent the appointment of a director or executive officer in the company has a duty of fairness toward the company. There is limited case law available to assist us in understanding the implications of these provisions that govern shareholders' actions. These provisions may be interpreted to impose additional obligations and responsibilities on our shareholders that are not typically imposed on shareholders of U.S. corporations.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful shareholder claims against us and may reduce the amount of money available to us.

The Israeli Companies Law and our articles of association permit us to indemnify our directors and officers for acts performed by them in their capacity as directors and officers. The Israeli Companies Law provides that a company may not exempt or indemnify a director or an officer nor enter into an insurance contract, which would provide coverage for any monetary liability incurred as a result of: (a) a breach by the director or officer of his duty of loyalty, except for insurance and indemnification where the director or officer acted in good faith and had a reasonable basis to believe that the act would not prejudice the company; (b) a breach by the director or officer of his duty of care if the breach was done intentionally or recklessly, except if the breach was solely as a result of negligence; (c) any act or omission done with the intent to derive an illegal personal benefit; or (d) any fine, civil fine, monetary sanctions, or forfeit imposed on the officer or director. Our articles of association provide that we may exempt or indemnify a director or an officer to the maximum extent permissible under law.

We have issued letters of indemnification to our directors and officers, pursuant to which we have agreed to indemnify them in advance for any liability or expense imposed on or incurred by them in connection with acts they perform in their capacity as a director or officer, subject to applicable law. The amount of the advance indemnity is limited to the higher of 25% of our then shareholders' equity, per our most recent annual financial statements, or $10 million.

Our indemnification obligations limit the personal liability of our directors and officers for monetary damages for breach of their duties as directors by shifting the burden of such losses and expenses to us. Although we have obtained directors' and officers' liability insurance, certain liabilities or expenses covered by our indemnification obligations may not be covered by such insurance or the coverage limitation amounts may be exceeded. As a result, we may need to use a significant amount of our funds to satisfy our indemnification obligations, which could severely harm our business or financial condition and limit the funds available to those who may choose to bring a claim against us. These provisions and resultant costs may also discourage us from bringing a lawsuit against directors and officers for breaches of their duties and may similarly discourage the filing of derivative litigation by our shareholders against the directors and officers even though such actions, if successful, might otherwise benefit our security holders.

Our Amended and Restated Articles of Association designate courts located either within the State of Israel, or the Federal District Courts of the United States, as the exclusive forum for certain litigation that may be initiated by our shareholders, which could limit our shareholders' ability to bring a favorable or convenient judicial forum for disputes with us.

Our Amended and Restated Articles of Association provide that, unless we consent in writing to the selection of an alternative forum, the Tel Aviv District Court (Economic Division in the State of Israel (or, if the Tel Aviv District Court

does not have jurisdiction, and no other Israeli court has jurisdiction, the federal district court for the District of New York) shall be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our shareholders, and (3) any action asserting a claim arising pursuant to any provision of the Companies Law or the Israeli Securities Law 5728-1968, in all cases subject to the court's having personal jurisdiction over the indispensable parties named as defendants. In addition, the federal district courts of the United States for the District of New York shall be the exclusive forum for any complaint asserting a cause of action arising under the Securities Act of 1933. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and consented to these provisions.

This forum selection provision may limit shareholders' ability to bring a claim in a judicial forum for disputes that it finds favorable or convenient for disputes with us or our directors, officers, or other employees, which may discourage lawsuits with respect to such claims. Alternatively, a court, including an Israeli court, could find these provisions of our Articles of Association to be inapplicable or unenforceable in respect of one or more of the specified types of actions or proceedings, which may require us to incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

General Risks

We must comply with the U.S. Foreign Corrupt Practices Act.

The U.S. Foreign Corrupt Practices Act (the "FCPA") applies to companies, such as us, with a class of securities registered under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The FCPA to which various of our operations may be subject generally prohibits companies and their intermediaries from engaging in bribery or making other improper payments to officials for the purpose of obtaining or retaining business. In various jurisdictions, our operations require that we and third parties acting on our behalf routinely interact with government officials, including medical personnel who may be considered government officials for purposes of these laws because they are employees of state-owned or controlled facilities. Our policies mandate compliance with these anti-bribery laws; however, we operate in many parts of the world that have experienced governmental or private corruption to some degree. As a result, the existence and implementation of a robust anti-corruption program cannot eliminate all risks that unauthorized reckless or criminal acts have been or will be committed by our employees or agents. If our employees or other agents are found to have engaged in such practices, we could suffer severe penalties. Violations of the FCPA, or allegations of such violations, could disrupt our business and result in a material adverse effect on our reputation, business, financial condition or results of operations.

Future issuances or sales of our ADSs could reduce the market price of our ADSs.

As of March 16, 2022, we had outstanding options to purchase 63,893,290 Ordinary Shares (equivalent to 6,389,329 of our ADSs) under our Amended and Restated Award Plan (2010) ("Award Plan"). As of March 16, 2022, we had 1,918,500 outstanding Restricted Share Units ("RSUs"), each with respect to one of our ADSs, which represents 10 of our Ordinary Shares. In addition, as of March 16, 2022, there were 97,718,090 Ordinary Shares (equivalent to 9,771,809 of our ADSs) reserved for issuance under our Award Plan (including Ordinary Shares subject to outstanding options under such plan). In addition, as of March 16, 2022 we have sold an aggregate of 332,454 ADSs under our current "at-the-market" equity offering program. Future substantial issuance or sale of our ADSs, or the perception that such sales may occur in the future, including sales of ADSs issuable upon vesting of RSUs and the exercise of options, warrants or other equity-based securities, may cause the market price of our ADSs to decline. Moreover, the issuance of ADSs upon the exercise of our options will also have a dilutive effect on our shareholders, which could further reduce the price of our ADSs.

The market price of our ADSs is subject to fluctuation, which could result in substantial losses by our investors. The COVID-19 pandemic has resulted in significant financial market volatility, and its impact on the global economy remains uncertain. A continuation or worsening of the pandemic could have a material adverse impact on the market price of our ADSs. This may affect the ability of our investors to sell their ADSs, and the value of an investment in our ADSs may decline.

The stock market in general and the market price of our ADSs on the Nasdaq, in particular, are subject to fluctuation, and changes in the price of our securities may be unrelated to our operating performance. The market price of our ADSs on the Nasdaq has fluctuated in the past, and we expect they will continue to do so. The market price of our ADSs is and will be subject to a number of factors, including but not limited to:

- our ability to execute our business plan, including commercialization of our current and future commercial products;
- announcements of technological innovations or new therapeutic candidates or new products approved for marketing by us or others;
- announcements by us of significant acquisitions, strategic partnerships, in-licensing, out-licensing, joint ventures or capital commitments;
- our ability to comply with the various covenants under our credit agreement with HCRM;
- expiration or terminations of licenses, research contracts or other commercialization or development agreements;
- public concern as to the safety of drugs we, our commercialization or development partners or others market or develop;
- the volatility of market prices for shares of biopharmaceutical companies generally;
- success or failure of research and development projects;
- departure of or major events adversely affecting key personnel;
- developments concerning intellectual property rights or regulatory approvals;
- variations in our and our competitors' results of operations;
- changes in earnings estimates or recommendations by securities analysts, if our ADSs are covered by analysts;
- changes in government regulations or patent proceedings and decisions;
- developments by our development or commercialization partners; and
- general market conditions, geopolitical conditions and other factors, including factors unrelated to our operating performance.

These factors and any corresponding price fluctuations may materially and adversely affect the market price of our ADSs and result in substantial losses by our investors.

Additionally, market prices for securities of biotechnology and pharmaceutical companies historically have been very volatile. The market for these securities has from time to time, experienced significant price and volume fluctuations for reasons unrelated to the operating performance of any one company. The COVID-19 pandemic has resulted in significant financial market volatility and uncertainty. A continuation or worsening of the levels of market disruption and volatility seen in the recent past could have an adverse effect on our ability to access capital, on our business, results of operations and financial condition, and on the market price of our ADSs. In the past, following periods of market volatility, shareholders have often instituted securities class action litigation and derivative actions. If we were involved in securities or other litigation, it could have a substantial cost and divert resources and attention of management from our business, even if we are successful.

We incur significant costs as a result of the listing of our ADSs on the Nasdaq, and we may need to devote substantial time and resources to new and current compliance initiatives and reporting requirements.

As a public company in the U.S., we incur significant accounting, legal and other expenses as a result of the listing of our securities on the Nasdaq. These include costs associated with the reporting requirements of the SEC and the requirements of the Nasdaq Listing Rules, as well as requirements under Section 404 and other provisions of the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"). These rules and regulations have increased our legal and financial compliance costs, introduced new costs such as investor relations, travel costs, stock exchange listing fees, and shareholder reporting, and

made some activities more time-consuming and costly. Any future changes in the laws and regulations affecting public companies in the U.S. and Israel, including Section 404 and other provisions of the Sarbanes-Oxley Act, the rules and regulations adopted by the SEC and the Nasdaq Listing Rules, as well as applicable Israeli reporting requirements, may result in an increase to our costs as we respond to such changes. These laws, rules, and regulations could make it more difficult and costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers and may require us to pay more for such positions.

We may fail to maintain effective internal control over financial reporting, which may adversely affect investor confidence in us and, as a result, may affect the value of our ADSs.

We have documented and tested our internal control systems and procedures in order for us to comply with the requirements of Section 404 of the Sarbanes-Oxley Act, which requires us to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting, and requires our auditor's attestation report on the effectiveness of our internal control over financial reporting. The continuous process of strengthening our internal control and complying with Section 404 of the Sarbanes-Oxley Act is complicated, expensive and time-consuming. While our assessment of our internal control over financial reporting resulted in our conclusion that as of December 31, 2021, our internal control over financial reporting was effective, we cannot predict the outcome of our testing or any subsequent testing by our auditor in future periods. If we fail to maintain the adequacy of our internal control, we may not be able to ensure that we can conclude on an ongoing basis that we have effective internal control over financial reporting. Even if we do conclude that our internal control over financial reporting is effective, our independent registered public accounting firm may still issue a report that is qualified or adverse if it is not satisfied with our internal control. Failure to maintain effective internal control over financial reporting could result in investigation or sanctions by regulatory authorities and could have a material adverse effect on our reputation, business, financial condition, results of operations or investor confidence in the accuracy and completeness of our financial reports, which would cause the price of our ADSs to decline.

ITEM 4. INFORMATION ON THE COMPANY

A. History and Development of the Company

Our legal and commercial name is RedHill Biopharma Ltd. Our company was incorporated on August 3, 2009, and was registered as a private company limited by shares under the laws of the State of Israel. Our principal executive offices are located at 21 Ha'arba'a Street, Tel-Aviv, Israel, and our telephone number is 972-3-541-3131.

In February 2011, we completed our initial public offering in Israel, pursuant to which we issued 14,302,300 Ordinary Shares, and 7,151,150 tradable Series 1 Warrants to purchase 7,151,150 Ordinary Shares for aggregate gross proceeds of approximately $14 million. On December 27, 2012, we completed the listing of our ADSs on the Nasdaq Capital Market, and on July 20, 2018, our ADSs were listed on the Nasdaq Global Market. On February 13, 2020, our Ordinary Shares were voluntarily delisted from trading on the Tel-Aviv Stock Exchange. Our ADSs are traded on the Nasdaq Global Market under the symbol "RDHL."

The Securities and Exchange Commission, or SEC, maintains an internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC at http://www.sec.gov.

Our website address is http://www.redhillbio.com. Information contained on, or that can be accessed through, our website does not constitute a part of this Annual Report.

Our capital expenditures for the years ended December 31, 2021, 2020 and 2019, were approximately $115,000, $406,000 and $168,000, respectively. Our current capital expenditures involve equipment and leasehold improvements.

B. Business Overview

We are a specialty biopharmaceutical company, primarily focused on gastrointestinal ("GI") and infectious diseases. Our primary goal is to become a leading specialty biopharmaceutical company through our commercial presence in the U.S. that supports commercialization of our current and potentially additional products approved for marketing in the U.S., and potential future commercialization of our therapeutic candidates, if approved.

We are currently focused primarily on the commercialization in the U.S. of the GI-related products, Movantik® (naloxegol), Talicia® (omeprazole, amoxicillin, and rifabutin) and Aemcolo® (rifamycin).

In addition, we continue to develop our pipeline of clinical-stage therapeutic candidates, including, among others, opaganib and RHB-107 (upamostat), as potential treatments for COVID-19. We look for opportunities to leverage our commercial presence and capabilities in the U.S. to support the potential future launch of our therapeutic candidates currently under development, if approved by the FDA, or any FDA-approved products that we may acquire the rights to in the future.

Our current pipeline consists of six therapeutic candidates, most of which are in late-stage clinical development. We generate our pipeline of therapeutic candidates by identifying, validating and in-licensing or acquiring products that are consistent with our product and corporate strategy and that have the potential to exhibit a favorable probability of therapeutic and commercial success. We have one product that we primarily developed internally which has been approved for marketing and, to date, none of our therapeutic candidates has generated meaningful revenues. We have out-licensed one of our commercial products, Talicia®, and one of our clinical-stage therapeutic candidates, opaganib, for specific territories outside the U.S. and we plan to commercialize our therapeutic candidates, upon approval, if any, through licensing and other commercialization arrangements outside the U.S. with pharmaceutical companies on a global and territorial basis or, in the case of commercialization in the U.S., independently with our dedicated commercial operations or in potential partnership with other commercial-stage companies. We also evaluate, on a case-by-case basis, co-development, co-promotion, licensing, acquisitions and similar arrangements.

Our Strategy

Our goal is to become a leading specialty pharmaceutical company in the commercialization and development of pharmaceuticals for the treatment of GI and infectious diseases.

Key elements of our strategy are to:

- advance our initiative to become a leading specialty biopharmaceutical company by leveraging our commercial presence in the U.S. to achieve successful commercialization of products approved for marketing, including Talicia® and our other commercial products, and future commercialization of our therapeutic candidates, if approved, and by identifying and acquiring rights to products that have been approved for marketing in the U.S. and investigational new drugs from pharmaceutical companies that are interested in divesting one or more of their products. Specifically, we seek to acquire rights to products that are already approved or commercialized in the U.S., preferably with a therapeutic focus on GI and infectious diseases, which would enable us to commercialize such products independently through our own marketing and commercialization capabilities. We identify such opportunities through our broad network of contacts and other sources in the pharmaceutical field;
- identify and acquire rights to products from pharmaceutical companies that have encountered cash flow or operational problems or that decide to divest one or more of their products for various reasons. Specifically, we seek to acquire rights to and develop products that are intended to treat pronounced clinical needs, have patent or other protections, and have potential target markets totaling tens of millions to billions of dollars. Additionally, we seek to acquire rights to and develop products based on different technologies designed to reduce our dependency on any specific product or technology. We identify such opportunities through our broad network of contacts and other sources in the pharmaceutical field;
- identify and enter into out-licensing or collaborative agreements with third parties to develop and/or commercialize our commercial products or therapeutic candidates in territories outside the U.S.;
- enhance existing pharmaceutical products, including broadening their range of indications, or launching innovative and advantageous pharmaceutical products, based on existing active ingredients. Because there is a

large knowledge base regarding existing products, the preclinical, clinical and regulatory requirements needed to obtain marketing approval for enhanced formulations are relatively well-defined. In particular, clinical trial designs, inclusion criteria and endpoints previously accepted by regulators may sometimes be re-used. In addition to reducing costs and time to market, we believe that targeting therapeutics with proven safety and efficacy profiles provides us a better prospect of clinical success;

- where applicable, utilize the FDA's 505(b)(2) regulatory pathway to potentially obtain more timely and efficient approval of our formulations of previously approved products. Under the 505(b)(2) process, we are able to seek FDA approval of a new dosage form, strength, route of administration, formulation, dosage regimen, or indication of a pharmaceutical product that has previously been approved by the FDA. This process enables us to partially rely on the FDA findings of safety or efficacy for previously approved drugs, thus avoiding the duplication of costly and time-consuming preclinical and various human studies. See "Item 4. Information on the Company – B. Business Overview – Government Regulations and Funding – Section 505(b)(2) New Drug Applications"; and
- cooperate with third parties to develop or commercialize therapeutic candidates in order to share costs and leverage the expertise of others.

The pharmaceutical and biotechnology industries are intensely competitive. Our therapeutic candidates, if commercialized, and our approved drugs, compete with existing drugs and therapies. In addition, there are many pharmaceutical companies, biotechnology companies, medical device companies, public and private universities, government agencies and research organizations actively engaged in the research and development of products targeting the same markets as our therapeutic candidates. Many of these organizations have substantially greater financial, technical, manufacturing and marketing resources than we do. In certain cases, our competitors may also be able to use alternative technologies that do not infringe upon our patents to formulate the active materials in our therapeutic candidates. They may, therefore, bring to market products that are able to compete with our candidates, or other products that we may develop in the future.

Our Approved and Commercial Products in the U.S.

We have established the headquarters of our U.S. commercial operations in Raleigh, North Carolina. Our U.S. operations promote Movantik® for opioid-induced constipation in adults, Talicia® for the treatment of *H. pylori* infection in adults and Aemcolo® for the treatment of travelers' diarrhea in adults. We also expect our U.S. operations to serve as the platform for potential launch of our proprietary, late-clinical stage therapeutic candidates in the U.S., if approved by the FDA, and potential in-licensed or acquired commercial-stage products in the U.S.

Our sales force consisted of approximately 120 employees as of December 31, 2021. The net revenues for the fiscal years ended December 31, 2021 and 2020 from the commercial products were approximately $85.8 million and $64.4 million, respectively. We continue to pursue the acquisition of additional commercial products, including, without limitation, through licensing or promotion transaction, asset purchase, joint venture with, acquisition of, or a merger with or other business combination with, companies with rights to commercial GI and other relevant assets and are continuously working to expand U.S. managed care access and coverage to our commercial products, where appropriate. We plan to pursue such opportunities in the U.S. and, if available, in other jurisdictions; however, we intend to focus our commercial activities in the U.S. We currently promote and commercialize three GI products in the U.S.

Movantik®

We acquired the worldwide rights (excluding Europe, Canada and Israel) to commercialize and develop Movantik® (naloxegol) from AstraZeneca in April 2020. Movantik® is a proprietary once-daily oral peripherally-acting mu-opioid receptor antagonist (PAMORA) approved by the FDA for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g. weekly) opioid dosage escalation. We initiated the promotion of Movantik® in the second quarter of 2020. In October 2020, we gained the rights to commercialize and develop Movantik® in Israel, and thus we now hold the worldwide rights to Movantik®, excluding Europe and Canada. See "Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – License Agreement for Movantik®."

Regulatory Status

Movantik® received FDA approval on September 16, 2014, for the treatment of OIC in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g. weekly) opioid dosage escalation. In connection with our in-license for Movantik®, we agreed to assume responsibility for completing any postmarketing requirements or commitments that may be required to retain approval. Accordingly, we are required to continue the post-marketing observational epidemiologic study to evaluate the major adverse cardiovascular events (MACE) of Movantik®.

Market and Competition

Movantik® is a peripherally-acting mu-opioid receptor antagonist indicated for the treatment of OIC. According to a DataMonitor report, OIC is the most common side effect of opioids, as tolerance does not arise over the long term, and is estimated that OIC in patients with non-cancer pain ranges between 40–50%.

Movantik® primarily competes with several branded therapies already approved and used extensively to treat OIC, including Amitiza® (lubiprostone, promoted by Takeda Pharmaceuticals) and two other oral PAMORA drugs, Relistor® (methylnaltrexone bromide, promoted by Salix Pharmaceuticals) and Symproic® (naldemedine, promoted by BioDelivery Sciences International, Inc.). Movantik® also competes with several OTC and prescription drugs, such as laxatives, including stool softeners, stimulants and the use of enemas. We may also be exposed to potential competitive products that may be under development to treat or prevent OIC. Our commercial success is dependent on continued reimbursement by commercial and government payors.

Talicia® (omeprazole magnesium, amoxicillin, and rifabutin) delayed-release capsules 10 mg/250 mg/12.5 mg

Talicia® is our proprietary new drug approved for marketing in the U.S. for the treatment of *H. pylori* infection in adults. Talicia® is a combination of three approved drug products – omeprazole, which is a proton pump inhibitor (prevents the secretion of hydrogen ions necessary for the digestion of food in the stomach), amoxicillin and rifabutin, which are antibiotics. Talicia® is administered to patients orally. Talicia® is the first product we developed that was approved for marketing in the U.S. We launched Talicia® in the U.S. in March 2020 with our dedicated sales force.

Chronic infection with *H. pylori* irritates the mucosal lining of the stomach and small intestine. The original discovery of the *H. pylori* bacteria and its association with peptic ulcer disease warranted the Nobel Prize in 2005. *H. pylori* infection has since been associated with a variety of outcomes, which include: dyspepsia (non-ulcer or functional), peptic ulcer disease (duodenal ulcer and gastric ulcer), primary gastric B-cell lymphoma, vitamin B12 deficiency, iron deficiency, anemia, and gastric cancer.

Gastric cancer is one of the most prevalent cancers worldwide and one of the most common causes of cancer-related deaths, accounting for approximately 768,000 deaths annually, according to the World Health Organization ("WHO") GLOBOCAN 2020 report. According to a 2010 report by Polk DB *et al.* published in Nature Reviews Cancer, *H. pylori*-induced gastritis is the strongest singular risk factor for cancers of the stomach, and eradication of *H. pylori* significantly decreases the risk of developing cancer in infected individuals without pre-malignant lesions.

In November 2014, Talicia® was granted QIDP designation by the FDA. The QIDP designation was granted under the FDA's Generating Antibiotic Incentives Now (GAIN) Act, which is intended to encourage the development of new antibiotic drugs for the treatment of serious or life-threatening infections that have the potential to pose a serious threat to public health. Under its QIDP designation, Talicia® is eligible for an additional five years of U.S. market exclusivity, on top of the standard exclusivity period, for a total of eight years of market exclusivity.

Talicia® is targeting a significantly broader indication than that of existing *H. pylori* therapies, as a treatment of *H. pylori* infection, regardless of ulcer status.

We acquired the rights to Talicia® pursuant to an agreement with Giaconda Limited. See "Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – Acquisition of Talicia®, RHB-104, and RHB-106."

On December 5, 2021, we entered into an exclusive license agreement with Gaelan Medical for Talicia®, in the UAE. See "Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements License Agreement with Gaelan Medical".

Regulatory Status

On November 1, 2019, Talicia® was approved by the FDA and is eligible for a total of eight years of U.S. market exclusivity.

Market and Competition

The American College of Gastroenterology clinical guidelines for the treatment of *H. pylori* infection published in 2017 generally exclude the majority of the U.S. population from treatment with current standard-of-care therapies which commonly include the antibiotic clarithromycin with amoxicillin or another antibiotic and a proton pump inhibitor. The American College of Gastroenterology recommends against using clarithromycin-based triple therapies in cases where the patient has prior macrolide exposure, in regions with unknown clarithromycin resistance or regions with 15% or more clarithromycin resistance. It is estimated that clarithromycin resistance in the U.S. exceeds 20% prevalence (Park JY, Dig Dis Sci. 2016). Such current clarithromycin and metronidazole-based standard-of-care treatments fail in approximately 25-40% of the patients due to the development of antibiotic resistance, based on Malfertheiner P. et al. (Gut 2012), O'Connor A. et al. (Helicobacter 2015) and Venerito M. et al. (Digestion 2013). According to a 2015 publication by Shiota et al., it is estimated that *H. pylori* resistance to clarithromycin, a standard-of-care antibiotic used for the treatment of *H. pylori,* more than doubled between 2009-2013. According to a 2021 publication by Graham et al., although clarithromycin is still widely used to treat *H. pylori*, by the year 2000, increasing resistance resulted in clarithromycin triple therapy becoming generally ineffective.

Talicia® is designed to address the high resistance of *H. pylori* bacteria to the antibiotics commonly used in current standard-of-care therapies. Talicia's approval was supported, in part, by the results of two positive Phase 3 studies in the U.S. for the treatment of *H. pylori*-positive adult patients complaining of epigastric pain and/or discomfort. The confirmatory Phase 3 study of Talicia® demonstrated 84% eradication of *H. pylori* infection with Talicia ® vs. 58% in the active comparator arm ($p<0.0001$). Further, in an analysis of data from this study, it was observed that subjects with measurable blood levels of drug at Day 13 had response rates of 90.3% in the Talicia® arm vs. 64.7% in the active comparator arm.

H. pylori bacterial infection affects over 50% of the adult population worldwide, according to a 2018 report by Kakelar HM et al., published in *Gastric Cancer*, and approximately 35% of the U.S. population, according to a report by Hooi JKY et al. published in 2017 in *Gastroenterology*. In the U.S., we estimate that approximately 2 million patients per annum are treated for *H. pylori* eradication, based on a 2019 custom study by IQVIA for us.

Talicia® faces competition in the U.S. from certain branded prescription therapies indicated for the treatment of *H. pylori* infection including, but not limited to, Pylera® (sold by Allergan plc), PrevPac® (sold by Takeda Pharmaceuticals) and Omeclamox-Pak® (sold by Cumberland Pharmaceuticals), as well as from the generic individual components of these branded therapies and other generic antibiotics and PPIs approved for the treatment of *H. pylori* infection. Additionally, the individual components of Talicia® are available in generic form and while rifabutin is not available in an equivalent dose, there is a risk that some physicians may prescribe the individual components of Talicia® in doses that are not equivalent to the approved drug and regimen. We may also be exposed to potential competitive products that may be under development to treat *H. pylori* infection.

In addition, Phathom Pharmaceuticals, Inc. ("Phathom Pharmaceuticals") has submitted two NDAs to the FDA for marketing approval of vonoprazan, in combination with amoxicillin and in combination with amoxicillin and clarithromycin for the eradication of *H. pylori* infection, with a target PDUFA date of May 3, 2022. Phathom

Pharmaceuticals has announced that, if approved, they expect to launch vonoprazan dual and triple therapies in the second half of 2022. Vonoprazan is an oral small molecule potassium competitive acid blocker (P-CAB) which has received marketing approval in Japan and other countries in Asia and Latin America.

We believe that Talicia® offers a significant benefit over other marketed drugs in part because of the resistance profile demonstrated in our Phase 3 program, which showed no bacterial resistance to rifabutin and high resistance to clarithromycin and metronidazole.

Aemcolo®

Aemcolo®, containing 194mg of rifamycin, is an orally administered, minimally absorbed antibiotic that is delivered to the colon, approved by the FDA in 2018 for the treatment of travelers' diarrhea caused by non-invasive strains of *E. coli* in adults ("Travelers' Diarrhea"). In October 2019, we entered into a license agreement, as amended, with a wholly-owned subsidiary of Cosmo pursuant to which we were granted exclusive rights to commercialize Aemcolo® in the U.S. (the "Cosmo License Agreement"). In December 2019, we launched the commercialization of Aemcolo® in the U.S. See "Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – Exclusive License Agreement for Aemcolo®."

Regulatory Status

Aemcolo® received FDA approval on November 16, 2018, for the treatment of travelers' diarrhea caused by noninvasive strains of *Escherichia coli* in adults. Cosmo transferred the Aemcolo® NDA and the IND to RedHill U.S., which were accepted on November 27, 2019. This acceptance also includes a commitment to complete any postmarketing requirements or commitments related to the NDA. There are two pediatric studies that are required to be completed to satisfy the PREA requirements and also with required milestone dates:

- Conduct a randomized, placebo-controlled study to evaluate the safety, tolerability, and efficacy of Aemcolo® (rifamycin) for the treatment of travelers' diarrhea in children from 6 to 11 years of age.
- Conduct a randomized, placebo-controlled study to evaluate the safety, tolerability, and efficacy of Aemcolo® (rifamycin) for the treatment of travelers' diarrhea in children from 12 to 17 years of age.

Market and Competition

Aemcolo® is a new pharmaceutical product employing rifamycin SV engineered with MMX® technology. The application of MMX® technology to rifamycin SV allows the antibiotic to be delivered directly into the colon, intended to avoid unwanted effects on the beneficial bacterial flora living in the upper portions of the gastrointestinal tract. The specific dissolution profile of Aemcolo® tablets increases the colonic disposition of the antibiotic so that an optimized intestinal concentration is achieved thus abating its systemic absorption in the lower intestine.

In October 2017, the FDA granted QIDP and Fast Track designations for Aemcolo®. With the QIDP designation, intended for antibacterial or antifungal drugs that treat serious or life-threatening infections, together with new chemical entity (NCE) designation, Aemcolo® enjoys marketing exclusivity until 2028.

Due to the significant decrease in travel as a result of the pandemic, the travelers' diarrhea market has been significantly impacted, and we have not generated meaningful revenues from the sale of Aemcolo®. We do not expect Aemcolo® to generate meaningful revenues until U.S. international travel returns to pre-COVID-19 pandemic levels, if at all, and there can be no assurance that we will generate meaningful revenues upon return of U.S. international travel to pre-pandemic levels.

In December 2021, we and Cosmo amended the Cosmo License Agreement such that either party may terminate the Cosmo License Agreement upon advance notice at any time.

We have implemented plans, including re-launching active field promotion of Aemcolo®, to support, and build on, the initial momentum that Aemcolo® was generating pre-COVID-19 travel restrictions. Based on our current plans, our return to full promotional activities is subject to the return of international travel.

Travelers' Diarrhea is the most common travel-related illness according to the FDA. The Centers for Disease Control and Prevention Yellow Book states that attack rates of Travelers' Diarrhea range up to 70% of travelers, depending on the destination and season of travel. Travelers' Diarrhea may often result in short-term morbidity adversely impacting travel plans. Untreated diarrhea can also lead to an underappreciated risk of chronic complications, including functional bowel disorders.

There are several competing drugs marketed in the U.S. intended for the treatment of Travelers' Diarrhea. One of the leading competitors is Xifaxan® (rifaximin, marketed by Salix Pharmaceuticals), a prescription drug approved for the treatment of Travelers' Diarrhea caused by non-invasive strains of *E. coli* in adults and pediatric patients, treatment of IBS-D and reduction in risk of overt hepatic encephalopathy recurrence in adults. Aemcolo® also competes with generic antibiotics such as fluoroquinolones and azithromycin. Aemcolo® also competes with prescription and OTC anti-diarrheal medications such as loperamide and bismuth subsalicylate, as well as probiotics and medical foods which may offer symptomatic relief. We may also be exposed to potentially competitive products, which may be under development to treat or prevent Travelers' Diarrhea, including new antibiotics, anti-diarrheals, and vaccines.

Our Therapeutic Candidates

Summary

The ongoing development programs of our six therapeutic candidates, most in late-stage clinical development, include "RHB-204", "opaganib", "RHB-107" (upamostat), "RHB-104", "RHB-102 (Bekinda®)" and "RHB-106" and related research and development programs, the most advanced of which are described below.

Name of Therapeutic Candidate	Proposed Indication	Potential Advantages Over Most Existing Treatments, if Approved	Development Stage	Rights to the Product
RHB-204	Pulmonary nontuberculous mycobacteria (NTM) infections caused by Mycobacterium avium complex (MAC)	Oral formulation targeting a major cause of pulmonary NTM infections	Phase 3 study ongoing	We filed patent applications internationally directed to the proposed commercial formulation and use
opaganib	Patients hospitalized with SARS-CoV-2 severe COVID-19 pneumonia	Oral administration, first-in-class SK2 selective inhibitor, with anti-inflammatory and anti-cancer activities	U.S. Phase 2 study completed and top-line data received; global Phase 2/3 completed and top-line data received and submitted regulatory packages to regulatory authorities	We filed patent applications to protect the proposed commercial use
opaganib	Advanced unresectable cholangiocarcinoma	Oral administration, first-in-class SK2 selective inhibitor, with anti-inflammatory and anti-cancer activities	Phase 2 study in the U.S. ongoing (ABC-108)	Worldwide exclusive license
opaganib	Prostate cancer	Oral administration, first-in-class SK2 selective inhibitor, with anti-inflammatory and anti-cancer activities in addition to failing treatment with abiraterone or enzalutamide	Investigator-sponsored Phase 2 study in the U.S ongoing	Worldwide exclusive license
RHB-107 (upamostat; formerly Mesupron)	Outpatients infected with SARS-Co-V-2 (COVID-19 disease)	Oral administration, inhibitor of human serine proteases with antiviral activity and established safety profile	Phase 2/3 study ongoing	We filed patent applications to protect the proposed commercial use
RHB-107 (upamostat; formerly Mesupron) and opaganib	Advanced unresectable cholangiocarcinoma	Combination of (RHB-107 (upamostat)) and (opaganib)	Preclinical evaluation ongoing	We filed patent applications internationally directed to the proposed commercial use
RHB-107 (upamostat; formerly Mesupron)	Gastrointestinal and other solid tumors	Oral administration, inhibitor of human serine proteases with established safety profile	Completed Phase 2 studies in pancreatic cancer and breast cancer; preclinical testing ongoing	Worldwide exclusive license; excludes China, Hong Kong, Taiwan, and Macao[1]
RHB-104	Crohn's disease	Novel mechanism of action and improved clinical benefit (targeting suspected underlying cause of Crohn's disease)	First Phase 3 study completed; supportive results from the open-label extension Phase 3 study	We filed patent applications internationally directed to the proposed commercial formulation and use
RHB-102 (Bekinda®) 24 mg	Acute gastroenteritis and gastritis	No other approved 5-HT3 serotonin receptor inhibitor for this indication; once-daily dosing	First Phase 3 study in the U.S. completed; confirmatory Phase 3 study in planning	We filed patent applications internationally to protect the proposed commercial formulation and its use
RHB-102 (Bekinda®) 12 mg	IBS-D	Potential 5-HT3 serotonin receptor inhibitor with improved safety, while maintaining efficacy	Phase 2 in the U.S. completed; Phase 3 program in planning	We filed patent applications internationally to protect the proposed commercial formulation and its use
RHB-106	Bowel preparation	Oral pill, avoid severe bad taste of chemical solutions, no known nephrotoxicity issues	Phase 2/3 studies in planning	We filed patent applications internationally to protect the proposed commercial formulation and its use

RHB-204

Nontuberculous Mycobacteria Infections

In November 2020, we initiated a Phase 3 study in RHB-204 for the treatment of pulmonary *Mycobacterium avium* complex (MAC) disease in adults with nodular bronchiectasis (also referred to hereafter as pulmonary nontuberculous mycobacteria (NTM) disease caused by MAC.

[1] We have received a Notice of Allowance from the United States Patent and Trademark Office for treatment of solid tumors with a combination of opaganib and RHB-107.

The study is intended to assess the efficacy and safety of RHB-204 as a potential first-line, stand-alone treatment for pulmonary NTM infections caused by MAC. The multi-center, randomized, double-blind, two-part, placebo-controlled, parallel-group Phase 3 study will be conducted at up to 40 sites across the U.S. The co-primary endpoints for Part 1 of the study are the proportion of patients with sputum culture conversion after 6 months of treatment, defined as 3 consecutive monthly negative sputum cultures with RHB-204, compared to placebo, and the mean change in the Quality-of-Life questionnaire - Bronchiectasis (QoL-B) Respiratory Symptoms domain score from baseline to Month 6 for RHB-204 compared to placebo. Subjects entering Part 2 of the study after Month 6 assessments will receive open-label RHB-204 until month 16 of treatment (12 months from sputum culture conversion), followed by post-treatment follow up of 3 months, with patient reported outcomes and durability of microbiological response assessed at Month 6, Month 16 and Month 19. An interim sample size re-estimate is planned once the study reaches approximately 50% enrolment. Given that NTM infection is a rare disease, recruitment of patients to the Phase 3 study is expected to be slow. The COVID-19 pandemic has also delayed recruitment significantly.

In January 2017, we announced that RHB-204 had been granted QIDP designation by the FDA for the treatment of pulmonary NTM infections, including eligibility for Accelerated Approval and Priority Review and an extended market exclusivity period, if approved for marketing in the U.S.

In October 2020, we announced that RHB-204 had been granted Orphan Drug designation by the FDA for the treatment of pulmonary NTM infections which would extend market exclusivity period to a total of 12 years, if approved for marketing in the U.S.

In January 2021 we announced that the FDA granted RHB-204 Fast Track designation, allowing RedHill access to early and frequent communications with the FDA, to expedite the RHB-204 development program, and to a rolling review of an NDA.

RHB-204 is a patented fixed-dose combination product of three antibiotics intended to simplify administration and optimize compliance, selected based on modelling to provide optimal balance of the potential safety and efficacy. Each capsule contains the same three antibiotics as RHB-104 (clarithromycin, clofazimine, and rifabutin), but at doses unique from RHB-104. Clarithromycin and rifabutin were selected because mycobacteria live within host cells, and these agents have intracellular activity against MAC. Further, rifabutin enhances the antimicrobial activity of clarithromycin due to increased levels of clarithromycin's active metabolite. Selection of clofazimine was based on its activity against MAC, preferential accumulation in macrophages and bactericidal activity demonstrated in a mouse model of tuberculosis. Moreover, the inclusion of rifabutin and clofazimine has shown to mitigate the emergence of resistance to clarithromycin compared to clarithromycin alone or in combination with only rifabutin or clofazimine in a clarithromycin-susceptible *M.avium* lung infection mouse model as well as exhibiting significant reductions in bacterial counts in the lung after four and eight weeks of treatment.

Market and Competition

Pulmonary NTM is an orphan disease affecting an estimated 110,000 patients in the U.S. in 2017, according to a 2017 analysis by Foster Rosenblatt. Although rare, the incidence and number of deaths from NTM disease have been steadily increasing globally, according to Ratnatunga CN *et al.* (Front. Immunol. 2020), with a rise in the number of globally documented NTM infections leading to NTM being recognized as emerging threat causing significant morbidity and mortality in both immune competent and immune compromised populations. Treatment options remain limited, lengthy and challenging (Ryu YJ *et al.* Tuberc Respir Dis, 2016; Ratnatunga CN *et al.* Front. Immunol. 2020).

NTM are naturally occurring organisms found in water and soil, which can cause chronic pulmonary infection. According to Prevots DR (Am J Respir Crit Care Med, 2010) and Winthrop KL (Am J Respir Crit Care Med, 2010), approximately 80% of pulmonary NTM cases in the U.S. are associated with MAC. In some people, infection with NTM may lead to a progressive lung disease characterized by fever, weight loss, chest pain, and blood in sputum. NTM disease is more common in the older adult population and individuals with a compromised immune system or underlying lung disease.

According to the American Lung Association, NTM are relatively resistant to antibiotics and can become more resistant if only one antibiotic is used. Effective treatment of NTM caused by MAC requires three drugs for at least 12 months of

treatment. Currently recommended treatment regimens, drug resistance patterns, and treatment outcomes differ according to the NTM species, and management is a lengthy complicated process with limited therapeutic options (Ryu YJ et al. 2016). There is currently no approved first-line therapy for NTM lung disease. Treatment is determined based on guidelines and includes multi-drug regimens with antibiotics not approved for NTM. Adherence to the guidelines for treating NTM lung disease is suboptimal, and potentially harmful antibiotic regimens are commonly prescribed. Management of NTM disease requires prolonged use of costly combinations of multiple drugs with a significant potential for toxicity.

In September 2018, the FDA approved Arikayce® (amikacin liposome inhalation suspension), a new drug developed by Insmed Incorporated, for the treatment of lung disease caused by MAC in a limited population of refractory patients which does not respond to conventional treatment. To the best of our knowledge, this is the first treatment approved specifically for pulmonary NTM infections caused by MAC. Arikayce® is indicated as a second-line therapy in refractory patients as part of a combination antibacterial drug regimen. The Arikayce® prescribing information includes a Boxed Warning regarding the increased risk of respiratory conditions, including hypersensitivity pneumonitis, bronchospasm, exacerbation of underlying lung disease and hemoptysis that have led to hospitalizations in some cases.

Several drug candidates are currently under development for the treatment of NTM infections, including but not limited to, LungFit® GO (Beyond Air Inc.), an inhaled Nitric Oxide and SRP720 (Spero Therapeutics, Inc.), an oral antimicrobial agent and Nuzyra® (Paratek Pharmaceuticals), an oral antibacterial agent. Additionally, Insmed Incorporated is conducting a clinical trial program with Arikayce® as a first-line treatment for patients with MAC lung disease. According to www.clinicaltrials.gov, there are several additional ongoing clinical studies evaluating treatments for NTM infections.

Clinical Development

Although each of the three components of RHB-204 is approved individually and has been tested extensively in humans (e.g. see RHB-104), the formulation and doses represented by RHB-204 is novel and has not previously been tested in humans. Initiation of the trial for pulmonary NTM lung infections was in November 2020. The appropriate regulatory path is currently under discussion.

The following chart summarizes the development history and status of RHB-204:

Trial name	Development phase	Purpose of the trial	Clinical trial sites	Planned number of subjects of the trial	Status of the trial
CleaR-MAC Trial	Phase 3	Evaluate the efficacy and safety of RHB-204 in adult subjects with documented MAC lung infection.	Up to 40	125	Recruiting

Opaganib

Opaganib, a new chemical entity, is a proprietary, first-in-class, orally-administered, sphingosine kinase-2 (SK2) selective inhibitor with observed anticancer, anti-inflammatory, and antiviral activities, targeting multiple oncology, viral, inflammatory, and gastrointestinal indications. The compound originally designated as ABC294640 received an international non-proprietary name, opaganib, in the Recommended INN: List 79, 2018.

Opaganib inhibits SK2, a lipid kinase that catalyzes the formation of the lipid signaling molecule sphingosine 1-phosphate ("S1P"). S1P promotes cancer growth and proliferation and pathological inflammation, including TNFα signaling and other inflammatory cytokine production. Specifically, by inhibiting the SK2 enzyme, opaganib blocks the synthesis of S1P which regulates fundamental biological processes such as cell proliferation, migration, immune cell trafficking and angiogenesis, and is also involved in immune-modulation and suppression of innate immune responses from T cells.

Opaganib's proposed antiviral mechanism, based on pre-clinical studies conducted with the molecule, inhibits the replication of positive-strand single-stranded ribonucleic acid ("RNA") viruses, of which coronavirus, and specifically SARS-CoV-2, is a member. By binding to SK2, opaganib inhibits SK2 recruited to the viral replication-transcription complex and thus blocks the intracellular viral replication process. Because SK2 is a human host factor, opaganib's

proposed action is expected to maintain effect against known and emerging SARS-CoV-2 variants of concern irrespective of mutations in the viral spike-protein. Additionally, preclinical *in vivo* studies have demonstrated opaganib's potential to decrease renal fibrosis, have shown decreased fatality rates from influenza virus infection, and amelioration of bacteria-induced pneumonia lung injury by reducing the levels of IL-6 and TNF-alpha in bronchoalveolar lavage fluids.

On March 30, 2015, we entered into an exclusive worldwide license agreement with Apogee Biotechnology Corporation ("Apogee"), pursuant to which Apogee granted us the exclusive worldwide development and commercialization rights to ABC294640 (which we then renamed to opaganib and, as noted above, received an international non-proprietary name, opaganib, in 2018) and additional intellectual property for all indications. See "Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – License Agreement for opaganib."

In March 2022, we entered into an exclusive license agreement with Kukbo for opaganib for the treatment of COVID-19 in South Korea. See " - Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – License Agreement with Kukbo".

The development of opaganib has been supported by grants and contracts from U.S. federal and state government agencies awarded to Apogee, including from the NCI, BARDA, the U.S. Department of Defense and the FDA Office of Orphan Products Development.

Market and Competition

Opaganib is currently being developed for several potential indications, including for the treatment of severe COVID-19 pneumonia, cholangiocarcinoma (bile duct cancer), and prostate cancer.

COVID-19 is a disease caused by a coronavirus virus, SARS-CoV-2. The clinical spectrum has not yet been well defined and ranges from asymptomatic infection to pneumonia and Acute Respiratory Distress Syndrome (ARDS) with multiorgan failure, that may lead to death. Patients over 65 years and those with significant comorbidities, such as diabetes, cardiac or pulmonary disease, are more susceptible for developing severe disease and have a relatively higher mortality rate compared to younger, otherwise healthy patients. To date, there have been over 460 million confirmed cases of COVID-19 worldwide, with almost 6 million reported deaths. Several therapies have been approved by the FDA for the treatment of COVID-19, some under emergency use authorization. These therapies include antiviral drugs such as remdesivir, molnupiravir and nirmatrelvir, anti-inflammatory drugs and monoclonal antibodies. The FDA recently granted Emergency Use Authorization for two oral antiviral drugs intended for patients with mild-to-moderate COVID-19. These therapies are intended for the outpatient setting and require treatment initiation within a limited window of five days from symptom onset. As of the filing of this report, no oral therapy has been approved to date for treatment of hospitalized patients with severe disease. Several vaccines for SARS-CoV-2 have also been approved by the FDA and other regulatory agencies to date. Multiple additional drug therapies and vaccines are currently under development for COVID-19.

Cholangiocarcinoma (bile duct cancer) is a highly lethal malignancy. According to the American Cancer Society report, approximately 8,000 people are diagnosed with intrahepatic and extrahepatic bile duct cancers annually in the U.S., with recent studies showing an increased incidence of cholangiocarcinoma, mainly attributed to recent advancements in the diagnosis of this disease (Gores GJ, Hepatology, 2003). Surgery with complete resection is currently known to be the only curative therapy for cholangiocarcinoma; however, only a minority of patients are classified as having a resectable tumor at the time of diagnosis. Additional treatment options include radiation therapy and chemotherapy, but the efficacy of these treatments in cholangiocarcinoma patients is also limited and the prognosis for relapse patients who have failed initial chemotherapy is very poor, with an overall median survival of approximately one year (Valle J, *et al.* New Eng J, Med 2010). In recent years, the FDA has approved two targeted drug therapies specifically for cholangiocarcinoma. In April 2020, the FDA approved Pemazyre® (pemigatinib, Incyte Corporation), the first drug approved specifically for cholangiocarcinoma, indicated for adults with advanced bile duct cancer whose cancer has grown after at least one previous chemotherapy treatment and whose tumors have a mutation in the FGFR2 gene. FGFR2 fusions have been found in the tumors of approximately 9% to 14% of patients with cholangiocarcinoma. In August 2021, the FDA approved Tibsovo® (ivosidenib, Servier Pharmaceuticals LLC) for adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma with an isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test. IDH1 mutations are estimated to occur in up to 20% of cholangiocarcinoma cases in the U.S. We believe there remains a high

unmet medical need for new therapies for the majority of cholangiocarcinoma patients. There are several drugs in late-stage clinical development for cholangiocarcinoma. The 5-year relative survival rates of intrahepatic and extrahepatic cholangiocarcinoma patients range between 2% to 25%, depending on the tumor type and stage at diagnosis, according to the American Cancer Society.

Prostate cancer is the second most common cancer and the second leading cause of cancer death in American men. The American Cancer Society estimates that approximately 268,000 new cases of prostate cancer will be diagnosed in 2022. Prostate cancer is more likely to develop in older men and in African-American men. Treatment options depend on each case and include surgery, radiotherapy, cryotherapy, chemotherapy, hormone therapy, and immunotherapy. There are several approved drugs indicated for treatment of prostate cancer, as well as several drugs in development for U.S. approval.

Clinical Development

COVID-19

Preclinical data have demonstrated both anti-inflammatory and antiviral activities of opaganib, with the potential to reduce inflammatory lung disorders, such as pneumonia, and mitigate pulmonary fibrotic damage. In September 2020, we announced that opaganib demonstrated potent inhibition of SARS-CoV-2, the virus that causes COVID-19, achieving complete blockage of viral replication in an in vitro model of human lung bronchial tissue. Additionally, preclinical *in vivo* studies have demonstrated that opaganib decreased fatality rates from influenza virus infection and ameliorated Pseudomonas aeruginosa-induced lung injury by reducing the levels of IL-6 and TNF-alpha in bronchoalveolar lavage fluids.

Preliminary results from a preclinical study with opaganib, administered at 250 mg/kg, demonstrated a reduction of thrombosis (blood clotting) in an acute respiratory distress syndrome (ARDS) animal model. The preclinical study was designed to assess the efficacy of opaganib in reducing the incidence of adverse thromboembolic events in situ in the lipopolysaccharide (LPS)-induced model of pulmonary inflammation, a reliable model of ARDS that can mimic COVID-19 inflammation. The preliminary results from our study show opaganib 250 mg/kg reduced blood clot length, weight and total thrombus score in a preclinical model of ARDS. We believe such preliminary results add to the known antiviral and anti-inflammatory activities of opaganib and provide the potential for a unique triple-action effect on the pathophysiological processes associated with COVID-19 disease.

In September 2020, Apogee was awarded a grant from Pennsylvania's COVID-19 Vaccines, Treatments and Therapies Program, which supports the rapid advancement of promising novel COVID-19 therapies.

ABC-201: Global Phase 2/3 Study

In July 2020, we initiated a global Phase 2/3 clinical trial evaluating opaganib in hospitalized patients with severe COVID-19 pneumonia. This global multi-center, randomized, double-blind, parallel-arm, placebo-controlled trial enrolled a total of 475 patients requiring hospitalization and treatment with supplemental oxygen. The study was approved in ten countries.

In September 2021, we reported that preliminary top-line data from the opaganib (ABC294640) global Phase 2/3 study in hospitalized patients with severe COVID-19 pneumonia showed that the study did not meet its primary endpoint. Analysis of the study efficacy endpoints did show trends in favor of the opaganib arm as compared to placebo across multiple endpoints, including the primary endpoint, despite not achieving statistical significance.

In October 2021, we reported new data from a further analysis of this study, showing that treatment with oral opaganib as compared to the placebo-controlled arm resulted in a 62% statistically significant reduction in mortality as well as statistically significant improved outcomes in time to room air and median time to hospital discharge in a group of 251 hospitalized, moderately severe COVID-19 patients, comprising 54% of the study participants.

These new results were from a post-hoc analysis of data from the 251 study participants requiring a Fraction of inspired Oxygen (FiO2) up to 60% at baseline. Patients with FiO2 ≤ 60% are still considered to be severely affected and typically require oxygen supplementation via a nasal cannula or face mask.

Analyses of the FiO2 up to 60% patient subset from the opaganib Phase 2/3 study, the median for FiO2 levels in the study, who were treated with either opaganib or placebo in addition to standard-of-care (including dexamethasone and/or remdesivir) demonstrated consistent benefit across endpoints, in this subset of hospitalized moderately severe patients. Given the post-hoc characteristics of this subset, statistical inferences of significance cannot be formally attributed (nominal values presented). We also conducted a sensitivity analysis to account for missing data interpretability:

- **Mortality**: Opaganib treatment resulted in a statistically significant 62% reduction in mortality (7/117 patients treated with opaganib vs. 21/134 for placebo; nominal p-value=0.019, Relative Risk 2.6) (Sensitivity Analysis: 5/117 vs. 16/134, 64% efficacy benefit; nominal p-value=0.033, Relative Risk - 2.8).

  A detailed analysis of baseline risk factors and their potential impact on the mortality outcome in the sensitivity analysis group has also been undertaken, showing that the benefit is robustly maintained irrespective of the subgroups/risk factors, confirming that the positive outcome observed is due to opaganib.

- **Reaching Room Air by Day 14 (primary endpoint of the study)**: 77% of opaganib-treated patients reached room air by Day 14 vs. 63.5% for placebo – an efficacy benefit of 21% with opaganib (nominal p-value=0.033).

- **Median time to discharge**: Patients treated with opaganib showed median time of 10 days to discharge vs. 14 days for the placebo arm, resulting in a saving of four days hospitalization per opaganib patient and saving a total of 524 cumulative days of hospitalization across the group by Day 42, nominal p-value=0.0195.

- **Safety**: Overall adverse events were balanced between the opaganib and placebo groups, suggesting good safety, with no new safety signals emerging, further supporting potential use in this patient population and earlier stage populations.

In January 2022, we reported new data from a prespecified analysis of all Phase 2/3 study patients with positive PCR at screening, demonstrating that opaganib improved the median time to viral RNA clearance by at least 4 days. Treatment with opaganib resulted in viral RNA clearance in a median of 10 days while the median for clearance in the placebo arm was not reached by the end of 14-days treatment for placebo (hazard ratio 1.34; nominal p-value=0.043, N=437/463). To the best of our knowledge, opaganib is the first oral novel drug candidate to show improved viral RNA clearance in patients with severe COVID-19 pneumonia. This data provides clinical evidence supporting opaganib's potential antiviral activity.

In February 2022, we reported additional results from two prespecified analyses from the Phase 2/3 study. The first analysis showed that opaganib significantly reduced mortality when given to patients who received remdesivir and corticosteroids, the best available standard-of-care (SoC) for hospitalized patients. This analysis, undertaken for all patients from the study who were receiving remdesivir and corticosteroids at baseline, demonstrated a significant 70.2% mortality benefit for opaganib-treated patients, with a mortality rate of 6.98% (n=3/43) for the opaganib arm + SoC versus 23.4% (n=11/47) for placebo + SoC by Day 42 (p-value=0.034).

The second analysis further showed that opaganib delivered a significant benefit in time to recovery, defined as achieving a score of 1 or less on the WHO Ordinal Scale by Day 14. The prespecified analysis showed opaganib delivered a significant 34% benefit in time to recovery, with 37.4% of opaganib-treated patients (n=86/230) reaching this event versus 27.9% of patients (n=65/233) treated with placebo + SoC (p-value=0.013, Hazard Ratio 1.49).

Top-line safety data for the Phase 2/3 clinical trial showed good tolerability of opaganib, with balanced adverse events between the study arms. Analysis of the top-line data is still ongoing, including further analysis of the potential for increased benefit of treatment with opaganib in patients at earlier stages of disease. We continue making regulatory progress, with opaganib data submissions initiated in the fourth quarter of 2021 in the U.S., Europe, UK and additional countries. Discussions remain ongoing and initial guidance on a confirmatory study and potential path to approval has been received from the EU's EMA, the U.S. FDA, UK's MHRA and others. Based on regulatory feedback from other

territories and external advice received, we are also planning potential emergency and marketing authorization applications in certain such countries in the first half of 2022.

We continue to further examine and analyze the data from this study along with all the information gathered during this study, including all safety, and secondary outcome measures.

We have submitted data packages for opaganib to the regulatory agencies in the U.S., EU, UK and other territories in the fourth quarter of 2021. Discussions remain ongoing and initial guidance on a confirmatory study and potential path to approval has been received from the EU's EMA, the U.S. FDA, UK's MHRA and others. Based on regulatory feedback from other territories and external advice received, the Company is also planning potential emergency and marketing authorization applications in certain such countries in the first half of 2022.

We are also continuing its discussions with U.S. and other government agencies and non-governmental organizations around potential funding to support the ongoing development of opaganib. Discussions are also ongoing with potential partners who are interested in the rights to opaganib in various territories.

ABC-110: U.S. Phase 2 Study

In December 2020, we announced that our randomized, double-blind, placebo-controlled U.S. Phase 2 trial with opaganib in patients hospitalized with COVID-19 pneumonia demonstrated positive safety and efficacy data. The trial, which was not powered for statistical significance, enrolled 40 patients requiring hospitalization and supplemental oxygen.

Top-line results from the study found opaganib to be safe, with no material safety differences between the opaganib and placebo treatment arms. Overall, fewer patients suffered from serious adverse events (SAEs) in the opaganib treatment arm than in the placebo arm. In this small sample size, there were few events of intubation or fatality, and these were balanced between the two arms.

The opaganib-treated arm demonstrated a consistent trend of greater improvement in reducing oxygen requirement by end of treatment on Day 14 across key primary and secondary efficacy outcomes, correlating with clinical improvement as defined by the WHO ordinal scale:

- A greater improvement in the proportion of patients reaching room air and no longer requiring oxygen support by Day 14 vs. the control arm (52.6% vs. 22.2%).
- A greater improvement in the proportion of patients with a 50% reduction in supplemental oxygen by Day 14 vs. the control arm (89.5% vs. 66.7%).
- A higher proportion of patients discharged by Day 14 vs. the control arm (73.7% vs. 55.6%).
- A greater reduction from baseline of the median total oxygen requirement (AUC) over 14 days vs. the control arm (68.0% vs. 46.7%).

The data is being provided for peer review.

Additionally, preclinical *in vivo* studies have demonstrated that opaganib decreased fatality rates from influenza virus infection and ameliorated Pseudomonas aeruginosa-induced lung injury by reducing the levels of IL-6 and TNF-alpha in bronchoalveolar lavage fluids.

Preclinical studies

In September 2021, we announced results of a preclinical study demonstrating opaganib’s efficacy in significantly decreasing renal fibrosis in a unilateral ureteral obstruction-induced renal interstitial fibrosis model. Reports suggest that over 20% of hospitalized COVID-19 patients experience acute renal failure. The aim of the *in vivo* efficacy study was to

verify the effect of opaganib on kidney inflammation and fibrosis in a unilateral ureteral obstruction (UUO) model – a well characterized model for renal fibrosis. Results from the study showed that opaganib significantly decreased renal fibrosis.

Opaganib demonstrated potent antiviral activity against SARS-CoV-2, the virus that causes COVID-19, completely inhibiting viral replication in an in vitro model of human lung bronchial tissue. In June 2021, we announced that preliminary results from a preclinical study demonstrated potent inhibition of the Beta and Gamma COVID-19 variants of concern by opaganib at non-cytotoxic doses. We further announced in August 2021 that opaganib demonstrated strong inhibition of the Delta variant replication while maintaining cell viability at relevant concentrations in a 3D tissue model of human bronchial epithelial cells. Based on opaganib's unique host-targeted mechanism and the preliminary results of this study, we believe opaganib is likely to also maintain its activity against emerging variants of COVID-19.

Compassionate use

In April 2020, at the beginning of the COVID-19 pandemic, we established a compassionate use program, providing opaganib on a compassionate-use basis to patients with severe COVID-19 in Israel and in Switzerland. A report was published in *medRxiv* describing the compassionate-use in Israel (2020), in which a small cohort (seven patients) with severe COVID-19 pneumonia requiring supplemental oxygen via high flow nasal cannula (HFNC) were treated with opaganib. The dose administered was 500 mg BID for up to 14 days. The outcomes of these patients were evaluated against matched controls at the same hospital center. No safety issues were observed in this small cohort. Additionally, a physician in Switzerland requested opaganib on a compassionate-use basis to treat ten COVID-19 patients. The data gathered from the physician is limited; however the outcomes suggest that the treatment was safe and well tolerated in this small cohort of patients.

ABC-108: Advanced Unresectable Cholangiocarcinoma

A Phase 2a clinical study with opaganib in patients with advanced, unresectable, intrahepatic, perihilar and extrahepatic cholangiocarcinoma is ongoing at Mayo Clinic's major campuses in Arizona and Minnesota, the Huntsman Cancer Institute, University of Utah Health and at Emory University. In September 2018, we announced that the study achieved its pre-specified efficacy goal for the first stage of the two-stage study design, and as a result, the study has continued to its second stage. Treatment with opaganib, Part 1 of the study, designed to enroll 39 evaluable patients, completed enrollment in January 2020. Preliminary data from this cohort indicated a signal of activity in a number of subjects with advanced cholangiocarcinoma. Enrollment is ongoing for a second cohort, evaluating opaganib in combination with hydroxychloroquine, an anti-autophagy agent. Opaganib received orphan drug designation from the FDA for the treatment of cholangiocarcinoma.

In October 2019, an expansion cohort for cotreatment of opaganib and hydroxychloroquine sulfate (HCQ) was submitted to the FDA. Enrollment of this cotreatment cohort, Part 2 of the study, began in July 2020. The cohort will consist of two phases: Phase 1, an accelerated dose escalation run-in with enrollment of up to 15 patients evaluable for safety and tolerability, and Phase 2, treatment of 20 patients evaluable in the Phase 1 determined dose to determine safety and tolerability.

The primary objective of Part 1 is to determine the response rate (RR) of cholangiocarcinoma defined as objective responses (OR), i.e. complete and partial responses (CR, PR) plus stable disease (SD) of at least four months to treatment with opaganib. The primary endpoint of Part 2 is to determine Durable Disease Control Rate (DDCR), defined as Disease Control Rate (DCR) of at least four months' duration to treatment with opaganib and HCQ.

In April 2017, the FDA granted to opaganib orphan drug designation for the treatment of cholangiocarcinoma. The orphan drug designation allows us to benefit from various development incentives to develop opaganib for this indication, including tax credits for qualified clinical testing, the waiver of a prescription drug user fee (PDUFA) upon submission of a potential NDA and, if approved, a seven-year marketing exclusivity period (subject to certain exceptions) for the treatment of cholangiocarcinoma.

EAP for the Treatment of Advanced Unresectable Cholangiocarcinoma

An EAP is for eligible participants who do not qualify for participation in, or who are otherwise unable to access, the ongoing clinical trial ABC-108 for advanced unresectable cholangiocarcinoma. This program is designed to provide access to opaganib for the treatment of cholangiocarcinoma prior to approval by the local regulatory agency. We cannot predict how long this program will continue, and we may decide for various reasons, including but not limited to resources and availability of opaganib, not to continue with the EAP.

ABC-103: Refractory or Relapsed Multiple Myeloma

A Phase 1b study with opaganib for the treatment of refractory or relapsed multiple myeloma was performed in heavily pretreated patients at Duke University Medical Center. A total of 13 patients were enrolled and treated in three dose cohorts. While efficacy was not the primary endpoint of the Phase 1b study, of ten evaluable subjects, one patient achieved a very good partial response. The study was supported by a $2 million grant from the National Cancer Institute (the "NCI") Small Business Innovation Research Program awarded to Apogee Biotechnology Corporation, in conjunction with Duke University, with additional support from us.

The study ended in line with the NCI grant expiration in May 2019. The Clinical Study Report was finalized in November 2020. Data demonstrated that oral administration of opaganib is generally safe and tolerable in patients with refractory or relapsed multiple myeloma. One patient in the 500 mg dose cohort showed a very good partial response and one patient showed stable disease for three months. The remaining patients had very short periods of stability, progressive disease or tumor assessment was missing. Mean progression-free survival (PFS) across dose cohorts was relatively the same number of weeks, and thus a conclusion on dosing strength in relation to improved survival could not be discerned. Additionally, there did not appear to be an effect of opaganib on plasma levels of sphingosine 1 phosphate (S1P), IL-6, or other cytokines measured in patients with refractory or relapsed MM. The small study size prohibits meaningful efficacy conclusions to be drawn.

The primary endpoints of the first portion of the study (Phase 1) were to assess safety and determine the maximum tolerated dose in this group of patients. Secondary objectives included assessment of antitumor activity and determination of the PK and pharmacodynamic (PD) properties of opaganib in refractory or relapsed multiple myeloma patients.

At the current stage, we have no intention to pursue the development of opaganib for this indication.

ABC-101: Advanced Solid Tumors

A Phase 1 study, first-in-man evaluation of opaganib in advanced solid tumors was completed in the summer of 2015. Final results demonstrated that the study, conducted at the Medical University of South Carolina (MUSC), successfully met its primary and secondary endpoints, demonstrating that the compound is well tolerated and can be safely administered to cancer patients at doses predicted to have therapeutic activity.

Twenty-one patients with advanced solid tumors were treated with opaganib in the study, the majority of who were GI cancer patients, including pancreatic, colorectal and cholangiocarcinoma cancers.

The study included the first-ever longitudinal analysis of plasma S1P levels as a potential pharmacodynamic biomarker for activity of a sphingolipid-targeted drug. Administration of opaganib resulted in a rapid and pronounced decrease in levels of S1P with several patients having prolonged stabilization of disease.

The study was supported by grants from the U.S. National Cancer Institute (NCI) awarded to MUSC Hollings Cancer Center, an NCI-Designated Cancer Center, and from the FDA Office of Orphan Products Development (OOPD) awarded to Apogee.

ABC-106: Advanced Hepatocellular Carcinoma

An investigator-sponsored Phase 2 study to evaluate the safety and efficacy of opaganib as a second-line monotherapy in patients with advanced hepatocellular carcinoma ("HCC") was initiated at MUSC Hollings Cancer Center, the Mayo Clinic campus at Arizona and the University of Maryland.

The study was led by Dr. Carolyn Britten, MUSC, and was planned to enroll up to 39 patients who have experienced tumor progression following treatment with first-line single-agent sorafenib (Nexavar®).

In September 2019, we announced that The National Cancer Institute (NCI) grant that was previously awarded to the MUSC to support a study with opaganib in hepatocellular carcinoma (HCC) had been diverted to support a Phase 2 study with opaganib for a different indication, prostate cancer (ABC-107). At the current stage, we have no intention to pursue the development of opaganib for the HCC indication.

ABC-107: Prostate Cancer

The investigator-sponsored study "A Phase 2 Study of the Addition of opaganib to Androgen Antagonists in Patients with Prostate Cancer Progression on Enzalutamide or Abiraterone" was initiated in March 2020 at MUSC Hollings Cancer Center and at Emory University. The study is led by Dr. Michael B. Lilly. The study is planned to enroll up to 70 patients and is supported by the National Cancer Institute grant awarded to MUSC.

This is a Phase 2 efficacy study of opaganib in patients with metastatic castration-resistant prostate cancer that is progressing during treatment with androgen signaling blockers, abiraterone or enzalutamide. The study will consist of an initial safety "run in" cohort in which patients will receive opaganib along with continuation of prior abiraterone or enzalutamide to document tolerability in this new patient population and to document the effects of opaganib on blood prostate-specific antigen (PSA) levels. Provided that there is no untoward toxicity in these patients, there will be two additional cohorts with up to 27 patients, with each of patients with worsening disease during abiraterone or enzalutamide treatment. These patients will continue previous androgen blocking agents (abiraterone or enzalutamide, and gonadotropin-releasing hormone GnRH receptor agonist/antagonist). The primary objective of the study is to measure the proportion of patients with disease control during opaganib plus abiraterone or enzalutamide treatment using a composite metric based on PSA, bone scan, and RECIST measurements per Prostate Cancer Working Group 3 (PCWG3) criteria.

In August 2021, we announced that based on a preliminary review of partial and unaudited data in the ongoing study, the study had met its primary endpoint of at least six subjects demonstrating disease control (defined as stable disease or better after 16 weeks on treatment) among at least 27 evaluable subjects.

Upon further review and analysis of the unaudited data in the ongoing study, we reported that the study did not meet its primary endpoint in the study arm evaluating opaganib in combination with enzalutamide. Patient enrolment continues for the study's other arm, evaluating a combination of opaganib and abiraterone. Accrual and data entry are ongoing and results for the study remain subject to further review and analysis.

Preclinical data have demonstrated both anti-inflammatory and antiviral activities of opaganib, demonstrating the potential to reduce inflammatory lung disorders, such as pneumonia, and mitigate pulmonary fibrotic damage.

ABC-104: Oncology Support, Radioprotectant: Prevention of Radiation-Associated Mucositis in the Treatment of Head and Neck Cancer

A Phase 1b study to evaluate opaganib as a radioprotectant in head and neck cancer patients undergoing therapeutic radiotherapy is currently on hold.

ABC-105: Moderate to Severe Ulcerative Colitis ("UC")

A Phase 2 study to evaluate the efficacy of opaganib in patients with moderate to severe UC by the proportion of patients who are in remission at the end of treatment is currently on hold.

ABC-109: Food Effect Study in Healthy Subjects

A Phase 1, randomized, open-label, single-dose, 3-treatment, 3-period, 6-sequence crossover study designed primarily to evaluate the effect of a standardized meal on the absorption and bioavailability of opaganib in healthy subjects, was completed in the U.S. in January 2018. The study also evaluated the effect of the administration of a solution of opaganib via nasogastric (NG) tube on the absorption and bioavailability of opaganib. Twenty-three eligible, healthy, male and female adult subjects were randomized to receive opaganib orally in a state of fast, fed or as a solution by NG tube (after tube feeding). Seventeen subjects received all three treatments. All three treatments, though maximum concentration was lower when the drug was given orally in the fed state as compared to fasted, nasogastric administration after tube feeding led to intermediate results. Subjects experienced fewer gastrointestinal side effects when the drug was given in the fed state than fasted, but the pharmacodynamic effect, as reflected in the decrease in sphingosine-1-phosphate, the product of the target enzyme, was no lower after fed than fasted administration. Thus, the results indicated that opaganib may be given after eating, with improved tolerance and no loss of pharmacodynamic effect.

The following chart summarizes the clinical trial history and status of opaganib:

Clinical trial name	Development phase of the clinical trial	Purpose of the clinical trial	Clinical trial site	Planned number of subjects of the trial	Nature and status of the trial	Schedule
ABC-201	Phase 2/3	A study for the treatment of Opaganib in patients with severe COVID-19 pneumonia	Multicenter study	464	Completed	Top-line results reported in Q3/2021
ABC-110	Phase 2	A study for the treatment of opaganib in patients with severe COVID-19 pneumonia	Multicenter study across the U.S.	40	Completed	Top-line results reported in 2020
ABC-108	Phase 2a	A study for the treatment of advanced, unresectable intrahepatic, perihilar and extrahepatic cholangiocarcinoma with opaganib and co-treatment with opaganib and HCQ	Multicenter study across the U.S.	Up to 105	Ongoing	Ongoing
ABC-107 (103193 MUSC Study ID)	Phase 2	An add-on study for prostate cancer patients who progressed on enzalutamide or abiraterone. The proportion of patients with disease control during treatment with opaganib and enzalutamide or abiraterone will be measured	Medical University of South Carolina, Charleston, U.S. and Emory University, Atlanta, Georgia, U.S.	Up to 60	Ongoing	Initiated in March 2020
ABC-103	Phase 1b/2	Safety and efficacy study in patients with refractory or relapsed multiple myeloma that have previously been treated with proteasome inhibitors and immunomodulatory drugs	Duke University, North Carolina, U.S.	Ended	Ended after Phase 1	Ended
ABC-101	Phase 1	Safety, PK and pharmacodynamic study in patients with advanced solid tumors	Medical University of South Carolina, Charleston, U.S.	22	Completed. Final results indicate the study drug is well tolerated and can be safely administered to cancer patients	Completed 2015
ABC-106	Phase 2	Investigator-Sponsored Safety and Efficacy Study in Patients with Advanced Hepatocellular Carcinoma Who Have Progressed on Sorafenib	Medical University of South Carolina, Charleston, U.S. and collaborating sites (Multicenter, U.S.)	From 12 to 39	Withdrawn and replaced with ABC-107 in prostate cancer (103193 MUSC Study ID)	Withdrawn
ABC-104	Phase 1b	Safety and efficacy study in the prevention of mucositis in combination with radiotherapy for treatment of squamous head and neck carcinoma	Multicenter study across the U.S.	Up to 32	TBD	TBD
ABC-105	Phase 2	A study for the treatment of moderate to severe ulcerative colitis	Multicenter study	Up to 94	TBD	TBD
ABC-109	Phase 1	Assessment of the effect of food on the absorption and bioavailability of opaganib; also as a solution via nasogastric (NG) tube under fed conditions	ICON Early Phase Services, San-Antonio, TX, U.S.	23	Completed	Completed 2018

We cannot predict with certainty our development costs, and such costs may be subject to changes. See “Item 3. Key Information – D. Risk Factors – Risks Related to Our Financial Condition and Capital Requirements.”

RHB-107 (upamostat; formerly Mesupron)

As mentioned under "Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – License Agreement for RHB-107" (upamostat; formerly Mesupron)", on June 30, 2014, we signed an exclusive license agreement with Wilex AG (which later changed its name to Heidelberg Pharma AG) forRHB-107 (INN: upamostat; formerly Mesupron) for all indications and for all uses. . Under this agreement, we are responsible for all development, regulatory and commercialization of RHB-107 in the entire world, excluding China, Taiwan, Macao, and Hong Kong.

RHB-107 is a proprietary, first-in-class, orally-administered potent inhibitor of several serine proteases, with a unique potency and specificity that suggests it may be a new non-cytotoxic approach to cancer therapy. In addition, work completed by us demonstrated its potential use in inflammatory digestive diseases, inflammatory lung diseases and infectious diseases.

Market and Competition

RHB-107 is currently being developed for the treatment of non-hospitalized symptomatic COVID-19, and has previously undergone non-clinical and clinical studies in several oncology indications, including metastatic breast cancer and advanced non-metastatic pancreatic cancer.

Non-Clinical and Clinical Development

Data from non-clinical studies conducted by us indicate that WX-UK1, the active metabolite of RHB-107, is a specific and potent inhibitor of several human serine proteases (e.g., trypsin-3, trypsin-2, trypsin-1, matriptase-1, and trypsin-6), some of which have been shown to play a role in inflammatory digestive diseases and lung diseases. Additional non-clinical studies indicated that several members of the type II transmembrane serine proteases (TTSPs), some of which are important factors in the spread of infectious diseases, were inhibited by WX-UK1.

Oncology

RHB-107's safety profile has been demonstrated in approximately 200 people, including in Phase 2 studies in oncology indications and COVID-19. Several Phase 1 studies and two Phase 2 proof-of-concept studies have been completed with RHB-107 in cancer patients. The first Phase 2 trial in locally advanced non-metastatic pancreatic cancer and the second trial in metastatic breast cancer established the therapeutic candidate's safety and tolerability profile. The Phase 2 trials with RHB-107 in both indications failed to demonstrate significant improvement in either progression-free survival or overall survival.

None of the prior studies used any molecular markers to target certain patient populations. Using technologies developed since the original clinical trials were performed, we are currently planning several preclinical studies, including biomarker analysis and mechanism of action studies. We expect that the findings from these studies can help us determine the patient populations to be studied in subsequent clinical trials.

In October 2017, the FDA granted RHB-107 orphan drug designation for the treatment of pancreatic cancer. The orphan drug designation allows us to benefit from various development incentives to develop RHB-107 for this indication, including tax credits for qualified clinical testing, waiver of a PDUFA upon submission of a potential marketing application and, if approved, a seven-year marketing exclusivity period (subject to certain exceptions) for the treatment of pancreatic cancer.

COVID-19

RHB-107 was studied in a 3D tissue model of human bronchial epithelial cells (EpiAirway™) which morphologically and functionally resembles the human airway and is similar to the model used to discover SARS-CoV-2. The study was designed to evaluate the *in vitro* efficacy of RHB-107 in inhibiting SARS-CoV-2 infection and included a positive control of camostat. Results from the study demonstrated strong inhibition of SARS-CoV-2 viral replication.

RHB-107-01: Global Phase 2/3 Study

A 2 – part, Phase 2/3 multicenter, randomized, double-blind, placebo-controlled, parallel-group study with RHB-107 is ongoing and aimed at evaluating treatment in patients with symptomatic COVID-19 early in the course of the disease, with a once-daily oral treatment that can be prescribed and used in the non-hospitalized patient population. The Phase 2 part of the study was designed to evaluate safety for dose selection and to provide preliminary assessment of parameters to be used for efficacy evaluation in Part B. A total of 61 patients were enrolled in Part A and randomized on a 1:1:1 basis to receive one of two dose levels of RHB-107 or a placebo control and was predominantly conducted in the U.S. (60/61 patients) as well as South Africa.

RHB-107 was administered once daily for 14 days, with patients receiving follow-up for eight weeks from first dosing. The primary endpoints were time to sustained recovery from symptomatic illness compared to placebo, as well as safety and tolerability of RHB-107. Several secondary and exploratory endpoints are also being assessed. In February 2021, we announced that the first patient had been dosed in the study.

In March 2022, we announced positive Phase 2 study results of Part A of the Phase 2/3 study, which enrolled a total of 61 patients who were randomized on a 1:1:1 basis to receive one of two dose levels of RHB-107 or a placebo control. Although not powered for efficacy assessment, the study showed highly promising efficacy results delivering a 100% reduction in hospitalization due to COVID-19, with zero patients on RHB-107 hospitalized with COVID-19 (0/41) compared to 15% on the placebo-controlled arm requiring hospitalization (3/20) (nominal p-value=0.0317). Furthermore, the study showed an 87.8% reduction in reported new severe COVID-19 symptoms, with only one patient on RHB-107 (2.4%, 1/41) compared to 20% (4/20) of patients on the placebo-controlled arm experiencing new COVID-19 related severe symptoms (nominal p-value=0.036).

The study met its primary outcome measure, demonstrating a favorable safety and tolerability profile of RHB-107. Study arms were well balanced with respect to baseline disease severity, risk factors and vaccination status. Patients were also tested for the specific viral strain (last patient randomized November 12, 2021), with the most common variant being Delta, found in 62.5% of the patients that had next generation sequencing (NGS).

Next steps for the study will follow data submission and discussion with regulators.

Ebola Virus Disease Therapy

We completed the first part of a preclinical *in-vivo* study (2 out of the 3 proposed actives). The preliminary results were evaluated in conjunction with the U.S. National Institute of Allergy and Infectious Diseases and demonstrated statistical significance of the combination of two of our molecular candidates. The second part of the study (all three actives combined) has not yet been initiated. In May 2018, we received a new U.S. patent for our experimental Ebola therapy. We continue to examine ways to work together with the National Institute of Health on various projects.

RHB-104

Crohn's Disease

RHB-104 is an investigational new drug intended to treat Crohn's disease, which is a serious inflammatory disease of the GI system that may cause severe abdominal pain and bloody diarrhea, malnutrition and potentially life-threatening complications.

RHB-104 is a patented combination of clarithromycin, clofazimine, and rifabutin, three generic antibiotic ingredients, in a single capsule. The compound was developed to treat MAP infections in Crohn's disease.

To date, Crohn's disease has been considered an autoimmune disease, but the exact pathological mechanism is unclear. Dr. Robert J. Greenstein suggested in *The Lancet Infectious Diseases*, 2003, that Crohn's disease is caused by MAP, the same organism responsible for causing a major disease in animal agriculture production, domestic and wild animals. This hypothesis is supported by an expanding number of scientific and clinical studies published in peer-reviewed journals

since a National Institute of Allergy and Infectious Diseases conference that focused on MAP in Crohn's disease took place in 1998. Specific genetic loci like NOD2/CARD15 have been implicated in the pathogenesis of Crohn's disease with mutations in NOD2 suspected of leading to defective recognition of MAP and increased compensatory immune activation in patients with Crohn's disease. Advances in diagnostic technology have led to increasingly higher identification of MAP, with studies, such as Naser S *et al.* The Lancet, 2004, Bull TJ *et al.* J Clin Microbiol, 2003 and Shafran I *et al.* Dig Dis Sci, 2002, demonstrating a high prevalence of MAP in Crohn's disease patients. However, there is currently no FDA-approved commercial diagnostic test for MAP.

In 2011, we obtained FDA "Orphan Drug" status for RHB-104 for the treatment of Crohn's disease in the pediatric population. See "Item 4. Information on the Company – B. Business Overview – Government Regulations and Funding – Orphan Drug Designation."

The formulation for RHB-104 and manufacturing of the all-in-one capsules for our clinical trials have been completed. Multiple batches of RHB-104 hard shell capsules packaged in 250 cc bottles with a cap and induction seal child resistant closure have been evaluated in long-term and accelerated stability studies under International Conference on Harmonization ("ICH") specified conditions.

We acquired the rights to RHB-104 pursuant to an asset purchase agreement with Giaconda Limited, an Australian company. See "Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – Acquisition of Talicia®, RHB-104, and RHB-106."

We continue to pursue the development program for a companion diagnostic for the detection of MAP bacteria in Crohn's disease patients. These efforts are in part based on detecting the presence of MAP bacterial DNA in human biological specimens. We do not know if or when such a diagnostic test would become available.

Market and Competition

According to GlobalData, a provider of market intelligence for the pharmaceutical sector, there were approximately 2.98 million diagnosed prevalent cases of Crohn's disease in the sixteen major pharmaceutical markets (the U.S., France, Germany, Italy, Spain, the UK, Japan, Australia, Brazil, Canada, China, India, Mexico, Russia, South Africa and South Korea) in 2021. This number of prevalent cases is expected to increase to 3.4 million by 2029.

Therapeutic interventions in Crohn's disease patients are based on the disease location, severity, and associated complications. Therapeutic approaches for the treatment of Crohn's disease are individualized according to the patient's symptomatic response and tolerance to the prescribed treatment. Since the existing treatments are not curative, the current therapeutic approaches are sequential and involve treatment of an acute disease or inducing clinical remission followed by maintenance of the response or remission to improve the patient's quality of life.

Currently, available drugs on the market for the treatment of Crohn's disease offer symptomatic relief, the effects of which are largely temporary or partial and are accompanied by numerous adverse effects. The most commonly prescribed drugs for treatment of Crohn's disease include 5 Aminosalicylates (5-ASA, such as mesalamine), corticosteroids (such as prednisone), immunosuppressant drugs (such as azathioprine and methotrexate) and biologic agents, including TNF-α inhibitors (such as Remicade®, Humira®, and Cimzia®), integrin inhibitors (such as Tysabri® and Entyvio®) and an IL 12 and IL23 antagonist (such as Stelara®). Additionally, several companies have developed for approval, or are in the process of developing, biosimilar drugs to compete with the approved biologic agents once their patent has expired. Salix Pharmaceuticals (a wholly-owned subsidiary of Bausch Health) also announced in January 2020 that they will initiate a Phase 2/3 study with the antibiotic rifaximin (Xifaxan®) for the treatment of Crohn's disease, however to the best of our knowledge, the study has not been initiated. Additionally, AbbVie Inc ("AbbVie") announced in December 2021 positive top-line results from its Phase 3 study with Rinvoq® (upadacitinib), a selective and reversible Janus kinase inhibitor, in moderate to severe Crohn's disease patients who had an inadequate response or were intolerant to biologic therapy. AbbVie has announced that it expects FDA marketing approval for Rinvoq® in 2022. If approved, it will be the first Janus kinase inhibitor approved for the treatment of Crohn's disease. Rinvoq® label includes an FDA black box warning for other approved indications due to safety concerns relating to serious heart-related side effects and cancer risks.

There are other companies currently conducting clinical trials with drug candidates in Crohn's disease. We may also be exposed to potentially competitive products, which may be under development to treat Crohn's disease, including new biological therapies and other new therapies.

Unlike drugs currently on the market for the treatment of Crohn's disease, which are immunosuppressive agents, RHB- 104 is intended to address the suspected cause of the disease - MAP bacterial infection. To the best of our knowledge, there are no drugs approved for marketing that target infections caused by MAP bacteria in Crohn's disease patients.

Clinical Development

A Phase 3 clinical trial for RHB-104 was conducted in Australia, sponsored by Pharmacia, a Swedish company (which merged with Pfizer), with the primary endpoint of evaluating the ratio of patients with recurrent symptoms of Crohn's disease following the initial induction of remission with 16 weeks of treatment with prednisolone initiated at 40 mg/day and weaned over the 16-week period. Subjects were subsequently assessed at 52, 104 and 156 weeks. The main secondary objective was the percentage of patients who achieved clinical remission at 16 weeks. The results of the trial were published by Professor Warwick Selby *et al.* in 2007 in the medical journal *Gastroenterology*. Although the study did not meet the main objective of showing a difference in relapse rate with long-term treatment, there was a statistically significant difference between the treatment groups in the percentage of subjects in remission at week 16. Professor Marcel Behr and Professor James Hanley from McGill University published a re-analysis of the study in *The Lancet Infectious Diseases* in June 2008, based on the intent-to-treat (ITT) principle and found that there was a significant statistical advantage for the active therapy over the placebo throughout the two-year period of administration that disappeared once the active therapy was discontinued.

In June 2011, we entered into an agreement with our Canadian service provider, which entered into a back-to-back agreement with PharmaNet Canada Inc. for the provision of clinical trial services for the RHB-104 adult studies in North America and Europe. PharmaNet was subsequently acquired by inVentiv Health which became Syneos Health ("Syneos"), and our agreements were transferred to Syneos.

In October 2012, we entered into an agreement with our Canadian service provider, which, in turn, entered into a back-to-back agreement with a Canadian manufacturer to complete the manufacturing and supply of RHB-104 for our clinical trials. In addition, we entered into additional manufacturing agreements directly with the Canadian manufacturer.

In July 2018, we announced positive top-line results from the first Phase 3 study with RHB-104 for Crohn's disease (the "MAP US study"), a randomized, double-blind, placebo-controlled first Phase 3 study with RHB-104 for Crohn's disease. The Phase 3 study enrolled 331 subjects with moderately to severely active Crohn's disease (defined as Crohn's Disease Active Index ("CDAI") between 220 and 450) in the U.S., Canada, Europe, Australia, New Zealand, and Israel. Subjects were randomized 1:1 to receive RHB-104 or placebo as an add-on therapy to baseline standard-of-care medications, including 5-ASAs, corticosteroids, immunomodulators or anti-TNF agents.

Our MAP US study successfully met its primary endpoint, as well as key secondary endpoints. Top-line results in the intent-to-treat (ITT) population demonstrated superiority of RHB-104 over placebo in achieving remission at week 26, defined as CDAI value of less than 150, the primary endpoint of the study. The proportion of patients meeting the primary endpoint was significantly greater in the RHB-104 group compared to placebo at week 26 (37% vs. 23%, p= 0.007). Moreover, while the secondary endpoints were not powered for significance in this induction of remission trial, key secondary endpoints were nevertheless met with statistically and clinically meaningful outcomes, demonstrating consistent benefit to Crohn's disease patients treated with RHB-104. RHB-104 was found to be generally safe and well tolerated.

In October 2018, we reported additional positive data from the MAP US study, including subgroup analysis of treatment with and without anti-TNF agents, presented at the United European Gastroenterology Week 2018.

In October 2019, we announced full week 52 results of blinded treatment in the MAP US study at the American College of Gastroenterology, which were consistent with the previously reported interim positive outcomes from the study. The study continued to meet its primary endpoint of clinical remission, defined as CDAI value of less than 150, at week 26 (36.7% vs. 22.4%, p=0.0048), key secondary endpoints of maintenance of remission at weeks 16 and 52 (25.9% vs. 12.1%,

p=0.0016) and, notably, durable clinical remission on all visits, week 16 through 52 (18.7% vs. 8.5%, p=0.0077) (in all cases, data presented as RHB-104 vs. placebo).

RHB-104 was found to be generally safe and well tolerated, with an overall balance in the type and frequency of adverse events between RHB-104 and placebo. RHB-104 was associated with a lower incidence of Clostridiodies (Clostridium) difficile infections compared with placebo. In the analysis of the complete safety information for the study, a top-line electrocardiogram monitoring report for the MAP US study, which was shared with the FDA, demonstrated evidence of progressive prolongation of the QTcF (corrected QT interval by Frederica's formula) interval across visits, with the largest mean placebo-corrected ΔQTcF (ΔΔQTcF) of 30.6ms at week 52 of treatment. Clofazimine, as well as clarithromycin (another active component of RHB-104), are known to be associated with QT prolongation. .

In October 2019, we also announced supportive top-line results from an open-label extension Phase 3 study (the "MAP US2 study"), which was conducted to evaluate the safety and efficacy of RHB-104 in subjects who remain with active Crohn's disease (CDAI ≥ 150) after 26 weeks of blinded study therapy in the Phase 3 MAP US study. These subjects had the opportunity to receive treatment with RHB-104 for a 52-week period in the open-label MAP US2 study. A total of 54 subjects entered the open-label extension study in the U.S., Canada, Europe, Israel, and New Zealand, and 30 subjects completed 52 weeks of treatment with RHB-104. The MAP US2 study's primary endpoint is disease remission at week 16, defined as CDAI of less than 150. Top-line results from the MAP US2 study demonstrated 28% clinical remission with RHB-104 at week 16 and 22% remission at week 52. Of the MAP US2 subjects who were previously randomized to the placebo arm (as an add-on to standard-of-care therapies) in the MAP US study and treated with RHB-104 for the first time in the MAP US2 study, 32% achieved remission at week 16.

We further announced in September 2019 that following additional guidance received from the FDA on the path for potential approval of RHB-104 for the treatment of Crohn's disease, we have intensified our collaborations with leading laboratories in the field of detection of MAP bacteria in Crohn's disease patients. We do not know if and when a diagnostic test for MAP would become available. Additional FDA guidance on the potential path to approval of RHB-104 is to be obtained prior to initiation of further clinical studies.

We have conducted several supportive studies with the current formulation of RHB-104, including a population pharmacokinetic study that was conducted as part of the Phase 3 MAP US study.

We believe that additional clinical studies will be required to support an NDA for RHB-104, if filed.

The following chart summarizes the clinical trial history and status of RHB-104 studies and its earlier individual active agents:

Clinical trial author/designation	Development phase of the clinical trial	Purpose of the clinical trial	Clinical trial site	Planned number of subjects of the trial	Nature and status of the trial	Schedule
Borody 2002	Phase 2a	Examining the effect of the treatment on Crohn's disease patients	Center for Digestive Disease, Australia	12	Performed	Completed 2002
Borody 2005	Phase 2	Examining the effect of the treatment on Crohn's disease patients	Center for Digestive Disease, Australia	52	Performed	Completed 2005
Selby	Phase 3	Examining the effect of the treatment with the product on Crohn's disease patients	20 clinical centers in Australia	213	The trial was performed and indicated promising improvement rates, although it did not meet the main trial objective, as defined	Published in 2007
Biovail PK Study 2007	PK Study	Optimize the formulation of RHB-104 on a PK basis	Toronto, Ontario	24	The trial compared two formulations to determine the optimum formulation for RHB-104	Completed 2007
MAP US Study	Phase 3	Assess the safety and efficacy of RHB-104 in Crohn's disease patients	U.S., Canada. Israel, Australia, New Zealand, and Europe	331	Completed	Completed 2020
MAP US2 Study	Phase 3	Assess the safety and efficacy of RHB-104 in Crohn's disease patients	U.S., Canada, Israel, New Zealand, and Europe	54	Completed	Completed 2021
Drug-Drug Interaction Study	PK Study	To assess the net PK effect of multiple doses of RHB-104 on CYP3A4 enzymes in healthy volunteers	Algorithme Pharma, Canada	36	Ended	Ended 2014
Food Effect Study	PK Study	Determine the effect of food on the bioavailability of RHB-104 in healthy volunteers	Algorithme Pharma, Canada	84	Completed	Completed 2014

We cannot predict with certainty our development costs, and such costs may be subject to change. See "Item 3. Key Information – D. Risk Factors – Risks Related to Our Financial Condition and Capital Requirements."

Multiple Sclerosis ("MS")

MS is an inflammatory, demyelinating, and neurodegenerative disease of the central nervous system of uncertain etiology that exhibits characteristics of both infectious and autoimmune pathology.

We had previously conducted a Phase 2a proof-of-concept study with RHB-104 for relapsing-remitting multiple sclerosis. At the current stage, we have no intention to pursue the development of RHB-104 for this indication.

RHB-102 (Bekinda®)

RHB-102 (Bekinda®) is an investigational once-daily bi-modal extended-release oral formulation of ondansetron, a leading member of the family of 5-HT3 serotonin receptor inhibitors. We are developing RHB-102 (Bekinda®) in multiple dosage strengths. RHB-102 (Bekinda®) is under development for the intended use in the following indications, which are novel and not yet FDA-approved indications for ondansetron targeting large potential markets:

1) Acute gastroenteritis and gastritis - 24 mg strength

2) Irritable Bowel Syndrome with Diarrhea (IBS-D) - lower dose strength for long-term administration

RHB-102 (Bekinda®) utilizes a technology called CDT® that uses salts to provide an extended-release of ondansetron. The CDT® platform enables extended drug release (i.e., the measured rate of introduction of active drug) at a relatively low manufacturing cost. The proposed commercial formulation and its use are protected by Company-filed patents and pending patent applications and are being pursued internationally.

Acute Gastroenteritis and Gastritis

Acute gastroenteritis and gastritis both involve inflammation of the mucous membranes of the GI tract. Symptoms of gastroenteritis and gastritis include nausea, vomiting, diarrhea, and abdominal pain. Acute gastroenteritis and gastritis are major causes of emergency room visits, particularly for pediatrics. If approved, RHB-102 (Bekinda®) could potentially decrease the number of emergency room visits for patients suffering from acute gastroenteritis and gastritis by offering them an effective and long-lasting treatment, which can be taken in the comfort of their home.

Market and Competition

A single dose of RHB-102 (Bekinda®) is intended to treat nausea and vomiting over a time window of approximately 24 hours. If approved for such use, this would be potentially advantageous for acute gastroenteritis and gastritis patients as it could help eliminate the need to take additional drugs (tablets) during the day or receiving intravenously administered drugs.

If RHB-102 (Bekinda®) is approved for the treatment of acute gastroenteritis and gastritis, it could potentially hold substantial advantages over existing treatments. If approved, RHB-102 (Bekinda®) could be prescribed by primary care physicians to patients early on, potentially preventing emergency room visits, dehydration and the need to provide IV fluids. There are an estimated 179 million cases of gastroenteritis in the U.S. annually (Scallan E *et al.* 2011).

To the best of our knowledge, there are no other 5-HT3 serotonin receptor inhibitors indicated or in the advanced clinical stage of development in the U.S. for this indication. Patients presenting at hospitals with gastroenteritis and gastritis are often treated primarily in IV administration with antiemetic drugs not indicated or approved for this condition, off-label, including 5-HT3 serotonin receptor inhibitors. If approved, RHB-102 (Bekinda®) will compete with several prescription and OTC anti-emetic drugs, including but not limited to, dimenhydrinate, Nauzene®, and Emetrol®, as well as off-label use of ondansetron and other 5-HT3 inhibitors.

We may also be exposed to potentially competitive products which may be under development to treat acute gastroenteritis. To the best of our knowledge, a product that potentially directly competes with RHB-102 (Bekinda®) is EUR-1025 for controlled release of ondansetron, based on a different technology of controlled release originally developed by Eurand N.V. (now owned by Adare Pharmaceuticals, Inc.) and which completed two pivotal pharmacokinetic studies intended to establish the bioequivalence of EUR-1025 versus Zofran® (ondansetron hydrochloride). To the best of our knowledge, EUR-1025 was being developed for the indication of postoperative-induced nausea and vomiting, for which Zofran® and generic ondansetron were already approved. To the best of our knowledge, there has not been further clinical development of EUR-1025 since the completion of the above-mentioned pharmacokinetic studies.

Clinical Development

In June 2017, we announced positive top-line results from the randomized, double-blind, placebo-controlled Phase 3 study (the "GUARD study") with RHB-102 (Bekinda®) 24 mg for acute gastroenteritis and gastritis. The study successfully met its primary endpoint and RHB-102 (Bekinda®) 24 mg was found to be safe and well tolerated in this indication. The GUARD study evaluated the efficacy and safety of RHB-102 (Bekinda®) 24 mg in treating acute gastroenteritis and gastritis in 321 adults and children over the age of 12. The primary endpoint of the study was the proportion of patients without further vomiting, without rescue medication, and who were not given intravenous hydration from 30 minutes post first dose of the study drug until 24 hours post-dose, compared to placebo. In September 2017, we met with the FDA to discuss the study results and the clinical and regulatory path toward potential marketing approval of RHB-102 (Bekinda®) 24 mg in the U.S. Following the guidance provided at the meeting and additional guidance provided thereafter, we are currently advancing preparations toward a confirmatory Phase 3 study to support a potential NDA with RHB-102 (Bekinda®) 24 mg for acute gastroenteritis and gastritis.

Final results from the GUARD study showed improvement to the primary efficacy outcome by 21% in the ITT population; 65.6% of RHB-102 (Bekinda®) treated patients as compared to 54.3% of placebo patients (p=0.04; n=192 in the RHB-102 (Bekinda®) group and n=129 in the placebo group). In the Per Protocol (PP) population, which included patients who met all protocol entry criteria and for which the diagnosis of gastroenteritis was confirmed (n=177 in the RHB-102 (Bekinda®) group and n=122 in the placebo group), RHB-102 (Bekinda®) improved the efficacy outcome by 27%; 69.5% of patients in the RHB-102 (Bekinda®) group vs. 54.9% in the placebo group, (p=0.01). An imbalance in baseline nausea was noted, with worse nausea in the RHB-102 (Bekinda®) treated group. In a post hoc analysis, when results were adjusted for baseline nausea, the p-value for the ITT population was 0.0152, and for the PP population was 0.0037. RHB-102 (Bekinda®) 24 mg was also shown to be safe and well tolerated; electrocardiogram results showed no adverse changes with treatment. The benefit observed with RHB-102 (Bekinda®) is evident across the spectrum of severity of nausea at baseline, including in patients with very severe nausea, suggesting that the drug works regardless of the initial severity of gastroenteritis.

The lead investigator for the Phase 3 study was Dr. Robert A. Silverman, MD, MS, Associate Professor at the Hofstra North Shore-LIJ School of Medicine and an emergency medicine specialist.

In September 2019, we had a follow-up meeting with the FDA regarding our efforts to design a study acceptable to the agency to seek the FDA's approval for pediatric labeling for RHB-102 (Bekinda®), as required by the FDA pursuant to the Pediatric Research Equity Act. The September 2019 meeting provided further clarity on the designs of the pediatric studies required by FDA, but the details have not yet been finalized.

The following chart summarizes the clinical trial history and status of RHB-102 (Bekinda®) for gastroenteritis and gastritis:

Clinical trial name	Development phase of the clinical trial	Purpose of the clinical trial	Clinical trial site	Planned number of subjects of the trial	Nature and status of the trial	Schedule
GUARD Study	Phase 3	Randomized double-blind placebo-controlled Phase 3 study in acute gastroenteritis and gastritis	21 sites in the U.S.	321	Evaluated the safety and efficacy of RHB-102 (Bekinda®) in acute gastroenteritis and gastritis	Completed 2017
TBD	Confirmatory Phase 3	Support a potential NDA with RHB-102 (Bekinda®) 24 mg for acute gastroenteritis and gastritis	TBD	TBD	TBD	TBD

We cannot predict with certainty our development costs, and such costs may be subject to changes. See "Item 3. Key Information – D. Risk Factors – Risks Related to Our Financial Condition and Capital Requirements."

Irritable Bowel Syndrome with Diarrhea (IBS-D)

Irritable bowel syndrome (IBS) is a multifactorial disorder marked by recurrent abdominal pain or discomfort and altered bowel function. According to the Mayo Clinic, certain factors that alter GI function can contribute to IBS symptoms, including stress, prior gastroenteritis, and changes in the gut microbiome, bile acids and short-chain fatty acids, which may stimulate 5-HT3 serotonin release and increase colonic permeability and motility.

In preliminary studies, ondansetron has demonstrated activity in IBS-D (Garsed K, Chernova J, Hastings M, et al. Gut Published Online First December 12, 2013). Unlike alosetron (a currently approved 5-HT3 antagonist in IBS-D), ondansetron has not been noted to cause ischemic colitis (FDA labeling for Lotronex® (alosetron), 2010; FDA labeling for Zofran® (ondansetron), 2014).

In light of the activity of ondansetron demonstrated in the preliminary studies described above, and because of its extended-release properties and once-daily dosing, we believe RHB-102 (Bekinda®) is a promising candidate for the treatment of IBS-D.

Market and Competition

IBS is one of the most common GI disorders. According to GlobalData, it is estimated that there were over 74 million diagnosed cases of IBS in the 16 major pharmaceutical markets in 2021 (age >= 18). Of the three subtypes of IBS, IBS-D is the most prevalent diagnosed subtype according to Pimentel M (Am J Manag Care, 2018), accounting for 40% of the patient population.

To the best of our knowledge, there is one other 5-HT3 serotonin receptor inhibitor indicated for this indication in the U.S. – alosetron (currently marketed under the brand name Lotronex® by Sebela Pharmaceuticals and generic versions marketed by other companies). However, alosetron is approved only for the treatment of IBS in women with severe chronic IBS-D and its indication is restricted to those patients for whom the benefit-to-risk balance is most favorable due to infrequent, but severe, adverse reactions. The active ingredient in RHB-102 (Bekinda®), ondansetron, is approved by the U.S. FDA as an oncology support antiemetic and has a good safety profile. Therefore, we believe that RHB-102 (Bekinda®), if approved for the treatment of IBS-D in the U.S., may provide improved safety while maintaining efficacy and has the potential to be a preferred 5-HT3 serotonin receptor inhibitor treatment for patients suffering from IBS-D. Ramosetron, another 5-HT3 serotonin receptor inhibitor (marketed under the brand name Irribow® by Astellas Pharma Inc. and generic versions marketed by other companies), is marketed for the treatment of IBS-D and for chemotherapy-induced nausea and vomiting in Japan, South Korea, China and India, and for and postoperative nausea and vomiting in South Korea and India. To the best of our knowledge, there is currently no clinical development of ramosetron for marketing approval in the U.S. for any indication.

If approved, RHB-102 (Bekinda®) will compete with several prescription drugs indicated for IBS-D, including but not limited to Xifaxan® (rifaximin), marketed in the U.S. by Bausch Health, and Viberzi® (eluxadoline), marketed in the U.S. by Allergan plc., as well as additional prescription drugs, generic drugs, and over-the-counter products indicated for IBS-D or for symptomatic relief of diarrhea and pain.

In addition, there are currently additional drug candidates in development by other companies for the treatment of IBS-D in the U.S.

Clinical Development

In January 2018, we announced positive final results from the Phase 2 clinical study of RHB-102 (Bekinda®) 12 mg for the treatment of IBS-D. The randomized, double-blind, placebo-controlled Phase 2 study evaluated the efficacy and safety of RHB-102 (Bekinda®) 12 mg in 126 subjects over 18 years old at 16 clinical sites in the U.S. The study successfully met its primary endpoint, improving the primary efficacy outcome of stool consistency.

RHB-102 (Bekinda®) was also shown to be safe and well tolerated in this indication. No serious adverse events or new or unexpected safety issues were noted in the study. In September 2018, we announced that we concluded a positive End-of-

Phase 2 Type B meeting with the FDA discussing the clinical and regulatory pathway toward potential FDA approval of RHB-102 (Bekinda®) for the treatment of IBS-D. We are currently finalizing the design of two pivotal Phase 3 studies with RHB-102 (Bekinda®) for the treatment of IBS-D.

The primary endpoint of the trial was the proportion of patients in each treatment group with response in stool consistency on study drug as compared to baseline. Response was defined as per FDA guidelines for the indication. Additional endpoints were analyzed including:

- proportion of patients in each treatment group who are pain responders, per FDA guidance definition;
- proportion of patients in each treatment group who are overall responders, per FDA guidance definition; and
- differences between treatment groups in:
  - abdominal pain
  - abdominal discomfort
  - frequency of defecation
  - incidence and severity of adverse events.

The RHB-102 (Bekinda®)12 mg Phase 2 study successfully met its primary endpoint, improving the primary efficacy outcome of stool consistency response (in accordance with the FDA guidance definition) by an absolute difference of 20.7%, with 56.0% responders of subjects treated with RHB-102 (Bekinda®) (n=75) vs. 35.3% responders of the placebo subjects (n=51) (p=0.036). While not powered for statistical significance of the secondary efficacy endpoints, the study suggested clinically meaningful improvement in both secondary efficacy endpoints of abdominal pain response and overall response (combined stool consistency and abdominal pain response). Final results from the Phase 2 study demonstrated that RHB-102 (Bekinda®) 12 mg improved the overall worst abdominal pain response rate by 11.5% vs. placebo (50.7% with RHB-102 (Bekinda®) 12 mg (n=75) vs. 39.2% with placebo (n=51); (p=0.278)) and the overall response improved by an absolute difference of 14.5% in favor of the RHB-102 (Bekinda®) 12 mg arm (40.0% with RHB-102 (Bekinda®) 12 mg (n=75) vs. 25.5% with placebo (n=51); (p=0.135)).

RHB-102 (Bekinda®) 12 mg was also shown to be safe and well tolerated. No serious adverse events or new or unexpected safety issues were noted in the study. In September 2018, we announced that we concluded a positive End-of-Phase 2/Pre-Phase 3 (Type B) meeting with the FDA discussing the clinical and regulatory pathway toward potential FDA approval of RHB-102 (Bekinda®) 12 mg for the treatment of IBS-D. We plan to finalize the design of two pivotal Phase 3 studies with RHB-102 (Bekinda®) for the treatment of IBS-D.

We have initiated formulation work to formulate RHB-102 at lower dosages to help support planned pediatric studies. In December 2019, we received confirmation from the FDA that it has agreed with our Initial Pediatric Study Plan (iPSP).

The following chart summarizes the clinical trial history and status of RHB-102 (Bekinda®) for IBS-D:

Clinical trial name	Development phase of the clinical trial	Purpose of the clinical trial	Clinical trial site	Planned number of subjects of the trial	Nature and status of the trial	Schedule
-	Phase 2	Randomized double-blind placebo-controlled Phase 2 study in IBS-D	16 sites in the U.S.	126	Evaluating the safety and efficacy of RHB-102 (Bekinda®) 12 mg in IBS-D	Completed 2018
TBD	Phase 3	Randomized double-blind placebo-controlled Phase 3 study in IBS-D	TBD	TBD	TBD	TBD

We cannot predict with certainty our development costs and such costs may be subject to change. See “Item 3. Key Information – D. Risk Factors – Risks Related to Our Financial Condition and Capital Requirements.”

RHB-106

RHB-106 is an investigational tablet intended for the preparation and cleansing of the GI tract prior to the performance of abdominal procedures, including diagnostic tests such as colonoscopy, barium enema or virtual colonoscopy, as well as surgical interventions, such as a laparotomy.

As noted above, we acquired the rights to RHB-106 pursuant to an agreement with Giaconda Limited. See "Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – Acquisition of Talicia®, RHB-104, and RHB-106."

In December 2019, we provided a notice of termination of the worldwide exclusive license agreement we had entered into on February 27, 2014, with Salix Pharmaceuticals, Ltd. (Salix, which was later acquired by Valeant Pharmaceuticals International, Inc. ("Valeant"), and subsequently renamed Bausch Health Companies Inc.). As a result of the termination of the Salix licensing agreement, we regained the exclusive worldwide rights to the RHB-106 encapsulated formulation for bowel preparation.

Market and Competition

It is estimated that approximately 19 million colonoscopies are performed annually in the U.S., according to a 2018 iDATA research report.

If approved, RHB-106 will compete with several products in the U.S., including but not limited prescription products such as PrepoPik® (marketed by Ferring Pharmaceuticals), Clenpiq ® (marketed by Ferring Pharmaceuticals), Suprep ® and Sutab ® (marketed Sebela Pharmaceuticals), OsmoPrep®, MoviPrep® and Plenvu ® (marketed by Bausch Health). There are additional bowel preparations in development by other companies.

To the best of our knowledge, the main competitors of RHB-106 are bowel cleansing products based on polyethylene glycol (PEG 3350). These products are delivered in the form of a water-soluble powder and require users to drink between 2-4 liters of solution before the performance of the gastroenterological procedure. In addition to the need to drink considerable amounts of a solution, a common side effect that raises difficulties with users is the accompanying harsh and unpleasant taste, leading to potential difficulties with patient compliance. RHB-106 offers the potential for improved patient compliance because it is tasteless and eliminates the need for drinking several liters of the ill-flavored electrolyte solution. RHB-106 also potentially has an advantage compared to currently available tablet products in the field in that it does not contain sodium phosphate, an active ingredient linked with a risk of nephrotoxicity.

Products administered in the form of tablets or capsules that were released on the market in the U.S., such as OsmoPrep®, are based on a chemical substance called sodium phosphate. In December 2008, the FDA published a severe warning against the use of these products due to rare but severe side effects linked to kidney damage. As a consequence of this development, the FDA required in 2008 that oral sodium phosphate products carry a severe warning (black box label). In November 2020, the FDA approved Sutab®, a new drug product administered in tablet form which does not contain sodium phosphate.

The potential advantage of RHB-106 over the current competitor products of the PEG 3350 type, MoviPrep®, as well as over products such as PicoPrep®, is that it is administered in an oral tablet, permits the patient to drink any clear liquid with the product and spares the patient the exposure to the unpleasant taste that may accompany these products. RHB-106 also does not fall under the black box warning against nephrotoxicity issued by the FDA in December 2008 with respect to currently marketed sodium phosphate capsule preparations.

Clinical Development

The following chart summarizes the clinical trial history and status of RHB-106:

Clinical trial name	Development phase of the clinical trial	Purpose of the clinical trial	Clinical site	Number of subjects of the trial	Nature and status of the trial	Performance schedule
-	Phase 2a	Comparison of the product's effectiveness and safety with an existing product	Center for Digestive Disease, Australia	60	Completed	Completed in 2005

Acquisition, Commercialization and License Agreements

Acquisition of Talicia®, RHB-104, and RHB-106

On August 11, 2010, we entered into an asset purchase agreement with Giaconda Limited, a publicly-traded Australian company, pursuant to which Giaconda Limited transferred all of its patents, tangible assets, production files, regulatory approvals and other data related to the "Heliconda", "Myoconda" and "Picoconda" products to us. We renamed these products Talicia®, RHB-104, and RHB-106, respectively. Giaconda Limited further transferred to us products in process, product samples and raw materials, as well as certain rights of first refusal with respect to intellectual property in relation to digestive condition treatments. The agreement excluded the transfer of the rights to two products of Giaconda Limited that are not related to Talicia®, RHB-104, and RHB-106. However, to the extent that the intellectual property associated with these two other products may be required for the research, development, manufacture, registration, import/export, use, commercialization, distribution, sale or offer for sale of any of Talicia®, RHB-104, and RHB-106, Giaconda Limited granted us an exclusive worldwide assignable right to such intellectual property for such purposes. The closing of this transaction occurred on August 26, 2010.

We paid Giaconda Limited in consideration for the assets purchased by us an initial amount of $500,000. We and Giaconda Limited also agreed that, until the expiration of the last patent transferred to us with respect to each product, we will pay to Giaconda Limited 7% of net sales from the sale of the relevant product/s by us and 20% of the consideration (including royalties received by us) from sublicensees, in each case, only after we recoup the amounts and expenses exceeding an approved budget.

Under the agreement, Giaconda Limited agreed that neither it, nor the developer of the products, nor any of their respective affiliates may compete with us or assist others to compete with us with respect to the products and acquired technology for the period provided for in the agreement.

The agreement provides that, should we elect not to proceed with the registration proceedings, or the maintenance of any patent transferred to us, we will notify Giaconda Limited and Giaconda Limited will have the right to proceed with the registration, maintenance, development and commercialization of such patent at its expense. Should Giaconda Limited exercise such right, it will be entitled to all amounts received in connection with sales relating to such patent.

The agreement also requires us to make a good faith, continuous and commercially reasonable effort to allocate appropriate financial resources to prepare, initiate and complete the clinical development of the products (with the exception of Picoconda by virtue of the Salix license agreement dated February 27, 2014) and file an application for regulatory marketing approval in accordance with industry standards. Development failures, negative regulatory decisions, or other reasons beyond our control will not constitute a breach of this obligation. Should we breach this obligation with respect to the development of any of the products and fail to cure the breach within 90 days from the date that Giaconda Limited sends us a default notice, Giaconda Limited may buy back all of the intellectual property rights with respect to such product for the original purchase price, plus the related development costs incurred by us through the date of the buy-back.

In connection with the license agreement with Salix (later acquired by Bausch Health), dated February 27, 2014, described below, we amended the asset purchase agreement and related agreements by excluding from the non-compete undertakings of Giaconda Limited and certain of its affiliate products, technology, and related activities in the purgative field and

excluded from such non-compete undertakings certain of Giaconda Limited's affiliates. Subsequently, we recognized revenues in 2014 and paid Giaconda Limited an additional amount of $1 million. On February 27, 2014, we amended the asset purchase agreement with Giaconda Limited to cancel the buyback right and agreed that we would pay Giaconda Limited 20% of all amounts received by us from Bausch Health under the license agreement, without first recouping amounts and expenses and notwithstanding the expiration of any relevant patents.

License Agreement for Movantik®

On February 23, 2020, we entered into the AstraZeneca License Agreement pursuant to which AstraZeneca granted us (by way of sublicense) exclusive, worldwide (excluding Europe, Canada and Israel) development and commercialization rights to Movantik® (naloxegol) and certain associated products. In October 2020, as part of an amendment to the AstraZeneca License Agreement, we also gained the rights to Movantik® in Israel.

Under the terms of the AstraZeneca License Agreement, as amended to date, we agreed to pay AstraZeneca an upfront payment of $52.5 million and an additional $16 million in gradual payments starting in March 2021 and ending in December 2022. In addition, we have assumed responsibility for certain milestone and royalty payments payable to Nektar depending on net sales (as defined in the AstraZeneca License Agreement) for the licensed product.

AstraZeneca transferred its co-commercialization agreement with Daiichi Sankyo, Inc. for Movantik® to us. In August 2020, we announced an amendment to the agreement with Daiichi Sankyo, Inc. which enables us to exercise full control over brand strategy and commercialization for Movantik® in the US, while also increasing capital. As part of the agreement, we will bear all responsibilities and costs for commercializing Movantik® in the U.S. During the term of the agreement, we will pay Daiichi Sankyo a mid-teen royalty rate on net sales of Movantik® in the U.S., in addition to three lump-sum payments in the amount of $5.1 million paid in January 2022, and $5 million to be paid in each of July 2022 and 2023. The term of this agreement shall continue until the end of the first calendar year during which annual net sales of Movantik® fall below the amount provided for in the agreement.

AstraZeneca granted us an exclusive, sublicensable license under AstraZeneca's patents and know-how to develop, sell and otherwise exploit Movantik® in the relevant territories under which RedHill was granted a license. We will take over and control the current consolidated litigation relating to ANDA filed under the Hatch-Waxman Act. We will bear all costs associated with the research, development, and commercialization of Movantik® in our territory.

The AstraZeneca License Agreement includes various representations, warranties, covenants, indemnities and other provisions customary for transactions of this nature. The AstraZeneca License Agreement also provides for the right of termination for either party in the event of an uncured material breach committed by the other party.

The foregoing summary is qualified in its entirety by reference to the AstraZeneca License Agreement, which is filed as an exhibit hereto.

Supply Agreement for Movantik®

On February 23, 2020, we entered into a supply agreement with AstraZeneca, pursuant to which AstraZeneca is assisting us with certain technology transfers to enable us to manufacture Movantik® through our own supply chain (including through third parties) and, pending completion of such technology transfers, supply us with our requirements for Movantik® on an interim basis. The agreement also provides for AstraZeneca to supply us with our requirements of related API for an agreed period, subject to the earlier depletion of AstraZeneca's API inventories. All products supplied by AstraZeneca under the agreement are required to have been manufactured in accordance with, and comply in all material respects with, certain standards.

The agreement will expire in accordance with its terms once the supply terms for Movantik® and associated API have each expired or terminated, and will automatically terminate if, and to the extent that, the AstraZeneca License Agreement is terminated. The agreement also provides for a right of termination for either party in the event of an uncured material breach committed by the other party, and we also have certain additional rights to terminate the agreement.

The agreement includes various representations, warranties, covenants, indemnities, limitations of liability and other provisions.

The foregoing summary is qualified in its entirety by reference to the supply agreement, which is filed as an exhibit hereto.

Exclusive License Agreement for Aemcolo®

On October 17, 2019, we entered into a strategic collaboration with Cosmo, which includes an exclusive license agreement for the U.S. rights to Aemcolo® and a simultaneous private investment by Cosmo of $36.3 million in the Company at $7.00 per ADS, with a 180-day transfer restriction.

Under the terms of the license agreement, Cosmo granted us the exclusive rights to commercialize Aemcolo® in the U.S. for travelers' diarrhea and agreed to act as the exclusive supplier of Aemcolo®. The license agreement also grants us certain rights related to the potential development of additional indications for Aemcolo®, as well as arrangements related to other pipeline therapeutic candidates of Cosmo. There are two pediatric studies that are required to be completed to satisfy the PREA requirements and also with required milestone dates. See "Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – Our Approved and Commercial Products in the U.S. – Aemcolo® – Regulatory Status."

Concurrently with the simultaneous private investment by Cosmo, as part of the license agreement we issued to a wholly-owned subsidiary of Cosmo 1,714,286 ADSs at an agreed value of $12.0 million, as an upfront payment for the rights granted under the license, corresponding to a price per ADS of $7.00, with a 180-day transfer restriction. These ADSs are in addition to the ADSs issued to Cosmo as part of the $36.3 million investment discussed above. In addition, we agreed to pay Cosmo a royalty percentage in the high twenties on net sales generated from the commercialization of Aemcolo® in the U.S. The license agreement further provides for potential regulatory and commercial milestone payments to Cosmo totaling up to $100.0 million, which, based on our current expectations and assumptions, are not currently expected to be made in the next 12 months. In connection with the subscription agreement, Cosmo nominated for appointment one member to our board of directors. Alessandro Della Chà, who was nominated by Cosmo to our board of directors, resigned from the board of directors in November 2021 for personal reasons. Upon Mr. Della Chà's resignation, Cosmo waived its right to nominate Mr. Della Chà's replacement to our board of directors.

The agreement includes various representations, warranties, covenants, indemnities, limitations of liability and other provisions. Cosmo contacted the Company to request we return the U.S. rights to Aemcolo®, and in December 2021, the parties signed an amendment to the Exclusive License Agreement providing that either party may terminate the agreement upon advance notice at any time.

On January 11, 2021, Cosmo announced that it had successfully completed a Phase 2 Proof of Concept ("POC") clinical trial of Rifamycin-MMX 600mg in patients with diarrhea-predominant irritable bowel syndrome ("IBS-D"). As part of our Exclusive License Agreement with Cosmo for the U.S. rights to Aemcolo® (rifamycin), we maintain certain rights, including a right of first refusal, in relation to Rifamycin-MMX 600mg in the U.S. Cosmo reported that results of the Phase 2 POC study show the achievement of statistical significance in all the study populations (intent-to-treat, full analysis study, modified full analysis study and per protocol) for the composite primary endpoint (substantial pain and diarrhea decrease) [OR 3.26 (1.39 - 7.67); p-value 0.0066] and for most secondary endpoints such as adequate relief of IBS-related symptoms [OR 2.18 (1.12 - 4.26); p-value 0.0227] and IBS-related bloating at the end of treatment period [OR 2.13 (1.11 - 4.07); p-value 0.0223].

The foregoing summary is qualified in its entirety by reference to the Exclusive License Agreement, as amended, with Cosmo, which is filed as an exhibit hereto.

License Agreement for opaganib

On March 30, 2015, we entered into an exclusive license agreement with Apogee, a privately-held biotech company located in Hummelstown, Pennsylvania, U.S., under which Apogee granted us the exclusive, worldwide development and commercialization rights to ABC294640 which we then renamed to Yeliva® and received an international non-proprietary

name, opaganib, in 2018) and additional intellectual property rights. Opaganib is a proprietary, first-in-class, orally-administered SK2 inhibitor, with anti-inflammatory and anti-cancer activities, targeting multiple oncology, inflammatory and GI indications. Under the terms of the agreement, as amended, we agreed to pay Apogee initial milestone payments of $3 million. In addition, we undertook to pay up to an additional $2 million in potential development milestone payments and potential tiered royalties starting in the low double-digits. Such potential royalties are due until the later of: (i) the expiration of the last to expire licensed patent that covers the product in the relevant country; and (ii) the expiration of regulatory exclusivity in the relevant country. Through December 31, 2020, we paid Apogee the initial amount of $3 million. The license agreement will stay in effect as of its effective date unless terminated earlier as described in the agreement. We are entitled to terminate the agreement at any time upon 30 days prior written notice to Apogee. The agreement also provides for the right of termination for each party in the event of a material breach committed by the other party.

License Agreement for RHB-107 (upamostat; formerly Mesupron)

On June 30, 2014, we entered into an exclusive license agreement with Wilex AG (which later changed its name to Heidelberg Pharma AG, "Heidelberg"), a German biopharmaceutical company focused on oncology, under which Heidelberg granted us the exclusive worldwide (excluding China, Hong Kong, Taiwan, and Macao) development and commercialization rights for all indications to RHB-107.

In consideration for the license, we paid Heidelberg an upfront payment of $1 million. We have agreed to pay Heidelberg tiered royalties on net revenues, ranging from mid-teens up to 30%.

The license agreement will stay in effect as long as we are required to make royalty payments. We are entitled to terminate the agreement at any time on 30 days written notice to Heidelberg. The agreement also provides the right of termination for each party in the event of a breach.

Limited Period Right of First Offer for License of opaganib, RHB-107 and Talicia® in Various Countries

In November 2021, we entered into a strategic transaction with Kukbo, a South Korean corporation, for the sale of our ADSs in a private placement of up to $10 million at a 20% premium to the prior 30 trading days' volume weighted average price. See "Item 5. B – Liquidity and Capital Resources". Under the terms of the agreement, we agreed to grant Kukbo a right of first offer, for a period of six months, for a license with respect to one or more of opaganib, RHB-107 and Talicia®, for one or more of the territories of South Korea, Japan, Indonesia, Vietnam, Thailand and Malaysia. Kukbo has the right to elect not to purchase the ADSs in the second tranche if no such license agreement is executed within six months of the closing of the first tranche. The right of first offer has been extended as part of the new license agreement with Kukbo until end of October 2022.

License Agreement with Kukbo

In March 2022, we entered into an exclusive license agreement with Kukbo. Under the terms of the exclusive license agreement, we will receive an upfront payment of $1.5 million and are eligible for up to $5.6 million in milestone payments as well as low double-digit royalties on net sales of oral opaganib in South Korea. Kukbo will receive the exclusive rights to commercialize opaganib in South Korea for COVID-19. The partnership with Kukbo also includes a right of first offer for our late-stage clinical assets, opaganib, RHB-107 and Talicia®, for one or more of the territories of South Korea, Japan, Indonesia, Vietnam, Thailand and Malaysia.

License Agreement with Gaelan Medical

On December 20, 2021, we entered into an exclusive license agreement with Gaelan Medical, a wholly owned subsidiary of the Ghassan Aboud Group (GAG), for Talicia®, in the UAE. Under the terms of the agreement, we are expected to receive an upfront payment of $2 million and are eligible for additional milestone payments as well as tiered royalties up to mid-teens on net sales of Talicia® in the UAE. Gaelan Medical will receive the exclusive rights to commercialize Talicia® in the UAE the later of (i) fifteen (15) years following the first commercial sale of Talicia® in the UAE and (ii) the expiration of the Regulatory Exclusivity in the UAE, if obtained. Gaelan Medical will also receive the right of first

refusal to commercialize Talicia in the Gulf Cooperation Council region (Saudi Arabia, Kuwait, Qatar, Bahrain and Oman) for a pre-determined period.

Additional License Agreement related to MAP diagnostic test for RHB-104

On December 27, 2014, we entered into a license agreement with the University of Minnesota (UoM) pursuant to which we were granted an exclusive license for all indications and medical uses to a patent-protected designation of certain DNA sequencing.

Licensing and Manufacturing Terms with Cosmo Pharmaceuticals

On August 12, 2020, we entered into a binding term sheet with Cosmo for an exclusive licensing and manufacturing agreement for multiple products. Since then, we and Cosmo have renegotiated the scope and terms of the collaboration, and in lieu of the terms of the term-sheet, we have entered into three manufacturing agreements with respect to Movantik®, RHB-204 and opaganib.

COVID-19 Impact on our Business

In an effort to contain and mitigate the spread of COVID-19, many countries around the world, including the U.S. and Israel, have imposed quarantines and restrictions on travel and mass gatherings to slow the spread of the virus and closed non-essential businesses and offices, and as of the date of this prospectus supplement, many local jurisdictions continue to have such restrictions in place. As many local jurisdictions continue to have such restrictions in place, our ability to continue to operate our business may also be limited. Such events may result in a period of office closures, business, supply and drug product manufacturing disruption, and in reduced operations, any of which could materially affect our business, financial condition and results of operations. Moreover, the COVID-19 pandemic may further divert the attention and efforts of the medical community to coping with COVID-19 and disrupt the marketplace in which we operate and may have a material adverse effect on our operations. In addition, SARS-CoV-2 infections of our employees may cause disruption to our operations.

We have put in place a comprehensive alternative commercial strategy to support our growth initiatives while adhering to government and health regulatory guidelines. To date, there have been no significant disruptions to our supply chain, and we currently have sufficient supply of commercial products on hand to meet U.S. commercial demand. However, we have experienced decreased commercial activities which have affected the sales of our commercial products due to slower initiation of certain promotional activities associated with a significant decrease in in-clinic patient visits, tests and treatments and the impact on our sales force's ability to engage with healthcare providers in an in-person setting, cancellation of events such as industry conferences and limited local and international travel. The ability to successfully commercialize Talicia® depends on in-clinic patient visits and the availability of diagnostics, both of which has have been negatively affected by the pandemic. In addition, the COVID-19 pandemic has adversely affected and may continue to adversely affect our clinical and pre-clinical trials, including our ability to initiate and complete our clinical and pre-clinical trials within the anticipated timelines, and delays or difficulties in enrolling patients in our clinical trials and recruiting clinical site investigators and clinical site staff. For example, the enrollment of patients for our Phase 3 study with RHB-204 in first-line pulmonary NTM infections has been slow, which has slowed the progress of the study. In addition, we may be unable to meet the timelines and milestones established for the contemplated postmarketing studies we are required to conduct for Aemcolo®, in which case we could be subject to FDA enforcement actions and civil monetary penalties, among others, unless the FDA agrees to an extension of the timelines and milestones. Moreover, the significant decrease in travel has significantly reduced the demand and sales of Aemcolo® for travelers' diarrhea.

Assessment of the complete extent of the impact of COVID-19 on our results will depend on future developments, which are highly uncertain and cannot be predicted, including new information that may emerge concerning the severity of COVID-19 and the actions to contain COVID-19 or treat its impact, among others. The continuation of the COVID-19 pandemic could materially disrupt our business and operations and have an adverse effect on the global markets and global economy generally, including on the availability and cost of employees, resources, materials, manufacturing and delivery efforts, and other aspects of the economy.

Expanded Access Program (EAP)

We have adopted an Expanded Access Program ("EAP"), allowing patients with life-threatening diseases potential access to our investigational new drugs that have not yet received regulatory marketing approval. Expanded access (sometimes referred to as "compassionate use") is possible outside of our clinical trials, under certain eligibility criteria, when a certain investigational new drug is needed to treat a life-threatening condition and when there is some clinical evidence suggesting that the drug might be effective for that condition. Patients who qualify for our EAP do not meet the eligibility criteria or are incapable of participating in our clinical trials for such therapeutic candidate or there is no clinical trial accessible to such patients. Following the adoption of the program, we continue to receive patient requests to obtain access to our investigational drugs. Subject to the evaluation of eligibility and all other necessary regulatory, reporting and other conditions and approvals required in all relevant jurisdictions, we provide certain patients with an investigational new drug under the EAP.

Under a compassionate use program, patients with severe COVID-19 (as classified by the WHO ordinal scale) were treated with opaganib in a leading hospital in Israel. Data from the treatment of these first patients with severe COVID-19 with opaganib have been published. We believe an analysis of treatment outcomes suggests substantial benefit to patients treated with opaganib under compassionate use in both clinical outcomes and inflammatory markers as compared to a retrospective matched case-control group from the same hospital. All patients in the opaganib-treated group were discharged from hospital on room air without requiring intubation and mechanical ventilation, whereas 33% of the matched case-control group required intubation and mechanical ventilation. Median time to weaning from high-flow nasal cannula was reduced to 10 days in the opaganib-treated group, as compared to 15 days in the matched case-control group.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our technology and therapeutic candidates, its therapeutic applications, and related technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions, and improvements that are important to the development of our business. We also rely on our trade secrets, know-how, and continuing technological innovation to develop and maintain our proprietary position. We vigorously defend our intellectual property to preserve our rights and gain the benefit of our technological investments.

Patents and Patent Applications

We have rights, either through assignment, asset purchase or in-licensing, to a total of approximately 450 issued patents and 150 patent applications. The patents and patent applications are registered in the U.S. and other key jurisdictions, the details of each family of patents being provided below. In addition, we have licensed rights to various platform technologies on a non-exclusive basis.

The patent positions of companies such as ours are generally uncertain and involve complex legal and factual questions. Our ability to maintain and solidify our proprietary position for our technology will depend on our success in obtaining effective claims and enforcing those claims once granted.

Movantik®

Following the closing of our in-license for Movantik®, we have in-licensed patents and trademarks from AstraZeneca AB as part of the AstraZeneca License Agreement. The Orange Book lists six U.S. patents, two of which are directed to the approved use for the treatment of opioid-induced constipation. However, the entire licensed patent portfolio consists of ten U.S. patents, one pending patent application, over fifty foreign patents and about a dozen pending foreign patent applications.

Talicia®

The patent portfolio protecting Talicia® currently includes six U.S. patents, one pending U.S. patent application, and over 20 foreign patents and patent applications. The patents currently provide patent protection through 2034. The Orange Book currently lists five U.S. patents.

Aemcolo®

This patent portfolio was in-licensed by us from Cosmo Technologies Ltd. as part of our license agreement for Aemcolo®. The U.S. patent portfolio consists of four issued patents and one pending patent application. The four issued patents protect the commercial product and its approved method of use. The Orange Book currently lists four U.S. patents.

RHB-104 – Inflammatory Bowel Disease

The patent portfolio protecting RHB-104 and its use in treating inflammatory bowel disease currently includes nine U.S. patents, , and 33 foreign patents and patent applications, providing patent protection through 2029.

We have also in-licensed U.S. Patent Nos. 7,074,559 and 7,867,704 from The University of Minnesota entitled "Mycobacterial Diagnostics." One U.S. patent will expire in 2022, and the other U.S. patent will expire in 2026. The acquired diagnostic technology is intended for the detection of *Mycobacterium avium subspecies paratuberculosis* (MAP) bacterium.

RHB-104 – Multiple Sclerosis ("MS")

The patent portfolio protecting the use of RHB-104 for treating relapsing-remitting multiple sclerosis includes one U.S. patent and over 20 foreign patents and patent applications, providing patent protection through 2032.

RHB-204 – Nontuberculous Mycobacterium (NTM) Infections

The patent portfolio protecting RHB-204 currently includes one U.S. patent, one pending U.S. patent application, one European patent application, and one pending Hong Kong application, providing protection through 2041. An international patent application, due to be converted into independent country-specific patent applications in 2022, is pending.

RHB-102 (Bekinda®) - Gastritis, Gastroenteritis and IBS-D

The patent portfolio protecting RHB-102 (Bekinda®) and its use currently includes three U.S. patents, two pending U.S. patent applications, and over 30 foreign patents and patent applications, providing patent protection through 2034.

RHB-106 - Bowel Preparation

The patent portfolio protecting RHB-106 and its use currently includes three issued U.S. patents, and 12 foreign patents and patent applications, providing patent protection through 2033.

Opaganib - Oncology, inflammatory and GI Indications

This patent portfolio was in-licensed by us from Apogee. Opaganib is a first-in-class, proprietary SK2 inhibitor, administered orally, with anti-cancer and anti-inflammatory activities, targeting a number of potential oncology, inflammatory and GI indications. These patents relate to sphingosine kinase inhibitors, pharmaceutical compositions, methods of preparing the inhibitors, methods of treating inflammatory diseases using the inhibitors, methods of treating cancer using the inhibitors, and methods for inhibiting sphingosine kinase.

The patent portfolio covering opaganib includes four U.S. patents and over eighteen foreign patents and patent applications, providing patent protection through 2028.

A new patent family seeking to protect the use of opaganib plus checkpoint inhibitors to treat cancer is pending in the US as well as 13 foreign jurisdictions. If patents are granted, it will provide protection for the combination treatment through 2040.

RHB-107 (upamostat; formerly Mesupron) – Oncology

The primary patent portfolio protecting the new chemical entity (WX-UK1), the pro-drug ("WX-671" or "RHB-107" or "upamostat"), formulations comprising upamostat, methods of synethesizing the compounds, and methods of using upamostat to treat cancer, was in-licensed by us from Wilex AG, now known as Heidelberg Pharma AG. RHB-107 is a first-in-class protease inhibitor administered by oral capsule. The portfolio includes fifteen issued U.S. patents and over sixty foreign patents and patent applications, providing patent protection through 2027.

Ebola

The patent portfolio covers RedHill's proprietary experimental therapy for the treatment of the Ebola virus disease. The portfolio consists of two U.S. patents, one pending U.S. patent application, five issued foreign patent applications and four pending international patents and patent applications.

SARS-CoV-2

This patent portfolio seeks covers the use of opaganib and RHB-107 for treating or preventing coronavirus infections. The portfolio currently consists of two issued U.S. patents, four pending U.S. patent applications and one pending PCT international patent application, providing patent protection through 2041.

RHB-108 – Combination Cancer Therapy

RedHill has also pursued patent protection in cancer therapy for various combination of drugs with different mechanisms of action which achieve synergistic effects. Currently, the portfolio includes three U.S. patents, one pending U.S. patent application, four issued foreign patent applications and six foreign pending patent applications.

Trademarks

Our principal trademarks, including RedHill, Redhill Biopharma, Talicia, Bekinda, Yeliva®, and their related logos, are registered with the United States Patent and Trademark Office. We have also filed registration applications for non-U.S. trademarks in other countries in which we do or plan to do business. Brand names appearing in this annual report are trademarks of RedHill Biopharma Ltd. except for:

- trademarks used or that may be or have been used under license by RedHill or its affiliates, such as Aemcolo®, a trademark of Cosmo Technologies Ltd.

- trademarks used or that may be or have been used under license by RedHill or its affiliates, such as Movantik®, a trademark of AstraZeneca AB.

Not all trademarks related to investigational agents have been authorized as of the date of this annual report by the relevant health authorities; for instance, the Bekinda® and Yeliva® trade names have not been approved by the FDA.

Government Regulations and Funding

Pharmaceutical companies are subject to extensive regulation by national, state and local agencies such as the FDA in the U.S., the Ministry of Health in Israel, or the EMA. The manufacture, clinical trials, distribution, marketing and sale of pharmaceutical products are subject to government regulation in the U.S. and various foreign countries. To manufacture both new therapeutic drug candidates for clinical trials and approved therapeutic drugs for sale and distribution in the U.S., we must follow the rules and regulations in accordance with current cGMP codified in 21 CFR 210 and 211. Additionally,

we are responsible for ensuring that the API in each therapeutic drug or therapeutic drug candidate is manufactured in accordance with ICH Q7 guidance that has been adopted by the FDA. Further, we are required to conduct clinical trials that present data indicating that our therapeutic drug candidates are safe and efficacious in accordance with the current good clinical practice and codified in 21 CFR 312. If we do not comply with applicable requirements, we may be fined, the government may refuse to approve our marketing applications or not allow us to manufacture or market our products, and we may be criminally prosecuted. We and our contract manufacturers and clinical research organizations may also be subject to regulations under other federal, state and local laws, including, but not limited to, the U.S. Occupational Safety and Health Act, the Resource Conservation and Recovery Act, the Clean Air Act and import, export and customs regulations as well as the laws and regulations of other countries. Further, the U.S. government has increased its enforcement activity regarding fraud and abuse and illegal marketing practices in the healthcare industry. As a result, pharmaceutical companies must ensure their compliance with the Foreign Corrupt Practices Act and federal healthcare fraud and abuse laws, including the False Claims Act.

These regulatory requirements impact our operations and differ in one country to another, so that securing the applicable regulatory approvals of one country does not imply the approval in another country. However, securing the approval of a more stringent body, *i.e.,* the FDA, may facilitate receiving the approval by a regulatory authority in a different country where the regulatory requirements are similar or less stringent. The approval procedures involve high costs and are manpower intensive, usually extend over many years and require highly skilled and professional resources.

FDA Approval Process for New Molecular Entities

Our therapeutic drug candidates are classified as New Molecular Entities. The steps required to be taken before therapeutic drug candidate may be marketed in the U.S. generally include:

- completion of preclinical laboratory and animal testing;
- the submission to the FDA of an investigational new drug, or IND, application which must be evaluated and found acceptable by the FDA before human clinical trials may commence;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug therapeutic candidate for its intended use; and
- the submission and approval of an NDA.

Clinical studies are conducted under protocols detailing, among other things, the objectives of the study, what types of patients may enter the study, schedules of tests and procedures, drugs, dosages, and length of study, as well as the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

In all the countries that are signatories of the Helsinki Declaration (including Israel), the prerequisite for conducting clinical trials (on human subjects) is securing the preliminary approval of the competent authorities of that country to conduct medical experiments on human subjects in compliance with the other principles established by the Helsinki Declaration.

The clinical testing of a therapeutic drug candidate generally is conducted in three sequential phases prior to approval, but the phases may overlap or be combined. However, safety information should be submitted before the initiation of a subsequent clinical phase. A fourth, or post-approval phase may include additional clinical studies. The phases are generally as follows:

Phase 1. In Phase 1 clinical studies, the therapeutic drug candidate is tested in a small number of healthy volunteers, though in cases where the therapeutic drug candidate may make the volunteer ill, clinical patients with the targeted condition may be used. These “dose-escalation” studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the therapeutic drug candidate in humans, side effects associated with increasing doses, and, in some cases, to gain early evidence on efficacy. The number of participants included in Phase 1 studies is generally in the range of 20 to 80.

Phase 2. In Phase 2 studies, in addition to safety, the sponsor evaluates the efficacy of the therapeutic drug candidate on targeted indications to determine dosage tolerance and optimal dosage and to identify possible adverse effects and safety

risks. Phase 2 studies typically are larger than Phase 1 but smaller than Phase 3 studies and may involve several hundred participants.

Phase 3. Phase 3 studies typically involve an expanded patient population at geographically-dispersed test sites and involve control groups taking a reference compound or a placebo (an inactive compound identical in appearance to the study compound). They are performed after preliminary evidence suggesting the effectiveness of the therapeutic candidate has been obtained and are designed to evaluate clinical safety and efficacy further, to establish the overall benefit-risk relationship of the therapeutic candidate and to provide an adequate basis for a potential product approval. Phase 3 studies usually involve several hundred to several thousand participants.

Phase 4. Phase 4 clinical trials are postmarketing studies designed to collect additional safety data as well as potentially expand a product indication. Postmarketing commitments may be required of, or agreed to by, a sponsor after the FDA has approved a therapeutic drug candidate for marketing. These studies are used to gain additional information from the treatment of patients in the intended therapeutic indication and to verify a clinical benefit in the case of drugs approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase 4 clinical trial requirement. These clinical trials are often referred to as Phase 4 post-approval or postmarketing commitments. Failure to promptly conduct Phase 4 clinical trials could result in the inability to deliver the product into interstate commerce, misbranding charges, and civil monetary penalties.

Clinical trials must be conducted in accordance with the FDA's GCP requirements. The FDA may order the temporary or permanent discontinuation of a clinical study at any time or impose other sanctions if it believes that the clinical study is not being conducted in accordance with FDA requirements or that the participants are being exposed to an unacceptable health risk. An institutional review board, or IRB, generally must approve the clinical trial design and patient informed consent at study sites that the IRB oversees and also may halt a study, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions. Additionally, some clinical studies are overseen by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board or committee. The FDA recommends that a data safety monitoring board should be used to perform regular interim analysis for long-term clinical studies where safety concerns may be unusually high. This group recommends whether or not a trial may move forward at designated checkpoints based on access to certain data from the study. The clinical study sponsor may also suspend or terminate a clinical trial based on evolving business objectives or competitive climate.

As a therapeutic candidate moves through the clinical testing phases, manufacturing processes are further defined, refined, controlled and validated. The level of control and validation required by the FDA would generally increase as clinical studies progress. We and the third-party manufacturers on which we rely for the manufacture of our therapeutic drugs and therapeutic drug candidates and their respective API are subject to requirements that drugs be manufactured, packaged and labeled in conformity with cGMP. In addition to our third-party API manufacturers, we are responsible for ensuring that our third-party excipient manufacturers conform to cGMP requirements. To comply with cGMP requirements, manufacturers must continue to spend time, money and effort to meet requirements relating to personnel, facilities, equipment, production and process, labeling and packaging, quality control, recordkeeping, and other requirements.

Assuming completion of all required testing in accordance with all applicable regulatory requirements, detailed information on the therapeutic candidate is submitted to the FDA in the form of an NDA, requesting approval to market the product for one or more indications, together with payment of a user fee, unless waived. An NDA includes all relevant data available from pertinent nonclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information on the chemistry, manufacture, control and proposed labeling, among other things. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the therapeutic candidate for its intended use to the satisfaction of the FDA.

If an NDA submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the Prescription Drug User Fee Act, or PDUFA, the FDA's goal is to complete its initial review and respond to the applicant within ten months of a completed submission for 90% of the submissions received, unless the application relates to an unmet medical need in a serious or life-threatening indication, in which case the goal may be within six months of a completed NDA submission. However, PDUFA goal dates are not legal mandates, and the FDA response may occur several months beyond

the original PDUFA goal date. Further, the review process and the target response date under PDUFA may be extended if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the NDA. The NDA review process can, accordingly, be very lengthy. During its review of an NDA, the FDA may refer the application to an advisory committee for review, evaluation, and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it typically follows such recommendations. Data from clinical studies are not always conclusive, and the FDA or any advisory committee it appoints may interpret data differently than the applicant.

After the FDA evaluates the NDA and conducts a pre-approval inspection of all manufacturing facilities where the drug therapeutic candidate or its API will be produced, it will either approve commercial marketing of the drug therapeutic candidate with prescribing information for specific indications or issue a complete response letter indicating that the application is not ready for approval and stating the conditions that must be met in order to secure approval of the NDA. If the complete response letter requires additional data and the applicant subsequently submits that data, the FDA nevertheless may ultimately decide that the NDA does not satisfy its criteria for approval. The FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategies, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct postmarketing testing. The FDA may also request a Phase 4 clinical trial to further assess and monitor the product's safety and efficacy after approval. Regulatory approval of products for serious or life-threatening indications may require that participants in clinical studies be followed for long periods to determine the overall survival benefit of the drug therapeutic candidate.

If the FDA approves one of our therapeutic drug candidates, we will be required to comply with a number of post-approval regulatory requirements. We would be required to report to the FDA, among other things, certain adverse reactions and production problems, and provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling for any of our products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes extensive procedural, substantive and recordkeeping requirements. If we seek to make certain changes to an approved therapeutic drug, such as certain manufacturing changes, we may need the FDA to review and approve before the change can be implemented. For example, if we change the manufacturer of a product or its API, the FDA may require stability or other data from the new manufacturer, which will take time and is costly to generate, and the delay associated with generating this data may cause interruptions in our ability to meet commercial demand, if any. At their discretion, physicians may prescribe approved pharmaceutical products for indications that pharmaceutical products have not been approved for use by the FDA. However, we may not label or promote pharmaceutical products for an indication that has not been approved. Securing FDA approval for new indications of an approved therapeutic drug requires a Section 505(b)(2) filing, is similar to the process for approval of the original indication and requires, among other things, submitting data from adequate and well-controlled studies that demonstrate the product's safety and efficacy in the new indication. Even if such studies are conducted, the FDA may not approve any change in a timely fashion, or at all.

We rely on, and expect to continue to rely on, third parties for the manufacture of clinical and future commercial, quantities of our therapeutic candidates. Future FDA and state inspections may identify compliance issues at these third-party facilities that may disrupt production or distribution or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing. Newly discovered or developed safety or efficacy data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and may also require the implementation of other risk management measures. Many of the foregoing could limit the commercial value of an approved product or require us to commit substantial additional resources in connection with the approval of a product. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Section 505(b)(2) New Drug Applications

As an alternate path to FDA approval of new indications or new formulations of previously-approved therapeutic drugs, a company may file a Section 505(b)(2) NDA, instead of a "stand-alone" or "full" NDA, somewhat similar to the process for approval of the original indication or reference drug and requires, among other things, submitting data from adequate and well-controlled studies that demonstrate the product's safety and efficacy in the new indication. Even if such studies are conducted, the FDA may not approve any change in a timely fashion, or at all. Section 505(b)(2) of the Food, Drug, and Cosmetic Act was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, otherwise known as the Hatch-Waxman Amendments. Section 505(b)(2) was enacted to allow a company to avoid duplicative testing by permitting the applicant to leverage previously performed pertinent clinical and non-clinical studies into the current NDA submission. Some examples of therapeutic drug candidates that may be allowed to follow a 505(b)(2) path to approval are candidates that have a new dosage form, strength, route of administration, formulation or indication.

The Hatch-Waxman Amendments permit the applicant to rely upon certain published nonclinical or clinical studies conducted for an approved product or the FDA's conclusions from a prior review of such studies. The FDA may require companies to perform additional studies or measurements to support any changes from the approved product. The FDA may then approve the new product for all or some of the labeled indications for which the reference product has been approved, as well as for any new indication supported by the NDA. While references to nonclinical and clinical data not generated by the applicant or for which the applicant does not have a right of reference are allowed, all development, process, stability, qualification and validation data related to the manufacturing and quality of the new product must be included in an NDA submitted under Section 505(b)(2).

To the extent that the Section 505(b)(2) applicant is relying on the FDA's conclusions regarding studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book publication. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The Section 505(b)(2) application also will not be approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the reference product has expired. Thus, the Section 505(b)(2) applicant may invest a significant amount of time and expense in the development of its products only to be subject to significant delay and patent litigation before its products may be commercialized.

Orphan Drug Designation

The Orphan Drug Act of 1983, or Orphan Drug Act, encourages manufacturers to seek approval for products intended to treat "rare diseases and conditions" with a prevalence of fewer than 200,000 patients in the U.S. or for which there is no reasonable expectation of recovering the development costs for the product. For products that receive orphan drug designation by the FDA, the Orphan Drug Act provides tax credits for clinical research, FDA assistance with protocol design, eligibility for FDA grants to fund clinical studies, waiver of the FDA application fee, and a period of seven years of marketing exclusivity for the product following FDA marketing approval.

GAIN Act

The FDA's Generating Antibiotic Incentives Now (GAIN) Act is intended to encourage the development of new antibiotic drug therapeutic candidates for the treatment of serious or life-threatening infections. For products that receive QIDP designation under the Act, the Act provides Fast-Track development status with an expedited development pathway and Priority Review status, which potentially provides shorter review time by the FDA of a future potential marketing application. Following FDA approval, an additional five years of U.S. market exclusivity applies, received on top of the standard exclusivity period.

Other Healthcare Laws and Compliance Requirements

In the U.S., we are subject to various federal and state laws and regulations regarding fraud and abuse in the healthcare industry, as well as industry standards and guidance, such as the codes issued by the Pharmaceutical Research and

Manufacturers of America (or "PhRMA Codes"), which some states reference or incorporate in their statutes and regulations. These laws, regulations, standards, and guidance may impact, among other things, our sales and marketing activities and our relationships with healthcare providers and patients. In addition, we may be subject to patient privacy regulations by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order, or recommendation of, an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the False Claim Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from the federal government, including Medicare, Medicaid, or other third-party payors, that are false or fraudulent;
- HIPAA, which imposes federal criminal and civil liability for executing, or attempting to execute, a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- the federal transparency laws, including the Physician Payments Sunshine Act, that requires applicable manufacturers of covered drugs to disclose payments and other transfers of value provided to physicians and teaching hospitals and physician ownership and investment interests;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and its implementing regulations, also imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines, state laws that require pharmaceutical manufacturers to report certain pricing or payment information, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and are not preempted by HIPAA, thus complicating compliance efforts.

The Healthcare Reform Law broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and certain other criminal healthcare fraud statutes. Specifically, a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the Healthcare Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only federal healthcare programs such as the Medicare and Medicaid programs.

Due to the breadth of some of these laws, it is possible that some of our current or future practices might be challenged under one or more of these laws. In addition, there can be no assurance that we would not be required to alter one or more of our practices to comply with these laws. Evolving interpretations of current laws or the adoption of new federal or state laws or regulations could adversely affect the arrangements we may have with sales personnel, healthcare providers, and patients. Our risk of being found in violation of these laws is increased by the fact that some of these laws are open to a variety of interpretations. If our past or present operations, practices, or activities are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, imprisonment, damages, fines, disgorgement, contractual remedies, reputational harm, diminished profits, and future earnings, if any, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

C. Organizational Structure

Our wholly-owned and only subsidiary, Redhill Biopharma Inc., was incorporated in Delaware on January 19, 2017.

D. Property, Plant and Equipment

We lease approximately 826 square meters of office space and eleven parking spaces in the "Platinum" building at 21 Ha'arba'a Street, Tel-Aviv, Israel. The projected yearly gross rental expenses are approximately $470,000 per year. Since 2018, we have been subleasing a portion of the office space to a tenant, and the lease payment is approximately $79,000 per year. The term under our lease agreement will expire on January 31, 2026. These offices have served as our corporate headquarters since April 2011.

We also entered into an operating lease agreement for the U.S. offices it uses. The agreement will expire on July 31, 2024. The projected yearly rental expenses are approximately $400,000 per year.

ITEM 4A. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

You should read the following discussion of our financial condition and results of operations in conjunction with the financial statements and the notes thereto included elsewhere in this Annual Report. The following discussion contains forward-looking statements that reflect our plans, estimates, and beliefs. Our actual results could differ materially from those discussed in the forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report, particularly those in "Item 3. Key Information – D. Risk Factors."

Company Overview

We are a specialty biopharmaceutical company, primarily focused on gastrointestinal ("GI") and infectious diseases. Our primary goal is to become a leading specialty biopharmaceutical company through our commercial presence in the U.S. that supports commercialization of our current and potentially additional products approved for marketing in the U.S., and potential future commercialization of our therapeutic candidates, if approved.

We are currently focused primarily on the commercialization in the U.S. of the GI-related products, Movantik® (naloxegol), Talicia® (omeprazole, amoxicillin, and rifabutin) and Aemcolo® (rifamycin).

In addition, we continue to develop our pipeline of clinical-stage therapeutic candidates, including, among others, opaganib and RHB-107 (upamostat), as potential treatments for COVID-19, and RHB-204, as a potential treatment of pulmonary nontuberculous mycobacteria (NTM) disease caused by MAC). We look for opportunities to leverage our commercial presence and capabilities in the U.S. to support the potential future launch of our therapeutic candidates currently under development, if approved by the FDA, or any FDA-approved products that we may acquire the rights to in the future.

Our therapeutic candidates are designed to exhibit greater efficacy and/or provide improvements over existing treatments in various ways, including by one or more of the following: by improving their effectiveness in treating an unmet medical need, improving their safety profile, reducing side effects, lowering the number of administrations, using a more convenient administration form or providing a cost advantage. Our current pipeline consists of six therapeutic candidates, most of which are in late-stage clinical development.

We generate our pipeline of therapeutic candidates by identifying, validating and in-licensing or acquiring products that are consistent with our product and corporate strategy and that have the potential to exhibit a favorable probability of therapeutic and commercial success. We have one product that we primarily developed internally which has been approved for marketing and, to date, none of our therapeutic candidates has generated meaningful revenues. We plan to commercialize our therapeutic candidates, upon approval, if any, through licensing and other commercialization arrangements outside the U.S. with pharmaceutical companies on a global and territorial basis or, in the case of commercialization in the U.S., independently with our dedicated commercial operations or in potential partnership with

other commercial-stage companies. We also evaluate, on a case-by-case basis, co-development, co-promotion, licensing, acquisitions and similar arrangements.

Since inception, we have funded our operations primarily through public and private offerings of our equity securities, loans, our strategic collaboration with Cosmo and revenues from our commercial activity. As of December 31, 2021, we had approximately $54.2 million of cash, cash equivalents, short-term investments and restricted cash.

The following is a description of our three current commercial products and six therapeutic candidates, most in late-stage clinical development:

Commercial Products

Movantik® is a proprietary once-daily oral peripherally-acting mu-opioid receptor antagonist (PAMORA) approved by the FDA for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g. weekly) opioid dosage escalation. We initiated the promotion of Movantik® in the second quarter of 2020. In April 2020, we acquired from AstraZeneca AB worldwide rights (excluding Europe, Canada and Israel) to commercialize and develop Movantik® (naloxegol) pursuant to a license agreement, dated February 23, 2020, (the "AstraZeneca License Agreement"), and in October 2020 we obtained the rights to commercialize and develop Movantik® in Israel. We initiated our U.S. commercialization activities for Movantik® in April 2020.

Talicia® is a proprietary new drug approved for marketing in the U.S. for the treatment of *H. pylori* bacterial infection in adults. Talicia® is a combination of three approved drugs, omeprazole, which is a proton pump inhibitor (prevents the secretion of hydrogen ions necessary for the digestion of food in the stomach), amoxicillin and rifabutin, which are antibiotics. Talicia® is administered to patients orally. On November 1, 2019, the FDA approved Talicia® for marketing in the U.S. for the treatment of *H. pylori* infection in adults and we launched Talicia® in the U.S. in March 2020. Talicia® is expected to receive a total of eight years of U.S. market exclusivity. Talicia® is the first therapeutic candidate we developed to be approved by the FDA.

Aemcolo® (containing 194 mg of rifamycin), is an orally-administered, minimally absorbed antibiotic that is delivered to the colon, approved by the FDA in 2018 for the treatment of travelers' diarrhea caused by non-invasive strains of *E. coli* in adults. We acquired the rights to market Aemcolo® in the U.S. from Cosmo pursuant to a license agreement under which we agreed to pay Cosmo a royalty percentage in the high twenties on net sales generated from the commercialization of Aemcolo® as well as potential regulatory and commercial milestone payments to Cosmo totaling up to $100.0 million, which, based on our current expectations and assumptions, are not currently expected to be made in the next 12 months.

In December 2019, we commenced the commercialization of Aemcolo® in certain territories in the U.S.

Therapeutic Candidates

RHB-204 is a patented fixed-dose combination product of three antibiotics that will simplify administration and optimize compliance. Each capsule contains the same components as RHB-104 (clarithromycin, clofazimine, and rifabutin) but at unique doses, selected based on modeling to provide optimal balance of the potential safety and efficacy.

Opaganib is an investigational new drug that is proprietary, first-in-class, orally administered SK2 selective inhibitor, with anti-viral, anti-inflammatory and anti-cancer activities, targeting multiple oncology, inflammatory and GI indications. On March 30, 2015, we entered into an exclusive worldwide license agreement with Apogee, pursuant to which Apogee granted us the exclusive worldwide development and commercialization rights to ABC294640 (which we then renamed to ABC294640 (Yeliva®)) and as noted above, received an international non-proprietary name, opaganib, in 2018) and additional intellectual property for all indications. Under the terms of the agreement, as amended, we agreed to pay Apogee initial milestone payments of $3 million, of which the total amount has been paid, as well as up to $2 million in potential development milestone payments, and tiered royalties starting in the low double-digits. For more information regarding this agreement, see "Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – License Agreement for opaganib." In March 2022, we entered into an exclusive license agreement

with Kukbo Co. Ltd. for opaganib in South Korea. Under the terms of the agreement, we will receive an upfront payment of $1.5 million and are eligible for up to $5.6 million in milestone payments as well as low double-digit royalties on net sales of oral opaganib. See “Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements - License Agreement with Kukbo”.

RHB-107 (upamostat; formerly Mesupron) (INN: upamostat) is a proprietary small molecule, first-in-class, potent serine protease inhibitor administered by oral capsule. We believe that RHB-107 has a unique potency and specificity that suggests it may be a new non-cytotoxic approach to cancer therapy, as well as other indications of high unmet need such as inflammatory digestive diseases and inflammatory lung diseases. On June 30, 2014, we acquired from Heidelberg the exclusive development and commercialization rights to RHB-107, excluding China, Hong Kong, Taiwan, and Macao, for all indications. We made an upfront payment to Heidelberg of $1.0 million with potential tiered royalties on net revenues, ranging from mid-teens up to 30%. We are responsible for all development, regulatory and commercialization of RHB-107. See “Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – License Agreement for RHB-107.”

RHB-104 is an investigational new drug intended to treat Crohn's disease, which is a serious inflammatory disease of the GI system that may cause severe abdominal pain and bloody diarrhea, malnutrition and potentially life-threatening complications. RHB-104 is a patented combination of clarithromycin, clofazimine, and rifabutin, three generic antibiotic ingredients, in a single capsule. The compound was developed to treat Crohn's disease through the targeting of MAP infection.

On August 11, 2010, we entered into an asset purchase agreement with Giaconda Limited, pursuant to which we acquired ownership rights in patents, tangible assets, production files, and regulatory approvals and other data and certain third-party agreements related to Talicia®, RHB-104, and RHB-106 in exchange for $500,000 and royalty payments of 7% of net sales and 20% of sublicense fees, in each case, only after we recoup the amounts and expenses exceeding the approved budget. See "Item 4. Information on the Company - B. Business Overview - Acquisition, Commercialization and License Agreements - Acquisition of Talicia®, RHB-104, and RHB-106."

RHB-102 (Bekinda®) is an investigational once-daily bi-modal extended-release oral formulation of ondansetron, a leading member of the family of 5-HT3 serotonin receptor inhibitors, intended to treat nausea, vomiting and diarrhea symptoms experienced in some people suffering from acute gastroenteritis, gastritis, and IBS-D.

RHB-106 is an investigational tablet intended for the preparation and cleansing of the GI tract prior to the performance of abdominal procedures, including diagnostic tests such as colonoscopy, barium enema or virtual colonoscopy, as well as surgical interventions, such as a laparotomy. We acquired ownership rights in patents, tangible assets, production files, and regulatory approvals and other data and rights in certain third-party agreements related to RHB-106 pursuant to the Asset Purchase Agreement with Giaconda Limited described above.

Impact of COVID-19

We have experienced decreased commercial activities due to the various precautionary measures taken in the United States in order to limit the spread of SARS-CoV-2, which have affected the sales of some of our commercial products due to slower initiation of some promotional activities associated with a significant decrease in in-clinic patient visits, tests and treatments and the impact on our sales force’s ability to engage with healthcare providers in an in-person setting, cancellation of events such as industry conferences and limited local and international travel. In addition, there may be a negative impact on our business as a result of COVID-19 within our commercial organization, including reduction in our sales force. The ability to successfully commercialize Movantik® Aemcolo® and Talicia® depends on in-clinic patient visits and the availability of diagnostics, both of which have been negatively affected by the pandemic, especially with respect to Aemcolo® and Talicia®, which we launched shortly before or at the time of the COVID-19 outbreak. In addition, the significant decrease in travel has significantly reduced the demand and sales of Aemcolo® for travelers’ diarrhea. We expect the decreased level of demand and sales of Aemcolo® to continue over the coming quarters due to the effects of the pandemic.

Assessment of the complete extent of the impact of COVID-19 on our results will depend on future developments, which are highly uncertain and cannot be predicted, including new information that may emerge concerning the severity of COVID-19 and the actions to contain COVID-19 or treat its impact, among others. The continuation of the COVID-19 pandemic could materially affect the sales of our commercial products and significantly impair our ability to fund our operations, satisfy our payment obligations and comply with our covenants under the Loan Agreement.

Components of Statements of Comprehensive Loss

Revenues

In 2021, 2020 and 2019, revenues consisted of revenues with respect to commercialization and promotional activities of our commercial products.

Cost of Revenues

Direct costs related to the revenues, such as cost of goods sold and royalties to third parties.

Research and Development Expenses

See "Item 5. Operating and Financial Review and Prospects – C. Research and Development, Patents and Licenses" below.

General and Administrative Expenses

General and administrative expenses consist primarily of compensation for employees, directors and consultants and professional services. Other significant general and administrative expenses include medical affairs, office-related expenses, travel, conferences, and others.

Selling, Marketing and Business Development Expenses

Selling, Marketing and Business Development expenses consist primarily of compensation for employees and consultants dedicated to marketing activities with the Company's commercialized and promoted products and professional services. Other significant selling, marketing and business development expenses include market research, market access, advertising, printed and digital media, product samples, car fleet, travel, conferences, office-related expenses, and others.

Financial Income and Expenses

Financial income and expenses consist of non-cash financing expenses in connection with changes in the fair value of derivative financial instruments, interest earned on our cash, cash equivalents, and short-term bank deposits, bank fees, interest, and finance changes for lease liabilities and other transactional costs and expense or income resulting from fluctuations of the U.S. dollar against other currencies, in which a portion of our assets and liabilities are denominated like NIS, for example.

A. Operating Results

History of Losses

Since inception in 2009, we have generated significant losses in connection with the research and development of our therapeutic candidates and from our commercial operations. We may continue to incur additional losses, which may be substantial over the next several years, as our commercial operations are expected to continue to expand. We also expect to continue and expand our research and development activities and commercial activities over time and this will require further resources. As a result, we expect to continue incurring operating losses, which may be substantial over the next several years, and we will need to obtain substantial additional funds. As of December 31, 2021, we had an accumulated deficit of approximately $367.9 million.

We expect to continue to fund our operations over the next several years through revenues generated from the commercialization of our commercial products, public or private equity offerings, debt financings, non-dilutive financings, commercialization of our therapeutic candidates, if approved, or products we may commercialize or promote in the future.

Segment Information

The Chief Executive Officer is the Company's Chief Operating Decision Maker ("CODM"). The CODM allocates resources and assesses the Company's performance based on the following segmentation: Commercial Operations and Research & Development, both on an Adjusted EBITDA basis. The Commercial Operations segment covers all areas relating to the commercial sales and is being performed by the Company's U.S. subsidiary. The Research and Development segment includes all activities related of research and development and licensing of therapeutic candidates and is being performed by the Company.

Effective December 31, 2021, the Company changed its operating segments to reflect the manner in which the Company's CODM reviews and assesses performance. Accordingly, the Company reports on revenue and segment Adjusted EBITDA. Disclosures regarding the Company's reportable segments for prior periods have been adjusted to conform to the current period presentation. The CODM does not review assets by operating segment. Adjusted EBITDA represents net loss before depreciation, amortization, and financial expenses (income), adjusted to exclude share-based compensation and the Aemcolo® intangible asset impairment.

The following table presents segment profitability and a reconciliation to the consolidated net loss and comprehensive loss for the periods indicated:

	Year Ended December 31,		
	2021	2020	2019
	U.S. dollars in thousands		
Commercial Operations Segment Adjusted EBITDA	(15,527)	(27,236)	(15,913)
Research And Development Adjusted EBITDA	(37,247)	(23,501)	(23,048)
Financial expenses (income), net	16,608	12,489	(897)
Share-based compensation to employees and service providers	10,212	4,202	3,027
Depreciation	1,914	1,710	997
Amortization and impairment of intangible assets	16,235	7,035	216
Consolidated Comprehensive loss	(97,744)	(76,173)	(42,304)

Comparison of the Year Ended December 31, 2021, to the Year Ended December 31, 2020

Net Revenues

Net Revenues for the year ended December 31, 2021, were $85.8 million, compared to $64.4 million for the year ended December 31, 2020. The increase was attributed mainly to an increase in units sold for both Movantik®, which was acquired by us in April 2020, and Talicia®, which we launched in March 2020.

Cost of Revenues

Cost of Revenues for the year ended December 31, 2021, was $49.4 million, compared to $36.9 million for the year ended December 31, 2020. The increase was mostly attributable to the recognition of approximately $9 million impairment related to the intangible asset of Aemcolo® for travelers' diarrhea, and in line with the increase in net revenues from our commercial products.

Gross Profit

Gross Profit for the year ended December 31, 2021, was $36.4 million, compared to $27.5 million for the year ended December 31, 2020. The increase was primarily attributable to the increase in net revenues, and partially offset by the recognized impairment of Aemcolo® intangible asset.

Research and Development Expenses

Research and Development Expenses were $29.5 million for the year ended December 31, 2021, as compared to $16.5 million for the year ended December 31, 2020. The increase was mainly attributable to the advancement of our COVID-19 programs with opaganib and RHB-107.

Selling, Marketing and General and Administrative Expenses

Selling, Marketing and Business Development Expenses for the year ended December 31, 2021, were $88.0 million, as compared to $74.7 million for the year ended December 31, 2020. The increase was mainly attributable to the expansion of commercialization activities related to Talicia® and Movantik® and to expenses related to share-based compensation.

Operating Loss

Operating Loss for the year ended December 31, 2021, was $81.1 million, compared to $63.7 million for the year ended December 31, 2020. The increase was mainly attributable to expenses related to the increased activities of both our segments – commercial operations and research and development.

Financial Expenses, net

Financial Expenses, net for the year ended December 31, 2021, was $16.6 million, compared to Financial Expenses, net of $12.5 million for the year ended December 31, 2020. The increase was mainly attributed to interest and royalty expenses related to the debt financing with HCRM entered into effect at the end of the first quarter of 2020.

Comparison of the Year Ended December 31, 2020, to the Year Ended December 31, 2019

This analysis can be found in Item 5 of the Company's Annual Report on Form 20-F for the year ended December 31, 2020.

B. Liquidity and Capital Resources

Liquidity and Capital Resources

Through our U.S. subsidiary, we currently commercialize Movantik®, Talicia® and Aemcolo®. However, our ability to generate profits from the commercialization of our commercial products still remains uncertain. To date, our commercial operations are still generating operational losses. Other than Talicia®, our therapeutic candidates are in research and development stage, and therefore do not yet generate revenues except for an upfront payment of $2 million received in December 2021 in connection with our grant of the exclusive rights to commercialize Talicia® in the UAE to Gaelan Medical Trade LLC. See "Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – License Agreement with Gaelan Medical Trade LLC". Since inception, we have funded our operations primarily through public and private offerings of our equity securities, loans, our strategic collaboration with Cosmo and revenues from our commercial activity. Other potential sources of liquidity in the future may include government grants or subordinated indebtedness, or other non-dilutive financings. As of December 31, 2021, we had approximately $54.2 million of cash, cash equivalents, short-term investments and restricted cash.

During the year ended December 31, 2021, we sold 87,628 of our ADSs under the at-the-Market (ATM) program for total gross proceeds of approximately $0.8 million, leaving an available balance under the ATM program of approximately $99.5 million.

On January 14, 2021, we closed an underwritten offering of 3,188,776 ADSs at a public offering price of $7.84 per share, for total net proceeds of approximately $23.1 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us in connection with the offering.

On March 4, 2021, we closed an underwritten offering of 4,647,433 ADSs at a public offering price of $8.00 per ADS, for total net proceeds of approximately $34.8 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us in connection with the offering, including the exercise by the underwriter of its overallotment option.

In November 2021, we entered into a strategic transaction with Kukbo Co. Ltd. ("Kukbo"), a South Korean corporation, for the sale of our ADSs in a private placement of up to $10 million at a 20% premium to the prior 30 trading days' volume weighted average price. Kukbo's strategic investment is to be made in two tranches, with the first tranche of $5 million already paid and the second tranche of $5 million to follow within six months, subject to satisfaction of certain conditions. As part of the first tranche, we issued 827,586 ADSs at a purchase price of $6.04. See "Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements –Limited Period Right of First Refusal for License of opaganib, RHB-107 and Talicia® in Various Countries" for additional information.

On November 18, 2021, we closed an underwritten offering of 4,686,036 ADSs. The underwriter purchased our ADSs at a price of $3.201 per ADS, for total net proceeds of approximately $14.8 million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us in connection with the offering.

Revenues generated from our U.S. commercial activities were approximately $85.8 million for the year ended December 31, 2021 and approximately $64.4 million for the year ended December 31, 2020.

Term Loan Facility

On February 23, 2020 (the "Credit Agreement Closing Date"), we, through our wholly-owned subsidiary, "RedHill U.S.", entered into a credit agreement (the "Credit Agreement") with HCRM, as Administrative Agent ("HCRM"), and the lenders from time to time party thereto. Pursuant to the terms of the Credit Agreement, RedHill U.S. received a $30 million loan following the signing of the Credit Agreement (the "Tranche A Loan"). An additional $50 million tranche was used to fund the acquisition of rights to Movantik® from AstraZeneca (together with the Tranche A Loan, the "Loans").

The Loans bear interest at an annual rate equal to the 3-month LIBOR rate plus 8.20% which will be decreased to 6.7% starting April 1, 2021, with a 1.75% 3-month LIBOR floor. The principal and interest under the Credit Agreement are payable quarterly in arrears on the last day of each March, June, September, and December (each an "HCRM Payment Date"). The Loans will mature on February 23, 2026 (the "Term Loan Maturity Date"), at which time, if not earlier repaid in full, the outstanding principal amount of the Loans, together with any accrued and unpaid interest, shall be due and payable in cash. Upon the prepayment or repayment of all or any portion of the Loans, RedHill U.S. must pay to the lenders under the Credit Agreement an exit fee in an amount equal to 4% of the aggregate principal amount of the Loans prepaid or repaid on such date. Pursuant to the Credit Agreement, HCRM will receive a royalty of 4% (on up to $75 million of our annual net revenues (the "Revenue Interest"). Payments of Revenue Interest will be made quarterly in arrears for nine years, beginning with the first fiscal quarter of 2021.

Pursuant to the terms of the Credit Agreement, on each HCRM Payment Date beginning with March 2023 (the "Amortization Date") through and including the Term Loan Maturity Date, RedHill U.S. must repay the Loans in equal installments. If, however, our net revenues for the trailing four quarters ending March 31, 2022, are less than $50 million, then at the sole discretion of the Required Lenders (as defined in the Credit Agreement), the Amortization Date shall be the HCRM Payment Date immediately following the two year anniversary of the Credit Agreement Closing Date.

We may elect to prepay the Loans at any time, subject to a prepayment premium that declines from 5% for the first four years of the Loans, to 2.5% in the fifth year, to 1.25% in the final year prior to maturity of the Loans. In addition, if we prepay any Loans prior to the third anniversary of the applicable borrowing date for such Loans, we are required to pay all required interest payments that would have been due on the principal amount of such Loans prepaid through and including the third anniversary of the applicable borrowing date for such Loans.

We also entered into a Security Agreement, a Pledge Agreement, an Israeli-law governed Fixed Charge Debenture and an Israeli-law governed Floating Charge Debenture in favor of HCRM, pursuant to which our obligations under the Credit

Agreement (and those of RedHill U.S.) are secured by a pledge of all of our holdings of the capital stock of RedHill U.S., substantially all of the assets of RedHill U.S., and all of our assets relating in any material respect to Talicia®.

The Credit Agreement contains certain affirmative covenants, including those relating to, among other things: financial statements; notices; payments of obligations; preservation of existence; maintenance of properties; maintenance of insurance; compliance with laws; inspection rights; and protection of our intellectual property. The Credit Agreement also contains certain negative covenants barring us and our subsidiaries from (with limited exceptions) taking certain actions including, among other things: certain fundamental transactions; issuing dividends and distributions; incurring indebtedness; incurring liens; making investments; engaging in transactions with affiliates; engaging in sale-leaseback transactions; and changing the nature of our business. The Credit Agreement also contains a financial covenant requiring us to maintain a minimum level of cash liquidity of $16 million, a covenant requiring us to maintain minimum net sales of $90 million for each 4-quarter period beginning on June 30, 2021, and a covenant requiring us to have a minimum of 119 sales representatives for our commercial products. In addition, the Credit Agreement contains a covenant restricting our ability to terminate or to permit certain changes to the respective roles and responsibilities as of February 23, 2020, of our chief executive officer, Dror Ben-Asher, and the chief commercial officer of RedHill U.S., Rick Scruggs.

The Credit Agreement contains defined events of default, in certain cases subject to a grace period, following which the lenders may declare any outstanding principal and unpaid interest immediately due and payable. These include, among other things: failure to pay principal, interest, or other amounts payable when due; any uncured breach of a representation, warranty, or covenant; any uncured cross-default under certain contracts; certain judgments being entered against us or our subsidiaries; certain bankruptcy or insolvency events; any Change of Control or Material Adverse Effect (in each case, as defined in the Credit Agreement); and certain regulatory events with respect to our products.

Additional Cash Requirements

In connection with our acquisition of worldwide rights (excluding Europe and Canada) to commercialize and develop Movantik® from AstraZeneca AB, we agreed to pay AstraZeneca an upfront payment of $52.5 million and an additional $16 million in gradual payments starting in March 2021 and ending in December 2022, of which $7.5 million is due by the end of 2022. In addition, we have assumed responsibility for certain milestone and royalty payments payable to Nektar depending on net sales (as defined in the license agreement with AstraZeneca) for the licensed product. The Company considers the likelihood of having to pay the milestone payments or increased royalties as negligible. For more information regarding this agreement, see “Item 4. Information on the Company – B. Business Overview – Acquisition, Commercialization and License Agreements – License Agreement for License Agreement for Movantik®.”

In connection with such license agreement, AstraZeneca transferred to us its co-commercialization agreement with Daiichi Sankyo, Inc. for Movantik®. In August 2020, we announced an amendment to the agreement with Daiichi Sankyo, Inc. which enabled us to exercise full control over brand strategy and commercialization for Movantik® in the U.S., and pursuant to which we pay Daiichi Sankyo a mid-teen royalty rate on net sales of Movantik® in the U.S., in addition to three lump-sum payments in the amount of $5.1 million already paid in January 2022 and $5 million to be paid in each of July 2022 and 2023.

In addition, we incur costs associated with our ongoing commercial operations, including salary and related benefits to our sales representatives and other employees, insurance and lease costs. Our labor costs in the U.S. may increase due to the overall tightening and increasingly competitive labor market in the U.S. employment market in response to the COVID-19 pandemic.

We are also obligated to make various payments upon the achievement of agreed-upon milestones or make certain royalty payments under our in-license agreements with Apogee with respect to opaganib and with Heidelberg with respect to RHB-107, under our asset purchase agreement with Giaconda Limited with respect to Talicia®, RHB-104, and RHB-106 and under our agreement with UCF or the University of Minnesota, pursuant to which we are obligated to make various payments upon the achievement of agreed-upon milestones or make certain royalty payments. See “ - Company Overview – Therapeutic Candidates” above. . All of our in-licensing agreements are terminable at-will by us upon prior written notice.

In addition, in connection with our purchase of inventory in the regular course of business as part of our ongoing commercialization of Movantik® we have future obligations to purchase API, bulk tables and finished goods under our Supply Agreement with AstraZeneca, and we have future obligations to purchase API, bulk tables and finished goods with respect to Talicia® for an aggregate purchase price of $22 million until 2025 in the ordinary course of business. We expect to purchase the inventory in the regular course of business as part of our ongoing commercialization of these products.

We estimate that so long as sufficient revenues to sustain our business operations in accordance with our plan are not generated from our current commercial products, our therapeutic candidates, upon approval, if any, out-licensing transactions or products that we may commercialize or promote in the future, we will need to raise substantial additional funds, as our current cash and short-term investments are not sufficient to continuously fund our commercial operations, satisfy our payment obligations and complete the research and development of all of our therapeutic candidates. However, additional financing may not be available on acceptable terms, if at all, including due to the decreased interest of investors in, and the decline in the prices of, securities of biopharmaceutical companies on the U.S. stock exchanges, including the ADSs. Our future capital requirements will depend on many factors including but not limited to:

- our ability to successfully commercialize commercial products and our therapeutic candidates, upon approval, if any, including securing commercialization agreements with third parties and favorable pricing and market share;
- we may consume available resources more rapidly than currently anticipated, resulting in the need for additional funding sooner than anticipated.
- the regulatory path of each of our therapeutic candidates;
- the progress, success, and cost of our clinical trials and research and development programs;
- the costs, timing, and outcome of regulatory review and obtaining regulatory approval of our therapeutic candidates and addressing regulatory and other issues that may arise post-approval;
- the costs of enforcing our issued patents and defending intellectual property-related claims;
- the costs of developing sales, marketing, and distribution channels; and
- consumption of available resources more rapidly than currently anticipated, resulting in the need for additional funding sooner than anticipated.

If we are unable to generate sufficient revenues from our commercial products, commercialize or out-license our therapeutic candidates or obtain future financing to sustain our business operations in accordance with our plan, we may be unable to satisfy our payment obligations or comply with our covenants under the Loan Agreement. In addition, we may be forced to delay, reduce the scope of, or eliminate one or more of our current commercial products and products that we may commercialize or promote in the future or our research, development programs for our therapeutic candidates, which may have a material adverse effect on our reputation, business, financial condition or results of operations. See "Item 3. Key Information – D. Risk Factors – Risks Related to Our Financial Condition and Capital Requirements." We will need to raise additional capital to achieve our strategic objectives of acquiring, in-licensing, developing and commercializing therapeutic candidates, upon approval, if any, commercializing our current commercial products and other products that we may commercialize or promote in the future, and our failure to raise sufficient capital or on favorable terms would significantly impair our ability to fund our operations, satisfy our payment obligations and comply with our covenants under the Loan Agreement, develop our therapeutic candidates, and commercialize products, such as our current commercial products or other products that we may commercialize or promote in the future, attract development or commercial partners or retain key personnel.

Cash Flow

Net Cash Used in Operating Activities

Net Cash Used in Operating Activities for the year ended December 31, 2021, was $65 million, compared to $48.6 million for the year ended December 31, 2020. The increase was attributable to the increase in operating expenses as detailed above.

Net Cash Used in Investing Activities

Net Cash Used in Investing Activities for the year ended December 31, 2021, was $8.1 million, primarily related to the changes in investment in current bank deposits. Net Cash Used in Investing Activities for the year ended December 31, 2020 was $35.6 million, primarily related to $52.5 million upfront payment to AstraZeneca for the acquisition of Movantik, partially offset by inflows from current bank deposits and financial assets at fair value through profit or loss.

Net Cash Provided by Financing Activities

Net Cash Provided by Financing Activities for the year ended December 31, 2021, was $73.5 million, comprised primarily of proceeds from public offerings, strategic investment by Kukbo. utilization of at-the-market facility and exercise of options. Net Cash Provided by Financing Activities for the year ended December 31, 2020, was $84.4 million, primarily from $78.1 million inflow from our credit agreement with HCRM and additional $23.9 million proceeds from issuance of our ADSs, partially offset by $16 million classified as restricted cash.

We did not have any material commitments for capital expenditures, including any anticipated material acquisition of plant and equipment or interests in other companies, as of December 31, 2021.

C. Research and Development, Patents and Licenses

Our research and development expenses consist primarily of costs of clinical trials, professional services, share-based payments and payroll, and related expenses. The clinical trial costs are mainly related to payments to third parties to manufacture our therapeutic candidates, to perform clinical trials with our therapeutic candidates and to provide us with regulatory services. We charge all research and development expenses to operations as they are incurred. We expect our research and development expenses to remain our primary expense in the near future as we continue to develop our therapeutic candidates.

Due to the inherently unpredictable nature of clinical development processes, we are unable to estimate with any certainty the costs we will incur in the continued development of the therapeutic candidates in our pipeline for potential commercialization.

Our future research and development expenses will depend on the clinical success of each therapeutic candidate, the rate of patient recruitment and the ongoing assessments of each therapeutic candidate's commercial potential. In addition, we cannot forecast with any degree of certainty which therapeutic candidates may be subject to future commercialization arrangements, when such commercialization arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements. See "Item 3. Key Information – D. Risk Factors – Risks Related to Regulatory Matters – If we or our development or commercialization partners are unable to obtain or maintain FDA or other foreign regulatory clearance and approval for our therapeutic candidates or products we may commercialize or promote, we or our commercialization partners will be unable to commercialize our therapeutic candidates, upon approval, if any, or products we may commercialize or promote."

As we obtain results from clinical trials, we may elect to discontinue or delay the development and clinical trials for certain therapeutic candidates in order to focus our resources on more promising therapeutic candidates or projects. Completion of clinical trials by us or our licensees may take several years or more, but the length of time generally varies according to the type, complexity, novelty and intended use of a therapeutic candidate. See "Item 3. Key Information – D. Risk Factors – Risks Related to Regulatory Matters."

We expect our research and development expenses to stay material as we continue the advancement of our clinical trials and therapeutic candidates' development. The lengthy process of completing clinical trials and seeking regulatory approvals for our therapeutic candidates requires substantial expenditures. Any failure or delay in completing clinical trials, or in obtaining regulatory approvals, could cause a delay in generating product revenue and cause our research and development expenses to increase and, in turn, have a material adverse effect on our operations. Due to the factors set forth above, we are not able to estimate with any high certainty if and when we would recognize any substantial revenues from our projects.

D. Trend Information

Other than as disclosed elsewhere in this Annual Report, we are not aware of any trends, uncertainties, demands, commitments or events that are reasonably likely to have a material effect on our net revenues, income from continuing operations, profitability, liquidity or capital resources, or that would cause reported financial information not necessarily to be indicative of future operating results or financial condition.

E. Critical Accounting Estimates

The preparation of financial statements requires management to make estimates which, by definition, will seldom equal the actual results and will affect the reported amounts in our consolidated financial statements and the accompanying notes. Some of the policies described in Note 2 of our consolidated financial statements involve a high degree of judgment or complexity. We believe that the most critical accounting policies and significant areas of judgment and estimation are in:

- Recognition and measurement of allowance for rebates and patient discount programs.
- Impairment reviews of intangible research and development assets.
- Estimated recoverable amount of the Aemcolo® asset.
- Estimated useful economic life of the acquired assets in the Movantik® acquisition.

Recognition and Measurement of Allowance for Rebates and Patient Discount Programs

We offer various rebate and patient discount programs, which result in discounted prescriptions to qualified patients. Rebates and discounts provided to the wholesalers and to the patients under these arrangements are accounted for as variable consideration, and recognized as a reduction in revenue, for which unsettled amounts are accrued. The allowance for these rebates is calculated based on historical and estimated utilization of the rebate and discount programs at the time the revenues are recognized. The main estimates used in recognizing and measuring this allowance relate to the amount of products sold to customers not yet prescribed to patients (units "in the channel") and the mix of rebate and discount programs estimated for future prescription utilization. We periodically evaluate our estimates against actual results and, if necessary, updates the estimates accordingly.

Impairment Reviews of Intangible Research and Development Assets

We review annually or when events or changes in circumstances indicate the carrying value of the research and development assets may not be recoverable.

When and if necessary, an impairment loss is recognized for the amount by which the asset's carrying amount exceeds its recoverable amount. The recoverable amount is determined using discounted cash flow calculations where the asset's expected post-tax cash flows are risk-adjusted over their estimated remaining useful economic life. The risk-adjusted cash flows are discounted using our estimated post-tax weighted average cost of capital ("WACC") which is 16%.

The main estimates used in calculating the recoverable amount include: outcome of the therapeutic candidates research and development activities; probability of success in gaining regulatory approval, size of the potential market and our asset's specific share in it and amount and timing of projected future cash flows.

Estimated recoverable amount of the Aemcolo® asset

The Aemcolo® asset was acquired in October 2019 in exchange of the Company's ADSs and was recognized at fair value at the acquisition date. Following the outbreak of the COVID-19 pandemic and its significant impact on worldwide travel, we expect a continued decrease in U.S. outbound travel and the potential market for Aemcolo®, for traveler's diarrhea. Accordingly, during 2020 we had recognized an impairment of approximately $0.8 million. In addition, in 2021, in line with continued performance of the product, we have again reevaluated the recoverable amount of the intangible asset related to Aemcolo®. Based mainly on estimates of the asset's peak market share and the period in which it will be reached (including the likelihood of early termination of the license before it will be reached), we considered the Aemcolo® asset to be entirely impaired. Accordingly, as of December 31, 2021, we recognized an impairment loss of $8.9 million.

Estimated Useful Life of the Acquired Assets in the Movantik® acquisition

In connection with the agreements mentioned in Note 1a(2) of our consolidated financial statements, we accounted for the acquisition of rights to Movantik® as an asset acquisition. Since all acquired assets are intended to generate revenues from sales of Movantik® and have a similar useful life, the Company attributed this consideration to a single intangible asset representing the acquired rights to Movantik®. The Company determined the asset's useful life, over which the asset will be amortized on a straight-line from its acquisition. The main estimate used in determining the useful life was the anticipated duration of sales of the product after its expected patent expiration. During 2021, as a result of reaching a litigation settlement related to Movnatik®'s IP, the Company has re-estimated the useful life of these assets to be 12.5 years from the date of acquisition.

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and Senior Management[1]

The following table sets forth the name, age and position of each of our executive officers and directors as of the date of this Annual Report.

Name	Age	Position(s)
Executive Officers		
Dror Ben-Asher	56	Chief Executive Officer and Chairman of the Board of Directors
Micha Ben Chorin	53	Chief Financial Officer
Reza Fathi, Ph.D.	67	Senior Vice President Research and Development
Gilead Raday	47	Chief Operating Officer
Adi Frish	52	Chief Corporate and Business Development Officer
Guy Goldberg	46	Chief Business Officer
Rick D. Scruggs	62	Chief Commercial Officer and Director
Dr. June Almenoff	66	Chief Medical Officer
Directors		
Dr. Shmuel Cabilly (3)	72	Director
Eric Swenden (1) (3)	78	Director
Dr. Kenneth Reed (2) (3)	68	Director
Ofer Tsimchi (1), (2) (3)	62	Director
Alla Felder (1), (2), (3)	48	Director

(1) Member of our audit committee; also serves as our financial statements committee.
(2) Member of our compensation committee.
(3) Independent director under Nasdaq Listing Rules.

Executive officers

Dror Ben-Asher has served as our Chief Executive Officer and as a director since August 2009. Since May 2011, Mr. Ben-Asher has also served as Chairman of our board of directors. From January 2002 to November 2010, Mr. Ben-Asher served as a manager at P.C.M.I. Ltd., an affiliate of ProSeed Capital Holdings CVA. Mr. Ben-Asher holds an LLB from the University of Leicester, U.K., an MJur. from Oxford University, U.K. and completed LLM studies at Harvard University.

Micha Ben Chorin has served as our Chief Financial Officer since January 2016. From 2014 until 2016, Mr. Ben Chorin served as Chief Financial Officer of Pyramid Analytics a business intelligence (BI) software company. From 2009 until 2013, he served as CFO of Starhome B.V., a leading international roaming vendor, from 2005 until 2009 as CFO of Winetworks, a wireless operator, and from 1998 until 2005 Mr. Ben Chorin served as Chief Financial Officer at GVT (currently Telefonica Brazil). Mr. Ben Chorin holds a B.A. from Tel-Aviv University and is a Certified Public Accountant.

[1] Senior management includes members of the Company's administrative, supervisory or management bodies, or nominees for such positions.

Reza Fathi, Ph.D., has served as our Senior Vice President Research and Development since May 2010. From 2005 to 2009, Dr. Fathi served as a Director of Research in XTL Biopharmaceuticals Inc., a biotechnology company engaged in developing small molecule clinical candidates for infectious diseases. Prior to that, from 2000-2005, Dr. Fathi served as Director of Research at Vivoquest, Inc. where he was responsible for developing a number of novel natural product-based combinatorial technologies for infectious diseases such as HCV and HIV. Between 1998-2000, he served as a Manager of Chemical Biology Research at the Institute of Chemistry and Chemical Biology (ICCB) at Harvard Medical School, pioneering chemical genetics to identify small molecules in cancer biology, and from 1991-1998 headed the Discovery Group at PharmaGenics, Inc. Dr. Fathi holds a Postdoctoral and Ph.D. in Chemistry from Rutgers University.

Gilead Raday has served as our Chief Operating Officer since April 2016. From December 2012, until March 2016, Mr. Raday served as Senior Vice President Corporate and Product Development. From November 2010 to December 2012, Mr. Raday served as our Vice President Corporate and Product Development. From January 2010 until October 2010, Mr. Raday served as Interim Chief Executive Officer of Sepal Pharma Plc., an oncology drug development company, and from January 2009 to December 2009, he was an independent consultant, specializing in business development and project management in the field of life sciences. From 2004 to 2008, Mr. Raday was a partner in Charles Street Securities Europe, LLP, an investment banking firm, where he was responsible for the field of life sciences. Mr. Raday previously served on the boards of Sepal Pharma Plc., ViDAC Limited, Morria Biopharmaceuticals Plc., Vaccine Research International Plc., TKsignal Plc., and Miras Medical Imaging Plc. He received his M.Sc. in Neurobiology from the Hebrew University of Jerusalem, Israel, and an M.Phil. in Bioscience Enterprise from Cambridge University, U.K.

Adi Frish has served as our Chief Corporate and Business Development Officer since October 2020. From December 2012 to October 2020 Mr. Frish served as our Senior Vice President Business Development and Licensing. From October 2010 to December 2012, Mr. Frish served as our Vice President Business Development and Licensing. From 2006 to 2010, Mr. Frish served as the Chief Business Development at Medigus Ltd., a medical device company in the endoscopic field, and from 1998 to 2006, Mr. Frish was an associate and a partner at the law firm of Y. Ben Dror & Co. Mr. Frish holds an LLB from Essex University, U.K. and an LLM in Business Law from the Bar-Ilan University, Israel.

Guy Goldberg has served as our Chief Business Officer since 2012. From 2007 to 2012, Mr. Goldberg served as Vice President and then as Senior Vice President of Business Operations at Eagle Pharmaceuticals, a specialty injectable drug development company, based in New Jersey. From 2004 to 2007, Mr. Goldberg was an associate at ProQuest Investments, a healthcare-focused venture capital firm, and from 2002 to 2004, Mr. Goldberg was a consultant at McKinsey & Company. Mr. Goldberg holds a B.A. in Economics and Philosophy from Yale University and a J.D. from Harvard Law School.

Rick D. Scruggs has served as our Chief Commercial Officer since February 2020 and served as our Chief Operations Officer, U.S. Operations since January 1, 2019, and as a member of our board of directors since January 1, 2016. Mr. Scruggs most recently served as Executive Vice President of Business Development at Salix until its acquisition by Valeant (now Bausch Health) in March 2015. Mr. Scruggs joined Salix in 2000, after working at Oclassen Pharmaceuticals Inc. and Watson Pharmaceuticals, and helped build Salix's commercial organization, serving in various sales and commercial trade-related positions. Mr. Scruggs was appointed as Executive Vice President in 2011 and was responsible for all business development activities as well as the worldwide distribution of Salix's innovative products and intellectual property. Mr. Scruggs also served as the Head of the board of directors of Oceana Therapeutics, Salix's European subsidiary. Mr. Scruggs holds a B.S. in Criminal Justice from the Appalachian State University in North Carolina.

Dr. June Almenoff, MD, PhD, has served as our U.S. Chief Medical Officer since May 2019. With over 20 years of experience in the pharmaceutical industry, Dr. Almenoff served in various senior executive roles, including the President and Chief Medical Officer of Furiex Pharmaceuticals (acquired by Actavis plc, now Allergan plc), whose lead product, Viberzi®, was approved by the FDA in 2015 for the treatment of irritable bowel syndrome with diarrhea (IBS-D). Prior to joining Furiex, Dr. Almenoff worked at GlaxoSmithKline plc, where she held various positions of increasing responsibility. She has recently served as a board member and advisor to numerous biopharma companies. She is currently a board member of the Harrington Investment Advisory Board of the Harrington Discovery Institute, Brainstorm Cell Therapeutics (Nasdaq: BCLI) Tenax Therapeutic (Nasdaq: TENX) and Avalo Therapeutics (Nasdaq: AVLO). Dr.

Almenoff has led or contributed to clinical and regulatory development strategy from pre-IND through Phase III & IV, and has also been a key contributor to several product approvals and commercial launches. Dr. Almenoff has also served as an advisor to numerous biopharma companies, venture capital and hedge funds. Dr. Almenoff holds a B.A. *(cum laude)* from Smith College and graduated from the M.D.-Ph.D. program at the Mt. Sinai School of Medicine. She completed post-graduate medical training at Stanford University Medical Center and served on the faculty of Duke University School of Medicine. She is an adjunct Professor at Duke, a Fellow of the American College of Physicians (FACP) and has authored over 60 publications.

Directors

Dr. Shmuel Cabilly has served as a member of our board of directors since August 2010. Dr. Cabilly is a scientist and inventor in the field of immunology. In the Backman Research Institute of the City of Hope, Dr. Cabilly initiated the development of a new breakthrough technology for recombinant antibody production, which was patented and known as the "Cabilly Patent." Dr. Cabilly was also a co-founder and a Chief Scientist of Ethrog Biotechnology, where he invented dry buffer technologies enabling the production of a liquid-free disposable apparatus for gel electrophoresis and a technology that enables the condensation of molecular separation zones to a small gel area. This technology was sold to Invitrogen in 2001. Dr. Cabilly serves as a board member at several companies, including BioKine Therapeutics Ltd., and Minovia Ltd. Dr. Cabilly holds a B.Sc. in Biology from the Ben Gurion University of Beer Sheva, Israel, an M.Sc. in Immunology and Microbiology from the Hebrew University of Jerusalem, Israel, and a Ph.D. in Immunology and Microbiology from the Hebrew University of Jerusalem, Israel.

Eric Swenden has served as a member of our board of directors since May 2010 and has served on our investment committee since May 2011. From 1966 until 2001 Mr. Swenden served in various positions including Chief Executive Officer (since 1985) and Executive Chairman (since 1990) of Vandemoortele Food Group, a privately held Belgium-based European food group with revenue of approximately EUR 2 billion. Mr. Swenden holds an M.A. in Commercial Science from the University of Antwerp, Belgium. The board of directors has determined that Mr. Swenden is a financial and accounting expert under Israeli law.

Dr. Kenneth Reed has served as a member of our board of directors since December 2009. Dr. Reed is a dermatologist practicing in private practice under the name of Kenneth Reed M.D. PC. Dr. Reed currently serves on the board of directors of Minerva Biotechnologies Corporation. Dr. Reed received his B.A. from Brown University in the U.S. and an M.D from the University of Medicine and Dentistry of New Jersey in the U.S. Dr. Reed is a board-certified dermatologist with over 25 years of clinical experience since completing the Harvard Medical School Residency Program in Dermatology. Dr. Reed is also a co-founder of Early Cell, a prenatal diagnostics company, Prescient Pharma and Lispiro.

Ofer Tsimchi has served as a director on our board of directors, a member of our audit committee and as the Chairman of our compensation committee since May 2011. From 2008 to 2012, Mr. Tsimchi served as the Chairman of the board of directors of Polysack Plastic Industries Ltd. and Polysack-Agriculture Products, and since 2006, he has served as a Partner in the Danbar Group Ltd., a holding company. Mr. Tsimchi currently serves on the board of directors of Caesarstone Ltd., Amutat Zionut 2000, Danbar Group Ltd, and Maabarot Products Ltd. Mr. Tsimchi received his BA in Economics and Agriculture from the Hebrew University of Jerusalem, Israel. The board of directors has determined that Mr. Tsimchi is a financial and accounting expert under Israeli law.

Alla Felder has served as a director on our board of directors and a chairperson of our audit committee and a member of our compensation committee since May 2019. Ms. Felder currently serves as a Director in numerous publicly listed leading Israeli companies across several industries, such as Ashtrom Properties Ltd., Israel Shipyards Ltd, Carmit Industries Ltd. Biolight Ltd. Photomyne Ltd. and IdoMoo Ltd. Ms. Felder also serves as the CFO of Weebit Nano Ltd, a high-tech company traded on the Australian stock exchange (ASX), and also provide financial and business advisory Ms. Felder also served on the board of Neuroderm Ltd., leading up to its acquisition by Mitsubishi Tanabe Pharma Corporation in 2017. From 1997 to 2010 Ms. Felder was with PriceWaterhouseCoopers where she served in her last role as a Senior Manager. Ms. Felder received a degree in Business Administration and Accounting from the College of Management Academic Studies Division in Rishon Lezion, Israel and an Executive Master's degree in the Science of Finance from the City University of New York.

B. Compensation

The aggregate compensation paid, and benefits-in-kind granted to or accrued on behalf of all of our directors and executive officers for their services, in all capacities, to us during the year ended December 31, 2021, was approximately $5.8 million. Out of that amount $2.9 million was paid as salary, $2.3 million was attributed to the value of the options granted to senior management during 2021, approximately $0.6 million was attributed to retirement plans and $0.1 million was attributed to other long-term benefits and $0.1 million for bonuses. No additional amounts have been set aside or accrued by us to provide pension, retirement or similar benefits.

The compensation terms for our directors and officers are derived from their employment agreements and comply with our Compensation Policy for Executive Officers and Directors as approved by our shareholders (the "Compensation Policy").

The table and summary below outline the compensation granted to our five highest compensated directors and officers during the year ended December 31, 2021. The compensation detailed in the table below refers to actual compensation granted or paid to the director or officer during the year 2021.

Name and Position of Director or Officer	Base Salary or Other Payment (1)	Value of Social Benefits (2)	Bonuses	Value of Equity-Based Compensation Granted (3)	All Other Compensation (4)	Total
Amounts in U.S. dollars are based on the 2021 monthly average representative U.S. dollar – NIS rate of exchange						
Dror Ben-Asher, Chief Executive Officer and Chairman of the Board of Directors (6)	716,838	139,973	—	464,200	27,862	1,348,873
Rick Scruggs, Chief Commercial Officer	611,250	15,296	94,050	358,092	15,750	1,094,438
Micha Ben Chorin, Chief Financial Officer	413,362	106,920	—	316,500	27,862	864,644
Gilead Raday, Chief Operating Officer	443,801	78,504	—	316,500	17,430	856,235
Adi Frish, Chief Corporate and Business Development Officer	408,815	96,891	—	316,500	13,944	836,150

(1) "Base Salary or Other Payment" means the aggregate yearly gross monthly salaries or other payments with respect to the Company's Executive Officers and members of the board of directors for the year 2021. Messrs. Ben-Asher and Scruggs do not receive extra compensation for the service as members of the board of directors.

(2) "Social Benefits" include payments to the National Insurance Institute, advanced education funds, managers' insurance and pension funds; vacation pay; and recuperation pay as mandated by Israeli law.

(3) Consists of the fair value of the equity-based compensation granted during 2021 in exchange for the directors and officers services recognized as an expense in profit or loss and is carried to the accumulated deficit under equity. The total amount is recognized as an expense over the vesting period of the options. See "Item 6, Directors, Senior Management and Employees, E. Share Ownership" for further information regarding the options.

(4) "All Other Compensation" includes, among other things, car-related expenses (including tax gross-up), communication expenses, basic health insurance, and holiday presents.

(5) Mr. Ben-Asher's employment terms as the Company's Chief Executive Officer provide that Mr. Ben-Asher is entitled to a monthly base gross salary of NIS 192,500 (approximately $58,995). Mr. Ben-Asher is further entitled to vacation days, sick days and convalescence pay in accordance with the market practice and applicable law, monthly remuneration for a study fund, contribution by the Company to an insurance policy and pension fund, and additional benefits, including communication expenses. In addition, Mr. Ben-Asher is entitled to reimbursement of car-related expenses from the Company. Mr. Ben-Asher's employment terms include an advance notice period of 12 months by the Company and 90 days by Mr. Ben-Asher. During such an advance notice period, Mr. Ben-Asher will be entitled to all of the compensation elements, and to the continuation of vesting of any options or restricted shares granted to him. Additionally, in the event Mr. Ben-Asher's employment is terminated in connection with a "change in control" he will be entitled to a special one-time payment equal to his then-current monthly salary and retirement benefits, including payments to an advanced study fund and pension arrangement and car expense reimbursement, multiplied by 18. A "change in control" is defined under the change in control employee retention plan (the "CIC Plan") as

follows: (1) the consummation of any merger, consolidation, reorganization, or similar transaction or series of related transactions of the Company with another entity, other than a merger, consolidation, reorganization, or similar transaction or series of related transactions which would result in the shareholders of the Company immediately preceding the transaction beneficially owning, immediately after the transaction, at least 50% of the combined voting power of the outstanding securities of the surviving or resulting entity (or its parent); (2) any "person" (as such term is used in Sections 13(d) and 14(d) of the U.S. Exchange Act of 1934 ("Exchange Act")) or "group" (two or more persons acting as a partnership, limited partnership, syndicate or other group for the purpose of acquiring, holding, or disposing of the applicable securities referred to herein) becomes the "beneficial owner" (as defined in Rule 13d-3 of the Exchange Act), directly or indirectly, of securities of the Company representing fifty percent (50%) or more of the total voting power represented by the Company's then-outstanding voting securities; (3) the election of a board of directors over a three-year period or less, the majority of which is not supported by at least a majority of the then existing board of directors of the Company; or (4) any sale, lease, exchange, or other transfer (in one transaction or a series of related transactions) of all or substantially all of the assets of the Company (other than to an entity controlled by the Company).

(6) Mr. Rick Scruggs' employment term as the Company's Chief Commercial Officer provide that Mr. Scruggs is entitled to a monthly base gross salary of approximately $52,250. Mr. Scruggs is further entitled to vacation days, sick days and convalescence pay in accordance with the market practice and applicable law, monthly remuneration for a study fund, contribution by the Company to an insurance policy and pension fund, and additional benefits, including communication expenses. Mr. Scruggs's employment terms include an advance notice period of 60 days by either party. During such an advance notice period, Mr. Scruggs will be entitled to all of the compensation elements, and to the continuation of vesting of any options or restricted shares granted to him. Additionally, in the event Mr. Scruggs's employment is terminated in connection with a "change in control" he will be entitled to a special one-time payment equal to his then-current monthly salary and retirement benefits, including payments to an advanced study fund and pension arrangement, multiplied by 12. A "change in control" is defined in the same manner as defined for Mr. Ben-Asher as described in footnote (5) above.

Employment Agreements

We have entered into employment or consultant agreements with each of our executive officers. All of these agreements contain customary provisions regarding non-competition, confidentiality of information and assignment of inventions. However, the enforceability of the non-competition provisions may be limited under applicable laws.

For information on exemption and indemnification letters granted to our directors and officers, please see "Item 6 – C. Board Practices – Exemption, Insurance and Indemnification of Directors and Officers."

Director Compensation

We currently pay our non-executive directors (i) an annual cash fee retainer of $40,000, (ii) a committee membership annual cash fee retainer of $10,000 to each Audit Committee member, $8,000 to each Compensation Committee member, and $1,500 to each Investment Committee member, and (iii) a committee chairperson annual cash fee retainer in an amount that is higher than the annual cash fee payable to other members of that committee (as described in clause (ii) above) by 50% to each of the Audit Committee and Compensation Committee chairs and by 10% to the Investment Committee chair (without duplication of the fees paid under clause (ii)).

Change in Control Retention Plan and Agreements

We have adopted a change in control employee retention plan and entered into employment agreements providing for compensation to Company employees, in the event of a change in control (as defined by the plan and the employment agreements), subject to the satisfaction of various conditions. Compensation to employees would be up to 12 months' salary depending on employee seniority and years with the Company.

Compensation Policy

On June 24, 2019, our shareholders approved the Compensation Policy for our directors and officers in accordance with the Israeli Companies Law, pursuant to which we are required to determine the compensation of our directors and officers, and which must be approved by our shareholders every three years. The policy was previously approved by our board of directors, upon the recommendation of our compensation committee. The shareholders approved amendments to the Compensation Policy on July 26, 2021.

The Compensation Policy is in effect for three years from the 2019 annual general meeting. Our Compensation Policy principles were designed to grant proper, fair and well-considered remuneration to our officers, in alignment with our long-term best interests and overall organizational strategy. Part of the rationale is that our Compensation Policy should encourage our officers to identify with our objectives, and an increase in officer satisfaction and motivation should retain the employment of high-quality officers in our service over the long term.

C. Board Practices

Appointment of Directors and Terms of Officers

Pursuant to our articles of association, the size of our board of directors shall be no less than five persons and no more than eleven persons, including any external directors whose appointment is required by law. The directors who are not external directors are divided into three classes, as nearly equal in number as possible. At each annual general meeting, which is required to be held annually, but not more than fifteen months after the prior annual general meeting, the term of one class of directors expires, and the directors of such class are re-nominated to serve an additional three-year term that expires at the annual general meeting held in the third year following such election (other than any director nominated for election by Cosmo pursuant to the Company's subscription agreement with Cosmo, whose term of office may expire earlier depending on the beneficial ownership by the Cosmo investor of the Cosmo shares). This process continues indefinitely. A simple majority shareholder vote may elect directors for a term of less than three years in order to ensure that the three groups of directors have as equal a number of directors as possible as provided above. The directors of the first class, currently consisting of Eric Swenden and Ofer Tsimchi, will hold office until our annual general meeting to be held in the year 2024. The directors of the second class, currently consisting of Dror Ben-Asher, Dr. Kenneth Reed and Alla Felder, will hold office until our annual general meeting to be held in the year 2022. The directors of the third class, currently consisting of Dr. Shmuel Cabilly and Rick Scruggs, will hold office until our annual general meeting to be held in the year 2023. Until the next annual general meeting, the board of directors may elect new directors to fill vacancies or increase the number of members of the board of directors up to the maximum number provided in our articles of association. Any director so appointed may hold office until the first general shareholders' meeting convened after the appointment. See "Item 6. Directors, Senior Management and Employees – C. Board Practices – Independent and External Directors – Israeli Companies Law Requirements" below for a description of the adoption by the Company of the corporate governance exemptions set forth in Regulation 5D of the Israeli Companies Regulations (Relief for Public Companies with Shares Listed for Trading on a Stock Market Outside of Israel), 5760-2000, including with respect to external directors.

Pursuant to the Israeli Companies Law, one may not be elected and may not serve as a director in a public company if he or she does not have the required qualifications and the ability to dedicate an appropriate amount of time for the performance of his duties as a director in the company, taking into consideration, among other things, the special needs and size of the company. In addition, a public company may convene an annual general meeting of shareholders to elect a director, and may elect such director, only if prior to such shareholders meeting, the nominee declares, among other things, that he or she possesses all of the required qualifications to serve as a director (and lists such qualifications in such declaration) and has the ability to dedicate an appropriate amount of time for the performance of his duties as a director of the company.

Under the Israeli Companies Law, entry by a public company into a contract with a non-controlling director as to the terms of his office, including exculpation, indemnification or insurance, requires the approval of the compensation committee, the board of directors and the shareholders of the company.

The Israeli Companies Law requires that the terms of service and engagement of the chief executive officer, directors or controlling shareholders (or a relative thereof) receive the approval of the compensation committee, board of directors, and shareholders, subject to limited exceptions. The appointment and terms of office of a company's officers, other than directors and the general manager (i.e., chief executive officer) are subject to the approval by first, the company's compensation committee; second, the company's board of directors, in each case subject to the company's compensation policy, and then approved by its shareholders. However, in special circumstances, they may approve the appointment and terms of office of officers inconsistent with such policy, provided that (i) they have considered those provisions that must be included in the compensation policy according to the Israeli Companies Law and (ii) shareholder approval is obtained (by a majority of shareholders that does not include the controlling shareholders of the company and any shareholders interested in the approval of the compensation). However, if the shareholders of the company do not approve a compensation arrangement with an officer inconsistent with the company's compensation policy, in special situations the compensation committee and the board of directors may override the shareholders' decision if each of the compensation committee and the board of directors provide detailed reasons for their decision. In addition, non-material amendments to the compensation of a public company's officers (other than the chief executive officer and the directors) may be approved by the chief executive officer of the company if the company's compensation policy establishes that non-material amendments within the parameters established in the compensation policy may be approved by the chief executive officer, so long as the compensation is consistent with the company's compensation policy. An amendment to the Israeli Companies Law requires that the board and shareholders (with approval by a "special majority" as further discussed below) adopt a compensation policy applicable to the company's directors and officers which must take into account, among other things, providing proper incentives to directors and officers, the risk management of the company, the officer's contribution to achieving corporate objectives and increasing profits, and the function of the officer or director. Under the Israeli Companies Law, a "special majority" requires (i) the vote of at least a majority of the shares held by shareholders who are not controlling shareholders or have a personal interest in the proposal (shares held by abstaining shareholders are not taken into account); or (ii) that the aggregate number of shares voting against the proposal held by such shareholders does not exceed 2% of the company's voting shareholders.

The compensation paid to a public company's chief executive officer is required to be approved by, first, the company's compensation committee; second, the company's board of directors; and third, unless exempted under the regulations promulgated under the Israeli Companies Law, by the company's shareholders (by a special majority vote as discussed above with respect to the approval of director compensation). However, if the shareholders of the company do not approve the compensation arrangement with the chief executive officer, the compensation committee and board of directors may override the shareholders' decision if each of the compensation committee and the board of directors provide a detailed report for their decision. The renewal or extension of the engagement with a public company's chief executive officer need not be approved by the shareholders of the company if the terms and conditions of such renewal or extension are no more beneficial than the previous engagement or there is no substantial difference in the terms and conditions under the circumstances, and the terms and conditions of such renewal or extension are in accordance with the company's compensation policy. The compensation committee and board of directors approval should be in accordance with the company's stated compensation policy; however, in special circumstances, they may approve compensation terms of a chief executive officer that are inconsistent with such policy provided that they have considered those provisions that must be included in the compensation policy according to the Israeli Companies Law and that shareholder approval was obtained (by a special majority vote as discussed above with respect to the approval of director compensation). The compensation committee may waive the shareholder approval requirement with regards to the approval of the initial engagement terms of a candidate for the chief executive officer position, if they determine that the compensation arrangement is consistent with the company's stated compensation policy, and that the chief executive officer did not have a prior business relationship with the company or a controlling shareholder of the company and that subjecting the approval of the engagement to a shareholder vote would impede the company's ability to employ the chief executive officer candidate. The engagement with a public company's chief executive officer need not be approved by the shareholders of the company with respect to the period from the commencement of the engagement until the next shareholder meeting convened by the company, if the terms and conditions of such engagement were approved by the compensation committee and the board of directors of the company, the terms and conditions of such engagement are in accordance with the company's compensation policy approved in accordance with the Israeli Companies Law, and if the terms and conditions of such engagement are no more beneficial than the terms and conditions of the person previously serving in such role or there is no substantial difference in the terms and conditions of the previous engagement versus the new one under the circumstances, including the scope of engagement.

We have a service contract with one of our directors, Dror Ben-Asher, that provides for benefits upon termination of his employment as director. For more information, see "Item 6. Directors, Senior Management and Employees – B. Compensation."

Independent and External Directors – Israeli Companies Law Requirements

We are subject to the provisions of the Israeli Companies Law. The Israeli Minister of Justice has adopted regulations exempting companies like us whose shares are traded outside of Israel from some provisions of the Israeli Companies Law.

Under the Israeli Companies Law, except as provided below, companies incorporated under the laws of Israel whose shares are either (i) listed for trading on a stock exchange or (ii) have been offered to the public in or outside of Israel and are held by the public (Public Company) are required to appoint at least two external directors.

Our board of directors has resolved to adopt the corporate governance exception set forth in Regulation 5D of the Israeli Companies Regulations (the "Regulation"). In accordance with the Regulation, a public company with securities listed on certain foreign exchanges, including the Nasdaq Stock Market, that satisfies the applicable foreign country laws and regulations that apply to companies organized in that country relating to the appointment of independent directors and composition of audit and compensation committees and have no controlling shareholder are exempt from the requirement to appoint external directors or comply with the audit committee and compensation committee composition requirements under the Israeli Companies Law. In accordance with our board of directors' resolution, pursuant to the Regulation, we intend to comply with the Nasdaq Listing Rules in connection with a majority of independent directors on the board of directors and in connection with the composition of each of the audit committee and the compensation committee, in lieu of such requirements of the Israeli Companies Law.

The Israeli Companies Law provides that a person may not be appointed as an external director if the person is a relative of the controlling shareholder or if the person or the person's relative, partner, employer, someone to whom he is subordinated directly or indirectly or any entity under the person's control, has, as of the date of the person's appointment to serve as external director, or had, during the two years preceding that date, any affiliation with us, our controlling shareholder, any relative of our controlling shareholder, as of the date of the person's appointment to serve as external director, or any entity in which, currently or within the two years preceding the appointment date, the controlling shareholder was the company or the company's controlling shareholder; and in a company without a controlling shareholder or without a shareholder holding 25% or more of the voting rights in the company, any affiliation to the chairman of the board of directors, to the general manager (Chief Executive Officer), to a shareholder holding 5% or more of the company's shares or voting rights, or to the chief officer in the financial or economic field as of the date of the person's appointment. The term "affiliation" includes:

- an employment relationship;
- a business or professional relationship maintained on a regular basis;
- control; and
- service as an officer, other than service as a director who was appointed in order to serve as an external director of a company when such company was about to make an initial public offering.

Under the Israeli Companies Law, an "officer" is defined as a general manager, chief business manager, deputy general manager, vice general manager, any person filing any of these positions in a company even if he holds a different title, director or any manager directly subordinate to the general manager.

However, a person may not serve as an external director if the person or the person's relative, partner, employer, someone to whom he is subordinated directly or indirectly or any entity under the person's control has a business or professional relationship with an entity which has an affiliation with is prohibited as detailed above, even if such relationship is not on a regular basis (excluding negligible relationship). In addition, an external director may not receive any compensation other than the compensation permitted by the Israeli Companies Law.

Regulations under the Israeli Companies Law provide for various instances and kinds of relationships in which an external director will not be deemed to have "affiliation" with the public company for which he serves or is a candidate for serving as an external director.

No person can serve as an external director if the person's positions or other businesses create, or may create, a conflict of interests with the person's responsibilities as a director or may impair his ability to serve as a director. In addition, a person who is a director of a company may not be elected as an external director of another company if, at that time, a director of the other company is acting as an external director of the first company.

Except for the cessation of classification of directors as external directors in connection with the adoption by certain companies listed on foreign stock exchanges, including the Nasdaq Stock Market, of the corporate governance exceptions set forth in the Regulation, as described above, until the lapse of two years from termination of office, a company, its controlling shareholder, or a company controlled by him may not engage an external director, his spouse, or child to serve as an officer in the company or in any entity controlled by the controlling shareholder and cannot employ or receive professional services for consideration from that person, and may not grant such person any benefit either directly or indirectly, including through a corporation controlled by that person. The same restrictions apply to relatives other than a spouse or a child, but such limitations may only apply for one year from the date such external director ceased to be engaged in such capacity. In addition, if at the time an external director is appointed all current members of the board of directors who are neither controlling shareholders nor relatives of controlling shareholders are of the same gender, then the external director to be appointed must be of the other gender.

Under the Israeli Companies Law, a public company is required to appoint as an external director, a person who has "professional expertise" or a person who has "financial and accounting expertise," provided that at least one of the external directors must have "financial and accounting expertise." However, if at least one of our other directors (1) meets the independence requirements of the Exchange Act, (2) meets the standards of the Nasdaq Stock Market for membership on the audit committee and (3) has financial and accounting expertise as defined in the Israeli Companies Law and applicable regulations, then neither of our external directors is required to possess financial and accounting expertise as long as both possess other requisite professional qualifications. The determination of whether a director possesses financial and accounting expertise is made by the board of directors.

Under the Israeli Companies Law regulations, a director having financial and accounting expertise is a person who, due to his education, experience and qualifications is highly skilled in respect of, and understands, business-accounting matters and financial reports in a manner that enables him to understand in depth the company's financial statements and to stimulate discussion regarding the manner in which the financial data is presented. Under the Israeli Companies Law regulations, a director having professional expertise is a person who has an academic degree in either economics, business administration, accounting, law or public administration or another academic degree or has completed other higher education studies, all in an area relevant to the main business sector of the company or in a relevant area of the board of directors position, or has at least five years of experience in one of the following or at least five years of aggregate experience in two or more of the following: a senior management position in the business of a corporation with a substantial scope of business, in a senior position in the public service or a senior position in the main field of the company's business.

Under the Israeli Companies Law, each Israeli public company is required to determine the minimum number of directors with "accounting and financial expertise" that such company believes appropriate in light of the company's type, size, the scope and complexity of its activities and other factors. Once a company has made this determination, it must ensure that the necessary appointments to the board of directors are made in accordance with this determination. Our board of directors determined that two directors with "accounting and financial expertise" is appropriate for us. Our board of directors currently has three directors with such "accounting and financial expertise."

External directors are to be elected by a majority vote at a shareholders' meeting, provided that either (1) the majority of shares voted at the meeting, including at least a majority of the votes of the shareholders who are not controlling shareholders (as defined in the Israeli Companies Law), do not have a personal interest in the appointment (excluding a personal interest which did not result from the shareholder's relationship with the controlling shareholder), vote in favor of the election of the director without taking abstentions into account; or (2) the total number of shares of the above-

mentioned shareholders who voted against the election of the external director does not exceed two percent of the aggregate voting rights in the company.

The initial term of an external director is three years and may be extended for two additional three-year terms under certain circumstances and conditions. Nevertheless, regulations under the Israeli Companies Law provide that companies, whose shares are listed for trading the Nasdaq Stock Market, may appoint an external director for additional three-year terms, under certain circumstances and conditions. External directors may be removed only in a general meeting, by the same percentage of shareholders as is required for their election, or by a court, and in both cases only if the external directors cease to meet the statutory qualifications for their appointment or if they violate their duty of loyalty to us. Each committee authorized to exercise any of the powers of the board of directors is required to include at least one external director and the audit committee is required to include all of the external directors.

An external director is entitled to compensation and reimbursement of expenses in accordance with regulations promulgated under the Israeli Companies Law and is otherwise prohibited from receiving any other compensation, directly or indirectly, in connection with serving as a director except for certain exculpation, indemnification and insurance provided by the company.

Committees

Israeli Companies Law Requirements

Our board of directors has established three standing committees, the audit committee, the compensation committee, and the investment committee.

Audit Committee

Under the Israeli Companies Law, the board of directors of a public company must appoint an audit committee. Except in the case of companies listed on foreign stock exchanges, including the Nasdaq Stock Market, which have adopted the corporate governance exceptions set forth in the Regulation, such as us, as described under "- Independent and External Directors – Israeli Companies Law Requirements", who are exempt from the audit committee composition requirements under the Companies Law, an audit committee of a public company under the Israeli Companies Law must be comprised of at least three directors including all of the external directors.

In addition, the Israeli Companies Law provides that the majority of the members of the audit committee, as well as the majority of members present at audit committee meetings, must be "independent" (as such term is defined below) and the chairman of the audit committee must be an external director. In addition, the following are disqualified from serving as members of the audit committee: the chairman of the board of directors, the controlling shareholder and her or his relatives, any director employed by the company or by its controlling shareholder or by an entity controlled by the controlling shareholder, a director who regularly provides services to the company or to its controlling shareholder or to an entity controlled by the controlling shareholder, and any director who derives most of its income from the controlling shareholder. Any persons not qualified from serving as a member of the audit committee may not be present at the audit committee meetings during the discussion and at the time decisions are made, unless the chairman of the audit committee determines that the presence of such person is required to present a matter to the meeting or if such person qualifies under an available exemption in the Israeli Companies Law.

An "independent director" is defined as an external director or a director who meets the following conditions: (i) satisfies certain conditions for appointment as an external director (as described above) and the audit committee has determined that such conditions have been met and (ii) has not served as a director of the company for more than nine consecutive years, with any interruption of up to two years in service not being deemed a disruption in the continuity of such service.

The role of the audit committee under the Israel Companies Law is to examine suspected flaws in our business management, in consultation with the internal auditor or our independent accountants and suggest an appropriate course

of action in order to correct such flaws. In addition, the approval of the audit committee is required to effect specified actions and related party transactions.

Additional functions to be performed by the audit committee include, among others, the following:

- the determination whether certain related party actions and transactions are "material" or "extraordinary" for purposes of the requisite approval procedures;
- to determine whether to approve actions and transactions that require audit committee approval under the Israel Companies Law;
- to assess the scope of work and compensation of the company's independent accountant;
- to assess the company's internal audit system and the performance of its internal auditor and if the necessary resources have been made available to the internal auditor considering the company's needs and size; and
- to determine arrangements for handling complaints of employees in relation to suspected flaws in the business management of the company and the protection of the rights of such employees.

Our audit committee also serves as our financial statements committee. The members of our audit committee are Alla Felder (chairperson), Ofer Tsimchi and Eric Swenden.

An amendment to the Israeli Companies Law allows a company whose audit committee's composition meets the requirements set for the composition of a compensation committee (as further detailed below) to have one committee acting as both audit and compensation committees. As of the date of this Annual Report, we have not elected to have one committee acting as both the audit and the compensation committees.

Compensation Committee

According to the Israeli Companies Law, the board of directors of a public company must establish a compensation committee. Except in the case of companies listed on foreign stock exchanges, including the Nasdaq Stock Market, which have adopted the corporate governance exceptions set forth in the Regulation, such as us, as described under "- Independent and External Directors – Israeli Companies Law Requirements", who are exempt from the compensation committee composition requirements under the Companies Law, the Israeli Companies Law requires that the compensation committee must consist of at least three directors and include all of the external directors who must constitute a majority of its members. The remaining members must be qualified to serve on the audit committee pursuant to the Israeli Companies Law requirements described above. The compensation committee chairman must be an external director and any persons not qualified from serving as a member of the compensation committee may not be present at the compensation committee meetings during the discussion and at the time decisions are made, unless the chairman of the compensation committee determines that the presence of such person is required to present a matter to the meeting or if such person qualifies under an available exemption in the Israeli Companies Law.

Our compensation committee, which consists of Ofer Tsimchi (chairman), Dr. Kenneth Reed and Alla Felder, administers issues relating to our global compensation plan with respect to our employees, directors, and consultants. Our compensation committee is responsible for making recommendations to the board of directors regarding the issuance of share options and compensation terms for our directors and officers and for determining salaries and incentive compensation for our executive officers and incentive compensation for our other employees and consultants. Each of the members of the compensation committee is "independent" as such term is defined in the Nasdaq Listing Rules.

Investment Committee

Our investment committee, which consists of Eric Swenden (chairman), Alla Felder and Ofer Tsimchi, assists the board in fulfilling its responsibilities with respect to our financial and investment strategies and policies, including determining policies and guidelines on these matters and monitoring implementation. It is also authorized to approve certain financial transactions and review risk factors associated with management of our finances and the mitigation of such risks, as well as financial controls and reporting and various other finance-related matters.

Nasdaq Stock Market Requirements

Under the Nasdaq Listing Rules, we are required to maintain an audit committee consisting of at least three members, all of whom are independent and are financially literate and one of whom has accounting or related financial management expertise.

The independence requirements of Rule 10A-3 of the Exchange Act implement two basic criteria for determining independence:

- audit committee members are barred from accepting directly or indirectly any consulting, advisory or other compensatory fee from the issuer or an affiliate of the issuer, other than in the member's capacity as a member of the board of directors and any board committee; and
- audit committee members may not be an "affiliated person" of the issuer or any subsidiary of the issuer apart from her or his capacity as a member of the board of directors and any board committee.

The SEC has defined "affiliate" for non-investment companies as "a person that directly, or indirectly through one or more intermediaries, controls, or is controlled by, or is under common control with, the person specified." The term "control" is intended to be consistent with the other definitions of this term under the Exchange Act, as "the possession, direct or indirect, of the power to direct or cause the direction of the management and policies of a person, whether through the ownership of voting securities, by contract, or otherwise." A safe harbor has been adopted by the SEC, under which a person who is not an executive officer or 10% shareholder of the issuer would be deemed not to have control of the issuer.

In accordance with the Sarbanes-Oxley Act of 2002 and the Nasdaq Listing Rules, the audit committee is directly responsible for the appointment, compensation, and performance of our independent auditors. In addition, the audit committee is responsible for assisting the board of directors in reviewing our annual financial statements, the adequacy of our internal control and our compliance with legal and regulatory requirements. The audit committee also oversees our major financial risk exposures and policies for managing such potential risks, discusses with management and our independent auditor significant risks or exposure and assesses the steps management has taken to minimize such risk.

As noted above, the members of our audit committee include Alla Felder, Ofer Tsimchi and Eric Swenden, with Ms. Felder serving as chairperson. All members of our audit committee meet the requirements for financial literacy under the Nasdaq Listing Rules. Our board of directors has determined that each of Ms. Alla Felder, Mr. Ofer Tsimchi and Mr. Eric Swenden is an audit committee financial expert as defined by the SEC rules and all members of the audit committee have the requisite financial experience as defined by the Nasdaq Listing Rules. Each of the members of the audit committee is "independent" as such term is defined in Rule 10A-3(b)(1) under the Exchange Act.

Diversity of the Board of Directors

We are committed to diversity among our Board. The ability to incorporate a wide range of viewpoints, backgrounds, skills, and experience is critical to our success. By bringing together individuals with varying backgrounds, expertise, and perspectives into an inclusive and collaborative work environment, we believe we can better achieve our corporate objectives and deliver long-term, sustained value for our shareholders.

We recognize that gender diversity is a significant aspect of diversity and acknowledge the important role that women with appropriate and relevant skills and experience can play in contributing to the diversity of thought on the Board. As such, when reviewing and assessing the qualifications of possible nominees to the Board, our Board is guided by the following considerations:

- the competencies and skills necessary for the Board as a whole should possess;
- the experience and skill each new nominee will bring to the Board;
- the diversity of the Board as a whole and whether the new nominee would enhance such diversity; and
- whether the nominees can devote sufficient time and resources to his or her duties as a Board member.

Due to the size of the Company and Board, our activities, and our current number of employees across two geographies, we have not yet set measurable objectives or adopted a formal policy for achieving gender diversity on the Board. However, our Board and the Company continues to monitor and consider the level of female representation on the Board and, where appropriate, aim to recruit qualified female candidates as part of the selection process to fill vacancies. We will consider establishing measurable objectives as it develops further.

Corporate Governance Practices

Internal Auditor

Under the Israeli Companies Law, the board of directors must appoint an internal auditor proposed by the audit committee. The role of the internal auditor is, among others, to examine whether our actions comply with the law and orderly business procedure. Under the Israeli Companies Law, the internal auditor may not be an interested party, an officer or a director, a relative of an interested party, or a relative of an officer or a director, nor may the internal auditor be our independent accountant or its representative. In January 2018, Ms. Sharon Cohen, Lead Engagement Partner, Head of LS & HC Industry at Deloitte Israel, was elected to serve as our internal auditor.

Duties of Directors and Officers and Approval of Specified Related Party Transactions under the Israeli Companies Law

Fiduciary Duties of Officers

The Israeli Companies Law imposes a duty of care and a duty of loyalty on all directors and officers of a company, including directors and executive officers. The duty of care requires a director or an officer to act with the level of care, according to which a reasonable director or officer in the same position would have acted under the same circumstances.

The duty of care includes a duty to use reasonable means to obtain:

- information on the appropriateness of a given action brought for the directors' or officer's approval or performed by such person by virtue of such person's position; and
- all other important information pertaining to the previous actions.

The duty of loyalty requires a director or an officer to act in good faith and for the benefit of the company and includes a duty to:

- refrain from any action involving a conflict of interest between the performance of the director's or officer's duties in the company and such person's personal affairs;
- refrain from any activity that is competitive with the company's business;
- refrain from usurping any business opportunity of the company to receive a personal gain for the director, officer or others; and
- disclose to the company any information or documents relating to a company's affairs which the director or officer has received due to such person's position as a director or an officer.

Under the Israeli Companies Law, subject to certain exceptions, directors' compensation arrangements require the approval of the compensation committee, the board of directors and the shareholders.

The Israeli Companies Law requires that a director or an officer of a company promptly and, in any event, not later than the first board meeting at which the transaction is discussed, disclose any personal interest that he may have, and all related material facts or document known to such person, in connection with any existing or proposed transaction by the company. A personal interest of a director or an officer (which includes a personal interest of the director's or officer's relative) is in a company in which the director or officer or the director's or officer's relative is: (i) a shareholder which holds 5% or more of a company's share capital or its voting rights, (ii) a director or a general manager, or (iii) in which the director or officer has the right to appoint at least one director or the general manager. A personal interest also includes a personal

interest of a person who votes according to a proxy of another person, even if the other person has no personal interest, and a personal interest of a person who gave a proxy to another person to vote on his behalf – in each case, regardless whether discretion with respect to how to vote lies with the person voting or not. In the case of an extraordinary transaction, the director's or the officer's duty to disclose also applies to a personal interest of the director or officer's relative.

Under the Israeli Companies Law, an extraordinary transaction is a transaction:

- other than in the ordinary course of business;
- other than on market terms; or
- that is likely to have a material impact on the company's profitability, assets or liabilities.

Under the Israeli Companies Law, once a director or an officer complies with the above disclosure requirement, the board of directors may approve an ordinary transaction between the company and a director or an officer, or a third party in which a director or an officer has a personal interest, unless the articles of association provide otherwise. A transaction that does not benefit the company's interest cannot be approved. Subject to certain exceptions, the compensation committee and the board of directors must approve the conditions and term of office of an officer (who is not a director).

If the transaction is an extraordinary transaction, both the audit committee and the board of directors, in that order, must approve the transaction. Under specific circumstances, shareholder approval may also be required. Whoever has a personal interest in a matter, which is considered at a meeting of the board of directors or the audit committee, may not be present at this meeting or vote on this matter. However, if the chairman of the board of directors or the chairman of the audit committee has determined that the presence of such person is required to present a matter at the meeting; such officer holder may be present at the meeting. Notwithstanding the foregoing, if the majority of the directors have a personal interest in a matter, a director who has the personal interest in this matter may be present at this meeting or vote on this matter, but the board of directors' decision requires the shareholder approval.

Controlling Shareholder Transactions and Actions

Under the Israeli Companies Law, the disclosure requirements which apply to a director or an officer also apply to a controlling shareholder of a public company and to a person who would become a controlling shareholder as a result of a private placement. A controlling shareholder includes a person who has the ability to direct the activities of a company, other than if this power derives solely from his/her position on the board of directors or any other position with the company. In addition, for such purposes, a controlling shareholder includes a shareholder that holds 25% or more of the voting rights in a public company if no other shareholder owns more than 50% of the voting rights in the company. Extraordinary transactions with a controlling shareholder or in which a controlling shareholder has a personal interest, including a private placement in which a controlling shareholder has a personal interest; and the terms of engagement of the company, directly or indirectly, with a controlling shareholder or his or her relative (including through a corporation controlled by a controlling shareholder), regarding the company's receipt of services from the controlling shareholder, and if such controlling shareholder is also a director or an officer of the company or an employee, regarding his or her terms of office and employment, require the approval of the audit committee, the board of directors and the shareholders of the company, in that order. The shareholders' approval must include either:

- a majority of the shareholders who have no personal interest in the transaction and who are participating in the voting, in person, by proxy or by written ballot, at the meeting (votes abstaining not being taken into account); or
- the total number of shares voted against the proposal by shareholders without a personal interest does not exceed 2% of the aggregate voting rights in the Company.

In addition, any such transaction whose term is more than three years requires the above-mentioned approval every three years, unless, with respect to transactions not involving the receipt of services or compensation, the audit committee approves a longer term as reasonable under the circumstances.

However, under regulations, promulgated pursuant to the Israeli Companies Law, certain transactions between a company and its controlling shareholders, or the controlling shareholder's relative, do not require shareholder approval.

For information concerning the direct and indirect personal interests of certain of our directors or officers and principal shareholders in certain transactions with us, see "Item 7. Major Shareholders – B. Related Party Transactions."

The Israeli Companies Law requires that every shareholder that participates, either by proxy or in person, in a vote regarding a transaction with a controlling shareholder indicate whether or not that shareholder has a personal interest in the vote in question, the failure of which results in the invalidation of that shareholder's vote.

The Israeli Companies Law further provides that an acquisition of shares or voting rights in a public company must be made by means of a tender offer if as a result of the acquisition the purchaser would become a holder of 45% of the voting rights of the company, unless there is a holder of more than 45% of the voting rights of the company or would become a holder of 25% of the voting rights unless there is another person holding 25% of the voting rights. This restriction does not apply to:

- an acquisition of shares in a private placement, if the acquisition had been approved in a shareholders meeting under certain circumstances;
- an acquisition of shares from a holder of at least 25% of the voting rights, as a result of which a person would become a holder of at least 25% of the voting rights; and
- an acquisition of shares from a holder of more than 45% of the voting rights, as a result of which the acquirer would become a holder of more than 45% of the voting rights in the company.

The Israeli Companies Law further provides that a shareholder has a duty to act in good faith toward the company and other shareholders when exercising his rights and duties and must refrain from oppressing other shareholders, including in connection with the voting at a shareholders' meeting on:

- any amendment to the articles of association;
- an increase in the company's authorized share capital;
- a merger; or
- approval of certain transactions with control persons and other related parties, which require shareholder approval.

In addition, any controlling shareholder, any shareholder who knows that it possesses power to determine the outcome of a shareholder vote and any shareholder who, pursuant to the provisions of a company's articles of association, has the power to appoint or prevent the appointment of a director or an officer in the company, or has any other power over the company, is under a duty to act with fairness toward the company. Under the Israeli Companies Law, the laws that apply to a breach of a contract will generally also apply to a breach of the duty of fairness.

Exemption, Insurance, and Indemnification of Directors and Officers

Exemption of Officers and Directors

Under the Israeli Companies Law, a company may not exempt an officer or director from liability with respect to a breach of his duty of loyalty, but may exempt in advance an officer or director from liability to the company, in whole or in part, with respect to a breach of his duty of care, except in connection with a prohibited distribution made by the company, if so provided in its articles of association. Our articles of association provide for this exemption from liability for our directors and officers.

Directors' and Officers' Insurance

The Israeli Companies Law and our articles of association provide that, subject to the provisions of the Israeli Companies Law, we may obtain insurance for our directors and officers for any liability stemming from any act performed by an officer or director in his capacity as an officer or director, as the case may be with respect to any of the following:

- a breach of such officer's or director's duty of care to us or to another person;

- a breach of such officer's or director's duty of loyalty to us, provided that such officer or director acted in good faith and had reasonable cause to assume that his act would not prejudice our interests;
- a financial liability imposed upon such officer or director in favor of another person;
- financial liability imposed on the officer or director for payment to persons or entities harmed as a result of violations in administrative proceedings as described in Section 52(54)(a)(1)(a) of the Israeli Securities Law ("Party Harmed by the Breach");
- expenses incurred by such officer or director in connection with an administrative proceeding conducted in this matter, including reasonable litigation expenses, including legal fees; or
- a breach of any duty or any other obligation, to the extent insurance may be permitted by law.

Pursuant to the Compensation Policy, we may obtain a directors' and officers' liability insurance policy, which would apply to our or our subsidiaries' directors and officers, as they may be, from time to time, subject to the following terms and conditions: (a) the total insurance coverage under the insurance policy may not exceed $100 million; and (b) the purchase of such policy must be approved by the Compensation Committee (and, if required by law, by the board of directors) which shall determine that such policy reflects the current market conditions and that it does not materially affect the Company's profitability, assets or liabilities. In addition, pursuant to our Compensation Policy, should we sell our operations (in whole or in part) or in case of a merger, spin-off or any other significant business combination involving us or part or all of our assets, we may obtain a director's and officers' liability insurance policy (run-off) for our directors and officers in office with regard to the relevant operations, subject to the following terms and conditions: (a) the insurance term may not exceed seven years; (b) the coverage amount may not exceed $100 million. ; and (c) the purchase of such policy must be approved by the Compensation Committee (and, if required by law, by the board of directors) which shall determine that such policy reflects the current market conditions and that it does not materially affect the Company's profitability, assets or liabilities. The Compensation Policy is in effect for three years from the 2019 annual general meeting.

Pursuant to the foregoing approvals, we carry directors' and officers' liability insurance. This insurance is renewed on an annual basis.

Indemnification of Officers and Directors

The Israeli Companies Law provides that a company may indemnify an officer or director for payments or expenses associated with acts performed in his capacity as an officer or director of the company, provided the company's articles of association include the following provisions with respect to indemnification:

- a provision authorizing the company to indemnify an officer or director for future events with respect to a monetary liability imposed on him in favor of another person pursuant to a judgment (including a judgment given in a settlement or an arbitrator's award approved by the court), so long as such indemnification is limited to types of events which, in the board of directors' opinion, are foreseeable at the time of granting the indemnity undertaking given the company's actual business, and in such amount or standard as the board of directors deems reasonable under the circumstances. Such undertaking must specify the events that, in the board of directors' opinion, are foreseeable in view of the company's actual business at the time of the undertaking and the amount or the standards that the board of directors deemed reasonable at the time;
- a provision authorizing the company to indemnify an officer or director for future events with respect to reasonable litigation expenses, including counsel fees, incurred by an officer or director in which he is ordered to pay by a court, in proceedings that the company institutes against him or instituted on behalf of the company or by another person, or in a criminal charge of which he was acquitted, or a criminal charge in which he was convicted of a criminal offense that does not require proof of criminal intent;
- a provision authorizing the company to indemnify an officer or director for future events with respect to reasonable litigation fees, including attorney's fees, incurred by an officer or director due to an investigation or proceeding filed against him by an authority that is authorized to conduct such investigation or proceeding, and that resulted without filing an indictment against him and without imposing on him financial obligation in lieu of a criminal proceeding, or that resulted without filing an indictment against him but with imposing on him a financial obligation as an alternative to a criminal proceeding in respect of an offense that does not require the proof of criminal intent or in connection with a monetary sanction;

- a provision authorizing the company to indemnify an officer or director for future events with respect to a Party Harmed by the Breach;
- a provision authorizing the company to indemnify an officer or director for future events with respect to expenses incurred by such officer or director in connection with an administrative proceeding, including reasonable litigation expenses, including legal fees; and
- a provision authorizing the company to indemnify an officer or director retroactively.

Limitations on Insurance, Exemption and Indemnification

The Israeli Companies Law and our articles of association provide that a company may not exempt or indemnify a director or an officer nor enter into an insurance contract, which would provide coverage for any monetary liability incurred as a result of any of the following:

- a breach by the officer or director of his duty of loyalty, except for insurance and indemnification where the officer or director acted in good faith and had a reasonable basis to believe that the act would not prejudice the company;
- a breach by the officer or director of his duty of care if the breach was done intentionally or recklessly, except if the breach was solely as a result of negligence;
- any act or omission done with the intent to derive an illegal personal benefit; or
- any fine, civil fine, monetary sanctions, or forfeit imposed on the officer or director.

In addition, under the Israeli Companies Law, exemption of, indemnification of, and procurement of insurance coverage for, our directors and officers must be approved by our audit committee and board of directors and, in specified circumstances, by our shareholders.

Letters of Indemnification

We may provide a commitment to indemnify in advance any director or officer of ours in the course of such person's position as our director or officer, all subject to the letter of indemnification, as approved by our shareholders from time to time and in accordance with our articles of association. We may provide retroactive indemnification to any officer to the extent allowed by the Israeli Companies Law. As approved by our shareholders on July 26, 2021, the amount of the advance indemnity is limited to the higher of 25% of our then shareholders' equity, per our most recent annual financial statements, or $10 million.

As part of the indemnification letters, we exempted our directors and officers, in advance, to the extent permitted by law, from any liability for any damage incurred by them, either directly or indirectly, due to the breach of an officer's or director's duty of care *vis-à-vis* us, within his acts in his capacity as an officer or director. The letter provides that so long as not permitted by law, we do not exempt an officer or director in advance from his liability to us for a breach of the duty of care upon distribution, to the extent applicable to the officer or director, if any. The letter also exempts an officer or director from any liability for any damage incurred by him, either directly or indirectly, due to the breach of the officer or director's duty of care *vis-à-vis* us, by his acts in his capacity as an officer or director prior to the letter of exemption and indemnification becoming effective.

D. Employees

As of December 31, 2021, we had 201 employees, of which 19 provide services in Israel and 182 in the U.S. In addition, we also receive services from 10 consultants, of which three are in the U.S., four in Canada and three in Israel.

	As of December 31,					
	2021		2020		2019	
	Company Employees	Consultants	Company Employees	Consultants	Company Employees	Consultants
Management and administration	17	—	15	—	13	—
Research and development	2	10	2	11	2	12
Commercial operations	182	—	165	—	128	—

While none of our employees are party to a collective bargaining agreement, certain provisions of the collective bargaining agreements between the Histadrut (General Federation of Labor in Israel) and the Coordination Bureau of Economic Organizations (including the Industrialists' Associations) are applicable to our employees by order of the Israel Ministry of Labor. These provisions primarily concern the length of the workday, minimum daily wages for professional workers, pension fund benefits for all employees, insurance for work-related accidents, procedures for dismissing employees, determination of severance pay and other conditions of employment. We generally provide our employees with benefits and working conditions beyond the required minimums.

We have never experienced any employment-related work stoppages and believe our relationship with our employees is good.

E. Share Ownership

The following table sets forth information regarding the beneficial ownership of our outstanding Ordinary Shares as of March 16, 2022, of each of our directors and executive officers individually and as a group based on information provided to us by our directors and executive officers. The information in this table is based on 526,842,294 Ordinary Shares outstanding as of such date. The number of Ordinary Shares beneficially owned by a person includes Ordinary Shares subject to options held by that person that were currently exercisable at, or exercisable within 60 days of March 17, 2022. The Ordinary Shares issuable under these options are treated as if they were outstanding for purposes of computing the

percentage ownership of the person holding these options but not the percentage ownership of any other person. None of the holders of the Ordinary Shares listed in this table have voting rights different from other holders of the Ordinary Shares.

	Number of Shares Beneficially Held	Percent of Class
Directors		
Dr. Kenneth Reed (1)	8,245,340	1.57 %
Dr. Shmuel Cabilly (2)	5,536,080	1.05%
Eric Swenden (3)	1,514,650	*
Ofer Tsimchi (4)	525,310	*
Alla Felder (5)	218,120	*
Executive officers		
Dror Ben-Asher (6)	7,254,370	1.38 %
Reza Fathi, Ph.D. (7)	2,395,290	*
Adi Frish (8)	2,117,370	*
Gilead Raday (9)	1,945,000	*
Guy Goldberg (10)	2,014,370	*
Micha Ben Chorin (11)	1,636,250	*
Rick D. Scruggs (12)	2,120,970	*
June Almenoff (13)	281,870	*
All directors and executive officers as a group (13 persons)	35,804,990	6.81 %

* Less than 1.0%

(1) Includes options to purchase 548,090 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.49 and $0.70 per share and the options expire between 2023 and 2031. Number of shares beneficially held also includes shares held by family members.

(2) Includes options to purchase 492,810 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.49 and $0.71 per share and the options expire between 2023 and 2031.

(3) Includes options to purchase 451,560 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.49 and $0.71 per share and the options expire between 2023 and 2031.

(4) Includes options to purchase 525,310 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.49 and $0.71 per share and the options expire between 2024 and 2031.

(5) Includes options to purchase 208,120 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.49 and $0.71 per share and the options expire between 2029 and 2031.

(6) Includes options to purchase 3,793,750 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.49 and $0.71 per share and the options expire between 2023 and 2031.

(7) Includes options to purchase 2,055,290 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.49 and $0.71 per share, and the options expire between 2022 and 2031.

(8) Includes options to purchase 1,906,250 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.49 and $0.71 per share and the options expire between 2022 and 2031.

(9) Includes options to purchase 1,945,000 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.49 and $0.71 per share and the options expire between 2022 and 2031.

(10) Includes options to purchase 1,984,370 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.49 and $0.71 per share, and the options expire between 2022 and 2031.

(11) Includes options to purchase 1,606,250 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.49 and $0.71 per share and the options expire between 2023 and 2031.

(12) Includes options to purchase 1,200,970 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.66 and $0.70 per share and the options expire between 2023 and 2031.

(13) Includes options to purchase 260,370 Ordinary Shares exercisable within 60 days of March 17, 2022. The exercise price of these options ranges between $0.70 and $0.71 per share and the options expire between 2023 and 2031.

Award Plans

Amended and Restated Award Plan

Our 2010 Amended and Restated Award Plan (2010) ("Award Plan") provides for the granting of Ordinary Shares, ADSs, stock options under various tax regimes in Israel and the U.S., RSUs, restricted shares, and other share-based awards to our directors, officers, employees, consultants and service providers and individuals who are their employees, and to the directors, officers, employees, consultants and service providers of our subsidiaries and affiliates. The Award Plan provides for awards to be issued at the determination of our board of directors in accordance with applicable laws. As of March 16, 2022, there were 83,078,290 Ordinary Shares issuable upon the exercise or vesting of outstanding awards under the Award Plan and 14,639,800 Ordinary Shares available for future issuance under the Award Plan. Our Award Plan provides that the maximum number of Ordinary Shares that may be issued under the Award Plan will automatically be increased on January 1, April 1, July 1 and October 1 of each calendar year such that immediately following such increase the maximum number of Ordinary Shares that may be issued under the Award Plan will be equal to sixteen and a half percent (16.5%) of the number of outstanding Ordinary Shares on a fully-diluted basis on the last day of immediately preceding fiscal quarter.

Administration of Our Amended and Restated Award Plan

Our Award Plan is administered by our compensation committee regarding the granting of awards and the terms of awards grants, including the exercise price, method of payment, vesting schedule, acceleration of vesting and the other matters necessary in the administration of these plans. Options and other awards granted under the Award Plan to eligible Israeli employees, directors and officers are granted under Section 102 of the Israel Income Tax Ordinance pursuant to which the options or the Ordinary Shares issued upon their exercise must be allocated or issued to a trustee and be held in trust for two years from the date upon which such options were granted in order to benefit from the provisions of Section 102. Under Section 102, any tax payable by an employee from the grant or exercise of the options is deferred until the transfer of the options or Ordinary Shares by the trustee to the employee or upon the sale of the options or Ordinary Shares, and gains may qualify to be taxed as capital gains at a rate equal to 25%, subject to compliance with specified conditions. See "Item 10. Additional Information – E. Taxation – Israeli Tax Considerations."

Options granted under the Award Plan as amended generally vest over a period of 4 years and expire ten (10) years after the grant date. The Award Plan, however, permits options to have a term of up to 10 years. If we terminate a grantee for cause (as such term is defined in the Award Plan) the right to exercise all the options granted to the grantee, the grantee's vested and unvested options will expire immediately, on the earlier of:

- termination of the engagement; or
- the date of the notice of the termination of the engagement.

Upon termination of employment for any other reason, other than in the event of death, disability, retirement after the age of 60, a merger or other change in control approved by the board of directors, or for cause, all unvested options will expire and all vested options will generally be exercisable for 90 days following termination, or such other period as determined by the plan administrator, subject to the terms of the Award Plan and the governing option agreement.

Upon termination in the event of a merger or other change in control approved by the board of directors, the grantee will be entitled at the time of termination to full acceleration of all the options granted prior to the event.

Under our Award Plan, as amended, in the event any person, entity or group that was not an interested party at the time of our initial public offering on the TASE becoming a controlling shareholder, all options granted by us under the plan will be accelerated, so that the grantee will be entitled to exercise all of those options. A "controlling shareholder" in this paragraph is a controlling shareholder, as defined in the Israel Securities Law, 1968. An "interested party" is defined in the Securities Law and includes, among others:

- a holder of 5% or more of the outstanding shares or voting rights of an entity;
- a person entitled to appoint one or more of the directors or chief executive officer of an entity;

- a director of an entity or its chief executive officer;
- an entity, in which an individual referred to above holds 25% or more of its outstanding shares or voting rights, or is entitled to appoint 25% or more of its directors; or
- a person who initiated the establishment of the entity.

Upon termination of employment due to death or disability, or retirement after the age of 60, subject to the board of directors' approval, all the vested options at the time of termination will be exercisable for 24 months, or such other period as determined by the plan administrator, subject to the terms of the Award Plan and the governing option agreement.

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major Shareholders

The following table sets forth certain information regarding the beneficial ownership of our outstanding Ordinary Shares as of March 16, 2022, by each person or entity known to beneficially own 5.0% or more of our outstanding Ordinary Shares. The information with respect to beneficial ownership of the Ordinary Shares is given based on information reported in such shareholder's Schedule 13G, and if no Schedule 13G was filed, based on the information provided to us by the shareholders.

The information in this table is based on 526,842,294 Ordinary Shares outstanding (equal to 52,684,229 ADSs) as of such date. In determining the number of Ordinary Shares beneficially owned by a person, we include any shares as to which the person has sole or shared voting power or investment power, as well as any Ordinary Shares subject to options or warrants held by that person that were currently exercisable at, or exercisable within 60 days of March 17, 2022. The Ordinary Shares issuable under these options and warrants are treated as if they were outstanding for purposes of computing the percentage ownership of the person holding these options and warrants but not the percentage ownership of any other person. None of the holders of the Ordinary Shares listed in this table have voting rights different from other holders of Ordinary Shares.

	Number of Shares Beneficially Held	Percent of Class
Cosmo Pharmaceuticals N.V. (1)	69,000,010	13.10 %
First Investments Holding Ltd. (2)	39,285,710	7.46 %

(1) The address of Cosmo Pharmaceuticals N.V. is Riverside II, Sir John Rogerson's Quay, Dublin, Ireland. Cosmo Technologies Ltd. a wholly-owned subsidiary of Cosmo Pharmaceuticals N.V., is the direct holder of 17,142,860 of the Ordinary Shares listed in the table.

(2) Mr. Vasile Timis may be deemed the beneficial owner of the shares held by First Investments Holdings Ltd. The address of First Investments Holding Ltd. is 2nd Floor, Strathvale House, 90 North Church Street, P.O. Box 1103, Cayman Islands.

On March 16, 2022, 10,828,572 ADSs (equivalent to 108,285,720 Ordinary Shares, or approximately 20.56% of our total issued and outstanding Ordinary Shares), were held of record by two record holders, of which none had a U.S. address. As of March 16 , 2022, there were no shareholders of record of our Ordinary Shares who was located in Israel. The number of record holders is not at all representative of the number of beneficial holders of our ADSs or Ordinary Shares because many of the ADSs and Ordinary Shares are held by brokers or other nominees.

B. Related Party Transactions

"Item 4. Information on the Company - B. Business Overview - Acquisition, Commercialization and License Agreements - Licensing and Manufacturing Terms with Cosmo Pharmaceuticals."

C. Interests of Experts and Counsel

Not applicable.

ITEM 8. FINANCIAL INFORMATION

A. Financial Statements and Other Financial Information

The financial statements required by this item are found at the end of this Annual Report, beginning on page F-1.

Legal Proceedings

From time to time, we may become a party to legal proceedings and claims in the ordinary course of business. On February 22, 2021, Aether Therapeutics Inc., filed a complaint against us in the United States District Court for the District of Delaware. We refer to this matter as the Aether Litigation. The complaint asserts that our marketing of the Movantik® product infringes U.S. Patent Nos. 6,713,488, 8,748,448, 8,883,817 and 9,061,024 held by Aether Therapeutics Inc., or the Aether Patents. Aether has asserted the Aether Patents against other entities previously involved in the marketing of the Movantik® product. The complaint requests customary remedies for patent infringement, including (i) a judgment that we have infringed, contributed to and induced infringement of the Aether Patents, (ii) damages, (iii) attorneys' fees and (iv) costs and expenses. We intend to vigorously defend ourselves against these claims. Given the stage of the Aether Litigation, we are unable to predict the likelihood of success of the claims of Aether Therapeutics Inc. against us or to quantify any risk of loss. The Aether Litigation could last for an extended period of time and require us to dedicate significant financial resources and management resources to our defense. An adverse ruling against us could materially and adversely affect our business, financial position, results of operations or cash flows and could also result in reputational harm. Even if we are successful in defending against these claims, the Aether Litigation could result in delays in future product developments, reputational harm or other collateral consequences

Dividend Policy

We have never declared or paid cash dividends to our shareholders. Currently, we do not intend to pay cash dividends, and we are prohibited from doing so under our Credit Agreement. We currently intend to reinvest any future earnings, if any, in developing and expanding our business. Any future determination relating to our dividend policy will be at the discretion of our board of directors and will depend on a number of factors, including future earnings, if any, our financial condition, operating results, contractual restrictions, capital requirements, business prospects, applicable Israeli law and other factors our board of directors may deem relevant.

B. Significant Changes

Except as otherwise disclosed in this Annual Report, no significant change has occurred since December 31, 2021.

ITEM 9. THE OFFER AND LISTING

A. Offer and Listing Details

Our Ordinary Shares were traded on the TASE under the symbol “RDHL” from February 2011 to February 2020 and were voluntarily delisted from trading on the TASE, effective February 13, 2020. They are listed but are not traded on the Nasdaq Global Market in connection with our ADSs. Our ADSs were traded on the Nasdaq Capital Market under the symbol “RDHL” from December 27, 2012, and have been listed on the Nasdaq Global Market under the same symbol since July 20, 2018.

B. Plan of Distribution

Not applicable.

C. Markets

Our ADSs, each representing ten Ordinary Shares and evidenced by an American depositary receipt, or ADR, are traded on the Nasdaq Global Market under the symbol "RDHL." The ADRs were issued pursuant to a Depositary Agreement entered into with The Bank of New York Mellon.

D. Selling Shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the Issue

Not applicable.

ITEM 10. ADDITIONAL INFORMATION

A. Share Capital

Not applicable.

B. Memorandum and Articles of Association

Securities Registers

The transfer agent and registrar for our ADSs is The Bank of New York Mellon, and its address is 101 Barclay Street, New York, NY.

Objects and Purposes

According to Section 4 of our articles of association, we shall engage in any legal business. Our number with the Israeli Registrar of Companies is 514304005.

Private Placements

Under the Israeli Companies Law, if (i) as a result of a private placement a person would become a controlling shareholder or (ii) a private placement will entitle investors to receive 20% or more of the voting rights of a company as calculated before the private placement, and all or part of the private placement consideration is not in cash or in public traded securities or is not in market terms and if as a result of the private placement the holdings of a substantial shareholder will increase or as a result of it a person will become a substantial shareholder, then, in either case, the allotment must be approved by the board of directors and by the shareholders of the company. A "substantial shareholder" is defined as a shareholder who holds five percent or more of the company's outstanding share capital, assuming the exercise of all of the securities convertible into shares held by that person. In order for the private placement to be on "market terms" the board of directors has to determine, on the basis of detailed explanation, that the private placement is on market terms, unless proven otherwise.

Board of Directors

Under our articles of association, resolutions by the board of directors are decided by a majority of votes of the directors present, or participating, in the case of voting by media, and voting, each director having one vote.

In addition, the Israeli Companies Law requires that certain transactions, actions, and arrangements be approved as provided for in a company's articles of association and in certain circumstances by the compensation or audit committee and by the board of directors itself. Those transactions that require such approval pursuant to a company's articles of association must be approved by its board of directors. In certain circumstances, compensation or audit committee and shareholder approval are also required. See "Item 6. Directors, Senior Management and Employees – C. Board Practices."

The Israeli Companies Law requires that a member of the board of directors or senior management of the company promptly and, in any event, not later than the first board meeting at which the transaction is discussed, disclose any personal interest that he or she may have, either directly or by way of any corporation in which he or she is, directly or indirectly, a 5% or greater shareholder, director or general manager or in which he or she has the right to appoint at least one director or the general manager, as well as all related material information known to him or her, in connection with any existing or proposed transaction by the company. In addition, if the transaction is an extraordinary transaction, (that is, a transaction other than in the ordinary course of business, otherwise than on market terms, or is likely to have a material impact on the company's profitability, assets or liabilities), the member of the board of directors or senior management must also disclose any personal interest held by his or her spouse, siblings, parents, grandparents, descendants, spouse's descendants, siblings and parents, and the spouses of any of the foregoing.

Once the member of the board of directors or senior management complies with the above disclosure requirement, a company may approve the transaction in accordance with the provisions of its articles of association. Under the provisions of the Israeli Companies Law, whoever has a personal interest in a matter, which is considered at a meeting of the board of directors or the audit committee, may not be present at this meeting or vote on this matter, unless it is not an extraordinary transaction as defined in the Israeli Companies Law. However, if the chairman of the board of directors or the chairman of the audit committee has determined that the presence of a director or an officer with a personal interest is required for the presentation of a matter, such officer holder may be present at the meeting. Notwithstanding the foregoing, if the majority of the directors have a personal interest in a matter, they will be allowed to participate and vote on this matter, but an approval of the transaction by the shareholders in the general meeting will be required.

Our articles of association provide that, subject to the Israeli Companies Law, all actions executed in good faith by the board of directors or by a committee thereof or by any person acting as a director or a member of a committee of the board of directors, will be deemed to be valid even if, after their execution, it is discovered that there was a flaw in the appointment of these persons or that any one of these persons was disqualified from serving in his or her office.

Our articles of association provide that, subject to the provisions of the Israeli Companies Law, the board of directors may appoint board of directors' committees. The committees of the board of directors report to the board of directors their resolutions or recommendations on a regular basis, as prescribed by the board of directors. The board of directors may cancel the resolution of a committee that has been appointed by it; however, such cancellation will not affect the validity of any resolution of a committee, pursuant to which we acted, vis-à-vis another person, who was not aware of the cancellation thereof. Decisions or recommendations of the committee of the board which require the approval of the board of directors will be brought to the directors' attention at a reasonable time prior to the discussion at the board of directors.

According to the Israeli Companies Law, a contract of a company with its directors, regarding their conditions of service, including the grant to them of exemption from liability from certain actions, insurance, and indemnification as well as the company's contract with its directors on conditions of their employment, in other capacities, require the approval of the compensation committee, the board of directors, and the shareholders by a Special Majority.

Description of Securities

Ordinary Shares

Our registered share capital is NIS 8,000,000, divided into (i) 794,000,000 registered Ordinary Shares of NIS 0.01 par value each, and (ii) 6,000,000 preferred shares of NIS 0.01 par value each.

The Ordinary Shares do not have preemptive rights, preferred rights or any other right to purchase our securities. Neither our articles of association nor the laws of the State of Israel restrict the ownership or voting of Ordinary Shares by non-residents of Israel, except for subjects of countries that are enemies of Israel.

Transfer of Shares. Fully paid Ordinary Shares are issued in registered form and may be freely transferred pursuant to our articles of association unless that transfer is restricted or prohibited by another instrument.

Notices. Under the Israeli Companies Law and our articles of association, we are required to publish notices in two Hebrew-language daily newspapers or our website at least 21 calendar days prior notice of a shareholders' meeting. However, under regulations promulgated under the Israeli Companies Law, we are required to publish a notice in two daily newspapers at least 35 calendar days prior any shareholders' meeting in which the agenda includes matters which may be voted on by voting instruments. Regulations under the Israeli Companies Law exempt companies whose shares are listed for trading both on a stock exchange in and outside of Israel, from some provisions of the Israeli Companies Law. An amendment to these regulations exempts us from the requirements of the Israeli proxy regulation, under certain circumstances.

According to the Israeli Companies Law and the regulations promulgated thereunder, for purposes of determining the shareholders entitled to notice and to vote at such meeting, the board of directors may fix the record date not more than 40 nor less than four calendar days prior to the date of the meeting, provided that an announcement regarding the general meeting be given prior to the record date.

Election of Directors. The number of directors on the board of directors shall be no less than five and no more than eleven, including any external directors whose appointment is required by law. The general meeting is entitled, at any time and from time to time, in a resolution approved by a majority of 75% or more of the votes cast by those shareholders present and voting at the meeting in person, by proxy or by a voting instrument, not taking into consideration abstaining votes, to change the minimum or maximum number of directors as stated above as well as to amend the board classification under our Articles. A simple majority shareholder vote is required to elect a director for a term of less than three years. For more information, please see "Item 6. Directors, Senior Management and Employees – C. Board Practices – Appointment of Directors and Terms of Office."

Dividend and Liquidation Rights. Our profits, in respect of which a resolution was passed to distribute them as a dividend or bonus shares, are to be paid pro rata to the amount paid or credited as paid on account of the nominal value of shares held by the shareholders. In the event of our liquidation, the liquidator may, with the general meeting's approval, distribute parts of our property in specie among the shareholders and he may, with similar approval, deposit any part of our property with trustees in favor of the shareholders as the liquidator, with the approval mentioned above deems fit. The terms of our term loan facility prohibit us from paying dividends.

Voting, Shareholders' Meetings and Resolutions. Holders of Ordinary Shares are entitled to one vote for each Ordinary Share held on all matters submitted to a vote of shareholders. The quorum required for an ordinary meeting of shareholders consists of at least two shareholders present, in person or by proxy, or who has sent us a voting instrument indicating the way in which he is voting, who hold or represent, in the aggregate, at least 25% of the voting rights of our outstanding share capital. A meeting adjourned for lack of a quorum is adjourned to the following day at the same time and place or any time and place as prescribed by the board of directors in the notice to the shareholders. At the reconvened meeting one shareholder at least, present in person or by proxy constitutes a quorum except where such meeting was called at the demand of shareholders. With the agreement of a meeting at which a quorum is present, the chairman may, and on the demand of the meeting he must, adjourn the meeting from time to time and from place to place, as the meeting resolves. Annual general meetings of shareholders are held once every year within a period of not more than 15 months after the last preceding annual general shareholders' meeting. The board of directors may call special general meetings of shareholders. The Israeli Companies Law provides that a special general meeting of shareholders may be called by the board of directors or by a request of two directors or 25% of the directors in office, whichever is the lower, or by shareholders holding at least 5% of our issued share capital and at least 1% of the voting rights, or of shareholders holding at least 5% of our voting rights.

An ordinary resolution requires approval by the holders of a majority of the voting rights present, in person or by proxy, at the meeting and voting on the resolution.

Allotment of Shares. Our board of directors has the power to allot or to issue shares to any person, with restrictions and conditions as it deems fit.

Acquisitions under Israeli Law

Full Tender Offer

A person wishing to acquire shares of an Israeli public company and who would as a result hold over 90% of the target company's issued and outstanding share capital is required by the Israeli Companies Law to make a tender offer to all of the company's shareholders for the purchase of all of the issued and outstanding shares of the company.

A person wishing to acquire shares of an Israeli public company and who would as a result hold over 90% of the issued and outstanding share capital of a certain class of shares is required to make a tender offer to all of the shareholders who hold shares of the same class for the purchase of all of the issued and outstanding shares of the same class.

If the shareholders who do not respond to or accept the offer hold less than 5% of the issued and outstanding share capital of the company or of the applicable class of the shares, and more than half of the shareholders who do not have a personal interest in the offer accept the offer, all of the shares that the acquirer offered to purchase will be transferred to the acquirer by operation of law. However, a tender offer will be accepted if the shareholders who do not accept it hold less than 2% of the issued and outstanding share capital of the company or of the applicable class of the shares.

Upon a successful completion of such a full tender offer, any shareholder that was an offeree in such tender offer, whether such shareholder accepted the tender offer or not, may, within six months from the date of acceptance of the tender offer, petition the Israeli court to determine whether the tender offer was for less than fair value and that the fair value should be paid as determined by the court. However, under certain conditions, the offeror may determine in the terms of the tender offer that an offeree who accepted the offer will not be entitled to petition the Israeli court as described above.

If the shareholders who did not respond or accept the tender offer hold at least 5% of the issued and outstanding share capital of the company or of the applicable class, the acquirer may not acquire shares of the company that will increase its holdings to more than 90% of the company's issued and outstanding share capital or of the applicable class from shareholders who accepted the tender offer.

The description above regarding a full tender offer will also apply, with necessary changes, when a full tender offer is accepted, and the offeror has also offered to acquire all of the company's securities.

Special Tender Offer

The Israeli Companies Law provides that an acquisition of shares of an Israeli public company must be made by means of a special tender offer if as a result of the acquisition the purchaser would become a holder of at least 25% of the voting rights in the company. This rule does not apply if there is already another holder of at least 25% of the voting rights in the company.

Similarly, the Israeli Companies Law provides that an acquisition of shares of a public company must be made by means of a special tender offer if as a result of the acquisition the purchaser would become a holder of more than 45% of the voting rights in the company, if there is no other shareholder of the company who holds more than 45% of the voting rights in the company.

These requirements do not apply if the acquisition (i) occurs in the context of a private offering, on the condition that the shareholders meeting approved the acquisition as a private offering whose purpose is to give the acquirer at least 25% of the voting rights in the company if there is no person who holds at least 25% of the voting rights in the company, or as a private offering whose purpose is to give the acquirer 45% of the voting rights in the company, if there is no person who

holds 45% of the voting rights in the company; (ii) was from a shareholder holding at least 25% of the voting rights in the company and resulted in the acquirer becoming a holder of at least 25% of the voting rights in the company; or (iii) was from a holder of more than 45% of the voting rights in the company and resulted in the acquirer becoming a holder of more than 45% of the voting rights in the company.

The special tender offer may be consummated only if (i) at least 5% of the voting power attached to the company's outstanding shares will be acquired by the offeror and (ii) the special tender offer is accepted by a majority of the votes of those offerees who gave notice of their position in respect of the offer; in counting the votes of offerees, the votes of a holder in control of the offeror, a person who has personal interest in acceptance of the special tender offer, a holder of at least 25% of the voting rights in the company, or any person acting on their or on the offeror's behalf, including their relatives or companies under their control, are not taken into account.

In the event that a special tender offer is made, a company's board of directors is required to express its opinion on the advisability of the offer or must abstain from expressing any opinion if it is unable to do so, provided that it gives the reasons for its abstention.

An officer in a target company who, in his or her capacity as an officer, performs an action the purpose of which is to cause the failure of an existing or foreseeable special tender offer or is to impair the chances of its acceptance, is liable to the potential purchaser and shareholders for damages resulting from his acts, unless such officer acted in good faith and had reasonable grounds to believe he or she was acting for the benefit of the company. However, officers of the target company may negotiate with the potential purchaser in order to improve the terms of the special tender offer and may further negotiate with third parties in order to obtain a competing offer.

If a special tender offer was accepted by a majority of the shareholders who announced their stand on such offer, then shareholders who did not respond to the special offer or had objected to the special tender offer may accept the offer within four days of the last day set for the acceptance of the offer. In the event that a special tender offer is accepted, then the purchaser or any person or entity controlling it and any corporation controlled by them must refrain from making a subsequent tender offer for the purchase of shares of the target company and may not execute a merger with the target company for a period of one year from the date of the offer unless the purchaser or such person or entity undertook to effect such an offer or merger in the initial special tender offer.

Merger

The Israeli Companies Law permits merger transactions if approved by each party's board of directors and, unless certain requirements described under the Israeli Companies Law are met, a majority of each party's shareholders, by a majority of each party's shares that are voted on the proposed merger at a shareholders' meeting.

The board of directors of a merging company is required pursuant to the Israeli Companies Law to discuss and determine whether in its opinion there exists a reasonable concern that, as a result of a proposed merger, the surviving company will not be able to satisfy its obligations toward its creditors, taking into account the financial condition of the merging companies. If the board of directors has determined that such a concern exists, it may not approve a proposed merger. Following the approval of the board of directors of each of the merging companies, the boards of directors must jointly prepare a merger proposal for submission to the Israeli Registrar of Companies.

For purposes of the shareholder vote, unless a court rules otherwise, the merger will not be deemed approved if a majority of the shares voting at the shareholders meeting (excluding abstentions) that are held by parties other than the other party to the merger, any person who holds 25% or more of the means of control (see "Management – Audit Committee – Approval of Transactions with Related Parties" for a definition of means of control) of the other party to the merger or anyone on their behalf including their relatives (see "Management – External Directors – Qualifications of External Directors" for a definition of relatives) or corporations controlled by any of them, vote against the merger.

In addition, if the non-surviving entity of the merger has more than one class of shares, the merger must be approved by each class of shareholders. If the transaction would have been approved but for the separate approval of each class of shares or the exclusion of the votes of certain shareholders as provided above, a court may still rule that the company has

approved the merger upon the request of holders of at least 25% of the voting rights of a company, if the court holds that the merger is fair and reasonable, taking into account the appraisal of the merging companies' value and the consideration offered to the shareholders.

Under the Israeli Companies Law, each merging company must send a copy of the proposed merger plan to its secured creditors. Unsecured creditors are entitled to receive notice of the merger, as provided by the regulations promulgated under the Israeli Companies Law. Upon the request of a creditor of either party to the proposed merger, the court may delay or prevent the merger if it concludes that there exists a reasonable concern that, as a result of the merger, the surviving company will be unable to satisfy the obligations of the target company. The court may also give instructions in order to secure the rights of creditors.

In addition, a merger may not be completed unless at least 50 days have passed from the date that a proposal for approval of the merger was filed with the Israeli Registrar of Companies and 30 days from the date that shareholder approval of both merging companies was obtained.

Anti-takeover Measures

The Israeli Companies Law allows us to create and issue shares having rights different from those attached to our Ordinary Shares, including shares providing certain preferred or additional rights to voting, distributions or other matters and shares having preemptive rights. We have 6,000,000 authorized unissued preferred shares. Our authorized preferred shares, and any other class of shares other than Ordinary Shares that we may create and issue in the future, depending on the specific rights that may be attached to them, may delay or prevent a takeover or otherwise prevent our shareholders from realizing a potential premium over the market value of their Ordinary Shares. The authorization of a new class of shares will require an amendment to our articles of association which requires the prior approval of a majority of our shares represented and voting at a general meeting. Shareholders voting at such a meeting will be subject to the restrictions under the Israeli Companies Law described in "– Voting." In addition, provisions of our articles of our association relating to the election of our directors for terms of three years make it more difficult for a third party to effect a change in control or takeover attempt that our management and board of directors oppose. See "Item 6. Directors, Senior Management and Employees – C. Board Practices – Appointment of Directors and Terms of Officers."

C. Material Contracts

For a description of other material agreements, please see "Item 4. Information on the Company – B. Business Overview."

D. Exchange Controls

Israeli law and regulations do not impose any material foreign exchange restrictions on non-Israeli holders of our Ordinary Shares. Dividends, if any, paid to holders of our Ordinary Shares, and any amounts payable upon our dissolution, liquidation or winding up, as well as the proceeds of any sale in Israel of our Ordinary Shares to an Israeli resident, may be paid in non-Israeli currency or, if paid in Israeli currency, may be converted into U.S. dollars at the rate of exchange prevailing at the time of conversion.

E. Taxation

Israeli Tax Considerations

General

The following is a summary of the material tax consequences under Israeli law concerning the purchase, ownership and disposition of our Ordinary Shares or American Depositary Shares (collectively, the "Shares").

This discussion does not purport to constitute a complete analysis of all potential tax consequences applicable to investors upon purchasing, owning or disposing of our Shares. In particular, this discussion does not take into account the specific circumstances of any particular investor (such as tax-exempt entities, financial institutions, certain financial companies,

broker-dealers, investors that own, directly or indirectly, 10% or more of our outstanding voting rights, all of whom are subject to special tax regimes not covered under this discussion). To the extent that issues discussed herein are based on legislation that has yet to be subject to judicial or administrative interpretation, there can be no assurance that the views expressed herein will accord with any such interpretation in the future.

Potential investors are urged to consult their own tax advisors as to the Israeli or other tax consequences of the purchase, ownership, and disposition of the Shares, including, in particular, the effect of any foreign, state or local taxes.

General Corporate Tax Structure in Israel

Israeli companies are generally subject to corporate tax on their taxable income at the rate of 23% for the 2021 tax year.

Taxation of Shareholders

Capital Gains

Capital gains tax is imposed on the disposition of capital assets by an Israeli resident and on the disposition of such assets by a non-Israeli resident if those assets are either (i) located in Israel; (ii) are shares or a right to a share in an Israeli resident corporation, or (iii) represent, directly or indirectly, rights to assets located in Israel, unless an exemption is available or unless an applicable double tax treaty between Israel and the seller's country of residence provides otherwise. The Israeli Income Tax Ordinance distinguishes between "Real Gain" and the "Inflationary Surplus". "Real Gain" is the excess of the total capital gain over Inflationary Surplus generally computed on the basis of the increase in the Israeli Consumer Price Index between the date of purchase and the date of disposition. Inflationary Surplus is not subject to tax.

Real Gain accrued by individuals on the sale of the Shares will be taxed at the rate of 25%. However, if the individual shareholder is a "Controlling Shareholder" (i.e., a person who holds, directly or indirectly, alone or together with another, 10% or more of one of the Israeli resident company's means of control) at the time of sale or at any time during the preceding 12-month period, such gain will be taxed at the rate of 30%.

Corporate and individual shareholders dealing in securities in Israel are taxed at the tax rates applicable to business income (23% in 2022), and a marginal tax rate of up to 50% in 2022 for individuals, including an excess tax (as discussed below).

Notwithstanding the foregoing, capital gains generated from the sale of our Shares by a non-Israeli shareholder may be exempt from Israeli tax under the Israeli Income Tax Ordinance provided that the following cumulative conditions are met: (i) the Shares were purchased upon or after the registration of the Shares on the stock exchange (this condition may not apply to shares purchased on or after January 1, 2009) and (ii) the seller does not have a permanent establishment in Israel to which the generated capital gain is attributed. However, non-Israeli resident corporations will not be entitled to the foregoing exemption if Israeli residents: (i) have a 25% or more interest in such non-Israeli corporation or (ii) are the beneficiaries of, or are entitled to, 25% or more of the income or profits of such non-Israeli corporation, whether directly or indirectly. In addition, such exemption would not be available to a person whose gains from selling or otherwise disposing of the securities are deemed to be business income.

In addition, the sale of the Shares may be exempt from Israeli capital gains tax under the provisions of an applicable double tax treaty. For example, the Convention Between the Government of the United States of America and the Government of the State of Israel with Respect to Taxes on Income, or the U.S.-Israel Double Tax Treaty, exempts a U.S. resident (for purposes of the U.S.-Israel Double Tax Treaty) from Israeli capital gain tax in connection with the sale of the Shares, provided that: (i) the U.S. resident owned, directly or indirectly, less than 10% of the voting power of the company at any time within the 12-month period preceding such sale; (ii) the U.S. resident, being an individual, is present in Israel for a period or periods of less than 183 days during the taxable year; and (iii) the capital gain from the sale was not derived through a permanent establishment of the U.S. resident in Israel; however, under the U.S.-Israel Double Tax Treaty, the taxpayer would be permitted to claim a credit for such taxes against the U.S. federal income tax imposed with respect to such sale, exchange or disposition, subject to the limitations under U.S. law applicable to foreign tax credits. The U.S.-Israel Double Tax Treaty does not relate to U.S. state or local taxes.

Payers of consideration for the Shares, including the purchaser, the Israeli stockbroker or the financial institution through which the Shares are held, are obligated, subject to certain exemptions, to withhold tax upon the sale of Shares at a rate of 25% of the consideration for individuals and corporations.

Upon the sale of traded securities, a detailed return, including a computation of the tax due, must be filed and an advance payment must be paid to the Israeli Tax Authority on January 31 and July 31 of every tax year in respect of sales of traded securities made within the previous six months. However, if all tax due was withheld at source according to applicable provisions of the Israeli Income Tax Ordinance and regulations promulgated thereunder, such return need not be filed, and no advance payment must be paid. Capital gains are also reportable on annual income tax returns.

Dividends

Dividends distributed by a company to a shareholder who is an Israeli resident individual will generally be subject to income tax at a rate of 25%. However, a 30% tax rate will apply if the dividend recipient is a Controlling Shareholder, as defined above, at the time of distribution or at any time during the preceding 12-month period. If the recipient of the dividend is an Israeli resident corporation, such dividend will generally be exempt from Israeli income tax provided that the income from which such dividend is distributed, derived or accrued within Israel.

Dividends distributed by an Israeli resident company to a non-Israeli resident (either an individual or a corporation) are generally subject to Israeli withholding tax on the receipt of such dividends at the rate of 25% (30% if the dividend recipient is a Controlling Shareholder at the time of distribution or at any time during the preceding 12-month period). These rates may be reduced under the provisions of an applicable double tax treaty. For example, under the U.S.-Israel Double Tax Treaty, the following tax rates will apply in respect of dividends distributed by an Israeli resident company to a U.S. resident: (i) if the U.S. resident is a corporation which holds during that portion of the taxable year which precedes the date of payment of the dividend and during the whole of its prior taxable year (if any), at least 10% of the outstanding shares of the voting stock of the Israeli resident paying corporation and not more than 25% of the gross income of the Israeli resident paying corporation for such prior taxable year (if any) consists of certain types of interest or dividends the tax rate is 12.5%; (ii) if both the conditions mentioned in clause (i) above are met and the dividend is paid from an Israeli resident company's income which was entitled to a reduced tax rate under The Law for the Encouragement of Capital Investments, 1959, the tax rate is 15%; and (iii) in all other cases, the tax rate is 25%. The aforementioned rates under the U.S.-Israel Double Tax Treaty will not apply if the dividend income is attributed to a permanent establishment of the U.S. resident in Israel.

Excess Tax

Individual holders who are subject to tax in Israel (whether any such individual is an Israeli resident or non-Israeli resident) and who have taxable income that exceeds a certain threshold in a tax year ((NIS 663,240 for 2022, linked to the Israeli Consumer Price Index) will be subject to an additional tax at the rate of 3% on his or her taxable income for such tax year that is in excess of such amount. For this purpose, taxable income includes taxable capital gains from the sale of securities and taxable income from interest and dividends, subject to the provisions of an applicable double tax treaty.

Estate and Gift Tax

Israel does not currently impose estate or gift taxes if the Israeli Tax Authority is satisfied that the gift was made in good faith and on condition that the recipient of the gift is not a non-Israeli resident.

Foreign Exchange Regulations

Non-residents of Israel who hold our Shares are able to receive any dividends, and any amounts payable upon the dissolution, liquidation and winding up of our affairs, repayable in non-Israeli currency at the rate of exchange prevailing at the time of conversion. However, Israeli income tax is generally required to have been paid or withheld on these amounts. In addition, the statutory framework for the potential imposition of currency exchange control has not been eliminated and may be restored at any time by administrative action.

U.S. Federal Income Tax Considerations

The following is a summary of the material U.S. federal income tax consequences relating to the ownership and disposition of our Ordinary Shares and ADSs by U.S. Holders, as defined below. This summary addresses solely U.S. Holders who acquire ADSs pursuant to this offering and who hold Ordinary Shares or ADSs, as applicable, as capital assets for tax purposes. This summary is based on current provisions of the Internal Revenue Code of 1986, as amended (the "Code"), current and proposed U.S. Treasury regulations promulgated thereunder, and administrative and judicial decisions as of the date hereof, all of which are subject to change, possibly on a retroactive basis. In addition, this section is based in part upon representations of the depositary and the assumption that each obligation in the deposit agreement and any related agreement will be performed in accordance with its terms. This summary does not address all U.S. federal income tax matters that may be relevant to a particular holder or all tax considerations that may be relevant with respect to an investment in our Ordinary Shares or ADSs.

This summary does not address tax considerations applicable to a holder of our Ordinary Shares or ADSs that may be subject to special tax rules including, without limitation, the following:

- dealers or traders in securities, currencies or notional principal contracts;
- banks, insurance companies and other financial institutions;
- real estate investment trusts;
- persons subject to the alternative minimum tax;
- tax-exempt organizations;
- traders that have elected mark-to-market accounting;
- corporations that accumulate earnings to avoid U.S. tax;
- pension plans;
- investors that hold the Ordinary Shares or ADSs as part of a "straddle," "hedge," or "conversion transaction" with other investments;
- regulated investment companies;
- persons that actually or constructively own 10 percent or more of our shares by vote or by value;
- persons that are treated as partnerships or other pass-through entities for U.S. federal income purposes and persons who hold the Ordinary Shares or ADSs through partnerships or other pass-through entities; and
- persons whose functional currency is not the U.S. dollars.

This summary does not address the effect of any U.S. federal taxation other than U.S. federal income taxation. In addition, this summary does not include any discussion of state, local, or foreign tax consequences to a holder of our Ordinary Shares or ADSs.

You are urged to consult your own tax advisor regarding the foreign and U.S. federal, state, and local and other tax consequences of an investment in Ordinary Shares or ADSs.

For purposes of this summary, a "U.S. Holder" means a beneficial owner of an Ordinary Share or ADS that is for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the U.S.;
- a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes) created or organized in the U.S. or under the laws of the U.S., any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust (1) if (a) a court within the U.S. is able to exercise primary supervision over the administration of the trust and (b) one or more U.S. persons have the authority to control all substantial decisions of the trust or (2) that has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

If an entity or arrangement that is classified as a partnership for U.S. federal tax purposes holds Ordinary Shares or ADSs, the U.S. federal tax treatment of its partners will generally depend upon the status of the partners and the activities of the

partnership. Entities or arrangements that are classified as partnerships for U.S. federal tax purposes and persons holding Ordinary Shares or ADSs through such entities should consult their own tax advisors.

In general, if you hold ADSs, you will be treated as the holder of the underlying Ordinary Shares represented by those ADSs for U.S. federal income tax purposes. Accordingly, gain or loss generally will not be recognized if you exchange ADSs for the underlying Ordinary Shares represented by those ADSs.

Distributions

Subject to the discussion under "—Passive Foreign Investment Companies" below, the gross amount of any distribution, including the amount of any Israeli taxes withheld from such distribution, see "Material Tax Considerations—Israeli Tax Considerations," actually or constructively received by a U.S. Holder with respect to an Ordinary Share (or, in the case of an ADS, received by the depositary) will be taxable to the U.S. Holder as foreign-source dividend income to the extent of our current and accumulated earnings and profits as determined under U.S. federal income tax principles. The U.S. Holder will not be eligible for any dividends received deduction in respect of the dividends paid by us. Distributions in excess of earnings and profits will be non-taxable to the U.S. Holder to the extent of the U.S. Holder's adjusted tax basis in its Ordinary Share or ADS. Distributions in excess of such adjusted tax basis will generally be taxable to the U.S. Holder as capital gain from the sale or exchange of property as described below under "—Sale or Other Disposition of Ordinary Shares or ADSs." If we do not report to a U.S. Holder the portion of a distribution that exceeds earnings and profits, then the distribution will generally be taxable as a dividend. The amount of any distribution of property other than cash will be the fair market value of that property on the date of distribution.

Qualified dividends received by non-corporate U.S. Holders will be subject to U.S. federal income tax at the preferential long-term capital gains rate of, currently, a maximum of 20%. Dividends distributed with respect to our Ordinary Shares or ADSs are qualified dividend only if we are treated as a "qualified foreign corporation" and such U.S. Holder has a holding period with respect to our Ordinary Shares or ADSs of at least 61 days during the 121-day period beginning 60 days before the ex-dividend date. We are a "qualified foreign corporation" if we are not a PFIC for the year in which the dividend is paid or for the preceding taxable year and either (a) we are eligible for the benefits under the U.S.-Israel Double Tax Treaty or (b) the Ordinary Shares or ADSs are readily tradable on an established securities market in the U.S. As discussed below in "—Passive Foreign Investment Companies," we do not anticipate being treated as a PFIC for this year; however, there can be no assurance that we will not be treated as a PFIC for our current taxable or future taxable years. You should consult your own tax advisor regarding the availability of this preferential tax rate under your particular circumstances.

The amount of any distribution paid in a currency other than U.S. dollars (a "foreign currency"), including the amount of any withholding tax thereon, will be included in the gross income of a U.S. Holder in an amount equal to the U.S. dollar value of the foreign currency calculated by reference to the exchange rate in effect on the date of the U.S. Holder's (or, in the case of ADSs, the depositary's) receipt of the dividend, regardless of whether the foreign currency is converted into U.S. dollars. If the foreign currency is converted into U.S. dollars on the date of receipt, a U.S. Holder generally should not be required to recognize a foreign currency gain or loss in respect of the dividend. If the foreign currency received in the distribution is not converted into U.S. dollars on the date of receipt, a U.S. Holder will have a basis in the foreign currency equal to its U.S. dollar value on the date of receipt. Any gain or loss on a subsequent conversion or other disposition of the foreign currency will be treated as U.S. source ordinary income or loss.

Subject to certain conditions and limitations, any Israeli taxes withheld on dividends may be creditable against a U.S. Holder's U.S. federal income tax liability, subject to generally applicable limitations. The rules relating to foreign tax credits and the timing thereof are complex. You should consult your own tax advisors regarding the availability of a foreign tax credit in your particular situation.

Sale or Other Disposition of Ordinary Shares or ADSs

Subject to the discussion under "—Passive Foreign Investment Companies" below, a U.S. Holder that sells or otherwise disposes of its Ordinary Shares or ADSs will recognize gain or loss for U.S. federal income tax purposes in an amount equal to the difference between the amount realized on the sale or other disposition and such U.S. Holder's adjusted basis

in the Ordinary Shares or ADSs. Such gain or loss generally will be capital gain or loss and will be a long-term capital gain or loss if the U.S. Holder's holding period of the Ordinary Shares or ADSs exceeds one year at the time of the sale or other disposition. Long-term capital gains realized by non-corporate U.S. Holders are generally subject to a preferential U.S. federal income tax rate. In general, gain or loss recognized by a U.S. Holder on the sale or other disposition or our Ordinary Shares or ADSs will be U.S. source gain or loss for purposes of the foreign tax credit limitation. However, if we were a PFIC, any such gain would be subject to the PFIC rules, as discussed below, rather than being taxed as capital gain. As discussed below in "—Passive Foreign Investment Companies," we do not anticipate being a PFIC for this year; however, there can be no assurance that we will not be treated as a PFIC for our current taxable year and future taxable years.

If a U.S. Holder receives foreign currency upon a sale or exchange of Ordinary Shares or ADSs, gain or loss will be recognized in the manner described above under "—Distributions." However, if such foreign currency is converted into U.S. dollars on the date received by the U.S. Holder, the U.S. Holder generally should not be required to recognize any foreign currency gain or loss on such conversion.

As discussed above under the heading "Material Tax Considerations—Israeli Tax Considerations—Taxation of Shareholders," a U.S. Holder who holds Ordinary Shares or ADSs through an Israeli broker or other Israeli intermediary may be subject to Israeli withholding tax on any capital gains recognized on a sale or other disposition of the Ordinary Shares or ADSs if the U.S. Holder does not obtain approval of an exemption from the Israeli Tax Authorities or does not claim any allowable refunds or reductions. U.S. Holders are advised that any Israeli tax paid under circumstances in which an exemption from (or a refund of or a reduction in) such tax was available will not be creditable for U.S. federal income tax purposes. U.S. Holders are advised to consult their Israeli broker or intermediary regarding the procedures for obtaining an exemption or reduction.

Medicare Tax on Unearned Income

Non-corporate U.S. Holders whose income exceeds certain thresholds are required to pay an additional 3.8% tax on their net investment income, which includes dividends paid on the Ordinary Shares or ADSs and capital gains from the sale or other disposition of the Ordinary Shares or ADSs.

Passive Foreign Investment Companies

Although we do not anticipate being treated as a PFIC for this year, it is possible that based on the value and composition of our assets, that we may be treated as a PFIC for U.S. federal income tax purposes for future taxable years. A non-U.S. corporation is considered a PFIC for any taxable year if either:

- at least 75% of its gross income for such taxable year is passive income; or
- at least 50% of the value of its assets (based on an average of the fair market values of the assets determined at the end of each quarter during a taxable year) is attributable to assets that produce or are held for the production of passive income.

For purposes of the above calculations, if a non-U.S. corporation owns, directly or indirectly, 25% or more of the total value of the outstanding shares of another corporation, it will be treated as if it (a) held a proportionate share of the assets of such other corporation and (b) received a proportionate share of the income of such other corporation directly. Passive income generally includes, among other things, dividends, interest, rents, royalties and certain capital gain, but generally excludes rents and royalties that are derived in the active conduct of a trade or business and which are received from a person other than a related person.

A separate determination must be made each taxable year as to whether we are a PFIC (after the close of each such taxable year). Because the value of our assets for purposes of the asset test will generally be determined by reference to the market price of the Ordinary Shares or ADSs, our PFIC status will depend in large part on the market price of the Ordinary Shares or ADSs, which may fluctuate significantly.

If we are a PFIC for any year during which a U.S. Holder holds Ordinary Shares or ADSs, such Ordinary Shares or ADSs generally will continue to be treated as Ordinary Shares or ADSs in a PFIC with respect to such U.S. Holder for all succeeding years during which such U.S. Holder holds the Ordinary Shares or ADSs, unless we cease to be a PFIC and such U.S. Holder makes a "deemed sale" election with respect to the Ordinary Shares or ADSs such U.S. Holder holds. If such election is made, a U.S. Holder will be deemed to have sold the Ordinary Shares or ADSs it holds at their fair market value on the last day of the last taxable year in which we qualified as a PFIC, and any gain from such deemed sale would be subject to the U.S. federal income tax treatment described below. After the deemed sale election, the Ordinary Shares or ADSs with respect to which the deemed sale election was made will not be treated as Ordinary Shares or ADSs in a PFIC unless we subsequently become a PFIC.

For each taxable year, we are treated as a PFIC with respect to a U.S. Holder, such U.S. Holder will be subject to special tax rules with respect to any "excess distribution" it receives and any gain it realizes from a sale or other disposition (including a pledge) of the Ordinary Shares or ADSs, unless it makes a "mark-to-market" election as discussed below. Distributions a U.S. Holder receives in a taxable year that are greater than 125% of the average annual distributions it received during the shorter of the three preceding taxable years or its holding period for the Ordinary Shares or ADSs will be treated as an excess distribution. Under these special tax rules, if a U.S. Holder receives any excess distribution or realizes any gain from a sale or other disposition of the Ordinary Shares or ADSs:

- the excess distribution or gain will be allocated ratably over the U.S. Holder's holding period for the Ordinary Shares or ADSs;
- the amount of excess distribution or gain allocated to the current taxable year, and any taxable year before the first taxable year in which we were a PFIC, must be included in the U.S. Holder's gross income (as ordinary income) for the current tax year; and
- the amount allocated to each other year will be subject to the highest marginal tax rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to such amounts allocated to each other year.

The tax liability for amounts allocated to years before the year of disposition or "excess distribution" cannot be offset by any losses for such years. Additionally, any gains realized on the sale of the Ordinary Shares or ADSs cannot be treated as capital gains.

If we are treated as a PFIC with respect to a U.S. Holder for any taxable year, to the extent any of our subsidiaries are also PFICs, such U.S. Holder will be deemed to own its proportionate share of any such subsidiaries that are PFICs, and such U.S. Holder may be subject to the rules described in the preceding two paragraphs with respect to the shares of such subsidiaries that are PFICs it would be deemed to own. As a result, a U.S. Holder may incur liability for any "excess distribution" described above if we receive a distribution from such subsidiaries that are PFICs or if any we dispose of, or are deemed to dispose of, any shares in such subsidiaries that are PFICs. You should consult your own tax advisor regarding the application of the PFIC rules to any of our subsidiaries.

Alternatively, a U.S. Holder of "marketable stock" (as defined below) in a PFIC may make a mark-to-market election for such stock to elect out of the general tax treatment for PFICs discussed above. If a U.S. Holder makes a mark-to-market election for the Ordinary Shares or ADSs, such U.S. Holder will include in income for each year we are a PFIC an amount equal to the excess, if any, of the fair market value of the Ordinary Shares or ADSs as of the close of such U.S. Holder's taxable year over such U.S. Holder's adjusted basis in such Ordinary Shares or ADSs. a U.S. Holder is allowed a deduction for the excess, if any, of the adjusted basis of the Ordinary Shares or ADSs over their fair market value as of the close of the taxable year. However, deductions are allowable only to the extent of any net mark-to-market gains on the Ordinary Shares or ADSs included in a U.S. Holder's income for prior taxable years. Amounts included in a U.S. Holder's income under a mark-to-market election, as well as gain on the actual sale or other disposition of the Ordinary Shares or ADSs, are treated as ordinary income. Ordinary loss treatment also applies to the deductible portion of any mark-to-market loss on the Ordinary Shares or ADSs, as well as to any loss realized on the actual sale or disposition of the Ordinary Shares or ADSs to the extent the amount of such loss does not exceed the net mark-to-market gains previously included for the Ordinary Shares or ADSs. A U.S. Holder's basis in the Ordinary Shares or ADSs will be adjusted to reflect any such income or loss amounts. If a U.S. Holder makes a valid mark-to-market election, the tax rules that apply to distributions by corporations which are not PFICs would apply to distributions by us, except the lower applicable tax rate for qualified

dividend income would not apply. If we cease to be a PFIC when a U.S. Holder has a mark-to-market election in effect, gain or loss realized by such U.S. Holder on the sale of the Ordinary Shares or ADSs will be a capital gain or loss and taxed in the manner described above under "—Sale or Other Disposition of Ordinary Shares or ADSs."

The mark-to-market election is available only for "marketable stock," which is a stock that is traded in other than de minimis quantities on at least 15 days during each calendar quarter, or regularly traded, on a qualified exchange or another market, as defined in applicable U.S. Treasury regulations. Any trades that have as their principal purpose meeting this requirement will be disregarded. The ADSs are listed on the NASDAQ Global Market and, accordingly, provided the ADSs are regularly traded, the mark-to-market election would be available to a U.S. Holder of ADSs if we are a PFIC. Once made, the election cannot be revoked without the consent of the IRS unless the Ordinary Shares or ADSs cease to be marketable stock. If we are a PFIC for any year in which the U.S. Holder owns the Ordinary Shares or ADSs but before a mark-to-market election is made, the interest charge rules described above will apply to any mark-to-market gain recognized in the year the election is made. If any of our subsidiaries are or become PFICs, the mark-to-market election will not be available with respect to the shares of such subsidiaries that are treated as owned by a U.S. Holder. Consequently, a U.S. Holder could be subject to the PFIC rules with respect to income of the lower-tier PFICs the value of which already had been taken into account indirectly via mark-to-market adjustments. You should consult your own tax advisors as to the availability and desirability of a mark-to-market election, as well as the impact of such election on interests in any lower-tier PFICs.

In certain circumstances, a U.S. Holder of stock in a PFIC can make a "qualified electing fund election" to mitigate some of the adverse tax consequences of holding stock in a PFIC by including in income its share of the corporation's income on a current basis. However, we do not currently intend to prepare or provide the information that would enable a U.S. Holder to make a qualified electing fund election.

Unless otherwise provided by the U.S. Treasury, each U.S. shareholder of a PFIC is required to file an annual information return on IRS Form 8621 (Information Return by a Shareholder of a Passive Foreign Investment Company or Qualifying Electing Fund) containing such information as the U.S. Treasury may require. A U.S. Holder's failure to file such annual information return could result in the imposition of penalties and the extension of the statute of limitations with respect to U.S. federal income tax. You should consult your own tax advisors regarding the requirements of filing such information returns under these rules, taking into account the uncertainty as to whether we are currently treated as or may become a PFIC.

YOU ARE STRONGLY URGED TO CONSULT YOUR OWN TAX ADVISOR REGARDING THE IMPACT AND APPLICATION OF THE PFIC RULES ON YOUR INVESTMENT IN THE ORDINARY SHARES OR ADSs.

Backup Withholding and Information Reporting

Payments of dividends with respect to Ordinary Shares or ADSs and the proceeds from the sale, retirement, or other disposition of Ordinary Shares or ADSs made by a U.S. paying agent or other U.S. intermediary will be reported to the IRS and to the U.S. Holder as may be required under applicable U.S. Treasury regulations. We, or an agent, a broker, or any paying agent, as the case may be, may be required to withhold tax (backup withholding), currently at the rate of 24%, if a non-corporate U.S. Holder that is not otherwise exempt fails to provide an accurate taxpayer identification number and comply with other IRS requirements concerning information reporting. Certain U.S. Holders (including, among others, corporations and tax-exempt organizations) are not subject to backup withholding. Backup withholding is not an additional tax. Any amount of backup withholding withheld may be used as a credit against your U.S. federal income tax liability provided that the required information is furnished to the IRS. U.S. Holders should consult their own tax advisors as to their qualification for exemption from backup withholding and the procedure for obtaining an exemption.

Individual U.S. Holders may be required to file certain U.S. information reporting returns with the IRS with respect to an investment in our Ordinary Shares or ADSs, including, among others, IRS Form 8938 (Statement of Specified Foreign Financial Assets). U.S. Holders paying more than $100,000 for our Ordinary Shares or ADSs may be required to file IRS Form 926 (Return by a U.S. Transferor of Property to a Foreign Corporation) reporting this payment. As described above under "—Passive Foreign Investment Companies," if we were determined to be a PFIC, each U.S. Holder would be

required to file an annual report containing certain information. Substantial penalties may be imposed upon a U.S. Holder that fails to comply with the required information reporting.

You should consult your own tax advisors regarding the backup withholding tax and information reporting rules.

EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF AN INVESTMENT IN OUR ORDINARY SHARES OR ADSs IN LIGHT OF SUCH INVESTOR'S PARTICULAR CIRCUMSTANCES.

F. Dividends and Paying Agents

Not applicable.

G. Statement by Experts

Not applicable.

H. Documents on Display

We are subject to the information reporting requirements of the Exchange Act, applicable to foreign private issuers, and under those requirements, we file reports with the SEC. Those other reports or other information are available to the public through the SEC's website at http://www.sec.gov.

As a foreign private issuer, we are exempt from the rules under the Exchange Act, related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act, to file annual, quarterly and current reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act. However, we are required to comply with the informational requirements of the Exchange Act, and, accordingly, file current reports on Form 6-K, annual reports on Form 20-F and other information with the SEC.

We maintain a corporate website at *www.redhillbio.com*. Information contained on, or that can be accessed through, our website does not constitute a part of this Annual Report.

I. Subsidiary Information

Not applicable.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Market risk is the risk of loss related to changes in market prices, including interest rates and foreign exchange rates, of financial instruments that may adversely impact our financial position, results of operations or cash flows. Our overall risk management program focuses on the unpredictability of financial markets and seeks to minimize potential adverse effects on our financial performance.

Risk of Interest Rate Fluctuation and Credit Exposure Risk

At present, our credit and interest risk arise from our term loan facility, cash and cash equivalents, deposits with banks and a portfolio of corporate bonds as well as accounts receivable. A substantial portion of our liquid instruments is invested in short-term deposits and corporate bonds in highly-rated institutions.

Our term loan facility indebtedness uses LIBOR as a benchmark for establishing the interest rate. The most popular LIBOR indices will be phased out by the end of June 2023. It is unclear whether new methods of calculating LIBOR will be established or if alternative benchmark reference rates will be adopted. The replacement of LIBOR with an alternative

benchmark reference rate may adversely affect interest rates and result in higher borrowing costs for us under current or future credit agreements. This could adversely affect our liquidity and financial condition, results of operations, and ability to acquire debt financing. We cannot predict the effect of the elimination of LIBOR or the establishment and use of alternative benchmark reference rates and the corresponding effects of our cost of capital.

We estimate that because the liquid instruments are invested mainly for the short-term and with highly-rated institutions, the credit and interest risk associated with these balances is low. The primary objective of our investment activities is to preserve principal while maximizing the income we receive from our investments without significantly increasing risk and loss. Our investments are exposed to market risk due to fluctuations in interest rates, which may affect our interest income and the fair market value of our investments. We manage this exposure by performing ongoing evaluations of our investments.

Market Price Risk

We may be exposed to market price risk because of investments in tradable securities, mainly corporate bonds, held by us and classified in our financial statements as financial assets at fair value through profit or loss. To manage the price risk arising from investments in tradable securities, we invest in marketable securities with high ratings and diversify our investment portfolio.

Foreign Currency Exchange Risk

Our foreign currency exposures give rise to market risk associated with exchange rate movements of the U.S. dollar, our functional and reporting currency, mainly against the NIS and other currencies. Although the U.S. dollar is our functional currency and reporting currency, a portion of our expenses is denominated in NIS and in Euro. Our NIS expenses consist principally of payments to employees or service providers and office-related expenses in Israel. Our Euro expenses consist primarily of payments to vendors related to our therapeutic candidates. We also hold short-term investments in currencies other than the U.S. dollar. We anticipate that a sizable portion of our expenses will continue to be denominated in currencies other than the U.S. dollar. If the U.S. dollar fluctuates significantly against the NIS, it may have a negative impact on our results of operations. We manage our foreign exchange risk by aligning the currencies for holding short-term investments with the currencies of expected expenses, based on our expected cash flows.

Portfolio diversification is performed based on risk level limits that we set. To date, we have not engaged in hedging transactions. In the future, we may enter into currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rates of our principal operating currencies. These measures, however, may not adequately protect us from the material adverse effects of such fluctuations.

(A) Set forth below is a sensitivity test to possible changes in U.S. dollars/NIS exchange rate on our assets and liabilities as of December 31, 2021:

Sensitive instrument	Income (loss) from change in exchange rate (U.S. dollars in thousands)		Value (U.S. dollars in thousands)	Income (loss) from change in exchange rate (U.S. dollars in thousands)	
	Down 2 %	Down 5 %		Up 5 %	Up 2 %
Cash and cash equivalents	3	7	29,475	(3)	(7)
Bank deposits	4	9	24,699	(4)	(9)
Accounts receivable (except prepaid expenses)	7	18	1,495	(7)	(18)
Accounts payable and accrued expenses	(12)	(28)	(32,560)	12	28
Total loss	2	6		(2)	(6)

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. Debt Securities

Not applicable.

B. Warrants and Rights

Not applicable.

C. Other Securities

Not applicable.

D. American Depositary Shares

Each of the American Depositary Shares, or ADSs, represents 10 Ordinary Shares. The ADSs trade on the Nasdaq Global Market.

The form of the deposit agreement for the ADSs and the form of American Depositary Receipt (ADR) that represents an ADS have been incorporated by reference as exhibits to this Annual Report on Form 20-F. Copies of the deposit agreement are available for inspection at the principal office of The Bank of New York Mellon, located at 101 Barclay Street, New York, New York 10286.

Fees and Expenses

***Persons depositing or withdrawing shares or American Depositary Shareholders must pay*:**	***For*:**
$5.00 (or less) per 100 American Depositary Shares (or portion of 100 American Depositary Shares)	● Issuance of American Depositary Shares, including issuances resulting from a distribution of shares or rights or other property ● Cancellation of American Depositary Shares for the purpose of withdrawal, including if the deposit agreement terminates
$0.05 (or less) per American Depositary Share	● Any cash distribution to American Depositary Shareholders
A fee equivalent to the fee that would be payable if securities distributed to you had been shares and the shares had been deposited for issuance of American Depositary Shares	● Distribution of securities distributed to holders of deposited securities which are distributed by the depositary to American Depositary Shareholders
$0.05 (or less) per American Depositary Shares per calendar year	● Depositary services
Registration or transfer fees	● Transfer and registration of shares on our share register to or from the name of the depositary or its agent when you deposit or withdraw shares
Expenses of the depositary	● Cable, telex and facsimile transmissions (when expressly provided in the deposit agreement) ● Converting foreign currency to U.S. dollars
Taxes and other governmental charges the depositary or the custodian have to pay on any American Depositary Share or share underlying an American Depositary Share, for example, stock transfer taxes, stamp duty or withholding taxes	● As necessary
Any charges incurred by the depositary or its agents for servicing the deposited securities	● As necessary

The depositary collects its fees for delivery and surrender of American Depositary Shares directly from investors depositing shares or surrendering American Depositary Shares for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of the distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions or by directly billing investors or by charging the book-entry system accounts of participants acting for them. The depositary may generally refuse to provide fee-attracting services until its fees for those services are paid.

From time to time, the depositary may make payments to us to reimburse us or share its revenue with us from the fees collected from American Depositary Shareholders or waive fees and expenses for services provided, generally relating to costs and expenses arising out of establishment and maintenance of the American Depositary Share program. In performing its duties under the deposit agreement, the depositary may use brokers, dealers or other service providers that are affiliates of the depositary and that may earn or share fees or commissions.

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

Not applicable.

ITEM 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

Not applicable.

ITEM 15. CONTROLS AND PROCEDURES

(a) Disclosure Controls and Procedures

We performed an evaluation of the effectiveness of our disclosure controls and procedures that are designed to ensure that information required to be disclosed on Form 20-F and filed with the SEC is recorded, processed, summarized and reported timely within the time period specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act, is accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. There can be no assurance that our disclosure controls and procedures will detect or uncover all failures of persons within the company to disclose information otherwise required to be set forth in our reports. Nevertheless, our disclosure controls and procedures are designed to provide reasonable assurance of achieving the desired control objectives. Based on our evaluation, our management, including our Chief Executive Officer and Chief Financial Officer, have concluded that our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act) as of the end of the period covered by this report are effective at such reasonable assurance level.

(b) Management's Annual Report on Internal Control over Financial Reporting

Our management, under the supervision of our Chief Executive Officer and Chief Financial Officer, is responsible for establishing and maintaining adequate internal control over our financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act of 1934, as amended. The Company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Internal control over financial reporting includes policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect our transactions and asset dispositions;
- provide reasonable assurance that transactions are recorded as necessary to permit the preparation of our financial statements in accordance with generally accepted accounting principles;

- provide reasonable assurance that receipts and expenditures are made only in accordance with authorizations of our management and board of directors (as appropriate); and
- provide reasonable assurance regarding the prevention or timely detection of unauthorized acquisition, use or disposition of assets that could have a material effect on our financial statements.

Due to its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. In addition, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we assessed the effectiveness of our internal control over financial reporting as of December 31, 2021, based on the framework for Internal Control-Integrated Framework set forth by The Committee of Sponsoring Organizations of the Treadway Commission (COSO) (2013).

Based on our assessment and this framework, our management concluded that the Company's internal control over financial reporting was effective as of December 31, 2021. Our auditor, Kesselman & Kesselman, Certified Public Accountants (Isr.), a member firm of PricewaterhouseCoopers International Limited, an independent registered public accounting firm, has provided an attestation report on our internal control over financial reporting, which is included herein. (See "– *Attestation Report of Registered Public Accounting Firm*.")

(c) Attestation Report of Registered Public Accounting Firm

Our independent registered public accounting firm has audited the consolidated financial statements included in this Annual Report on Form 20-F, and as part of its audit, has issued its audit report on the effectiveness of our internal control over financial reporting. This report is included in pages F-1 to F-4 of this Annual Report on Form 20-F and is incorporated herein by reference.

(d) Changes in Internal Control Over Financial Reporting

There were no material changes in our internal control over financial reporting that occurred during the year ended December 31, 2021, that have materially affected or are reasonably likely to materially affect our internal control over financial reporting.

ITEM 16. [RESERVED]

ITEM 16A. AUDIT COMMITTEE FINANCIAL EXPERT

Our board of directors has determined that Ms. Alla Felder, Mr. Ofer Tsimchi and Mr. Eric Swenden are audit committee financial experts. Ms. Felder, Mr. Tsimchi and Mr. Eric Swenden are independent directors for the purposes of the Nasdaq Listing Rules.

ITEM 16B. CODE OF ETHICS

As of the date of this Annual Report, we have adopted a code of ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. This code of ethics is posted on our website, https://s28.q4cdn.com/226515471/files/doc_downloads/gov_docs/Standards-of-Business-Conduct-and-Ethics.pdf. We intend to post on our website any amendments or waivers to the code of ethics that apply to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions.

ITEM 16C. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Fees Paid to Independent Registered Public Accounting Firm

The following table sets forth, for each of the years indicated, the aggregate fees billed by our independent registered public accounting firm for professional services.

Services Rendered	Year Ended December 31, 2021	2020
	(U.S. dollars in thousands)	
Audit fees (1)	258	210
Audit-related fees (2)	118	52
Tax fees (3)	7	22
Total	383	284

(1) Audit fees consist of services that would normally be provided in connection with statutory and regulatory filings or engagements, including services that generally only the independent accountant can reasonably provide.
(2) Audit-related fees relate to work regarding prospectus supplements and ongoing consultation.
(3) Tax fees relate to tax compliance, planning, and advice.

Audit Committee Pre-Approval Policies and Procedures

Our audit committee's specific responsibilities in carrying out its oversight of the quality and integrity of the accounting, auditing and reporting practices of the Company include the approval of audit and non-audit services to be provided by the external auditor. The audit committee approves in advance the particular services or categories of services to be provided to the Company during the following yearly period and also sets forth a specific budget for such audit services. All non-audit services are pre-approved by the audit committee.

ITEM 16D. EXEMPTIONS FROM THE LISTING STANDARDS FOR AUDIT COMMITTEES

Not applicable.

ITEM 16E. PURCHASES OF EQUITY SECURITIES BY THE ISSUER AND AFFILIATED PURCHASERS

Members of our board of directors and senior management, including the Company's Chairman & CEO, CFO, Chief Commercial Officer, Chief Business Officer and Chief Corporate & Business Development Officer, purchased ADSs in open-market transactions during calendar year 2021 as described in the table below. We did not repurchase any ADSs during the year.

Period	Total Number of Shares Purchased	Average Price Paid Per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	Maximum Number of Shares that May Yet Be Purchased Under the Plans or Programs
September 15, 2021 until September 30, 2021	90,991 ADSs	$4.93 per ADS	None	None
October 1, 2021 until October 18, 2021	97,752 ADSs	$4.87 per ADS	None	None
December 1 until December 13	58,887 ADSs	$2.97 per ADS	None	None

ITEM 16F. CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT

Not applicable.

ITEM 16G. CORPORATE GOVERNANCE

Nasdaq Stock Listing Rules and Home Country Practices

As a foreign private issuer, we are permitted to follow Israeli corporate governance practices instead of the Nasdaq Listing Rules, provided that we disclose which requirements we are not following and the equivalent Israeli requirement. We rely on this "foreign private issuer exemption" with respect to the following items:

- *Shareholder Approval* - We seek shareholder approval for all corporate actions requiring such approval in accordance with the requirements of the Israeli Companies Law, which are different from the shareholder approval requirements of the Nasdaq Listing Rules. The Nasdaq Listing Rules require that we obtain shareholder approval for certain dilutive events, such as for the establishment or amendment of certain equity-based compensation plans and arrangements, issuances that will result in a change in control of a company, certain transactions other than a public offering involving issuances of 20% or more of the shares or voting power in a company, and certain acquisitions of the stock or assets of another company involving issuances of 20% or more of the shares or voting power in a company or if any director, officer or holder of 5% or more of the shares or voting power of the company has a 5% or greater interest in the company or assets to be acquired or consideration to be paid and the transaction could result in an increase in the outstanding common shares or voting power by 5% or more;
- Under the Israeli Companies Law, shareholder approval is required for any transaction, including any grant of equity-based compensation, to a director or a controlling shareholder, but is not generally required to establish or amend an equity-based compensation plan. Similarly, shareholder approval is required for a private placement that is deemed an "extraordinary private placement" or that involves a director or controlling shareholder. An "extraordinary private placement" is a private placement in which a company issues securities representing 20% or more of its voting rights prior to the issuance and the consideration received pursuant to such issuance is not comprised, in whole or in part, solely of cash or securities registered for trade on an exchange or which is not made pursuant to market conditions, and as a result of which the shareholdings of a 5% holder of the shares or voting rights of the company increases or as a result of which a person will become a holder of 5% of the shares or voting rights of the company or a controlling shareholder after the issuance;
- *Quorum* - As permitted under the Israeli Companies Law, pursuant to our articles of association, the quorum required for an ordinary meeting of shareholders consists of at least two shareholders present in person or by proxy who hold or represent at least 25% of the voting rights of our shares (and at an adjourned meeting, with some exceptions, any number of shareholders), instead of 33 1/3% of the issued share capital required under the Nasdaq Listing Rules; and
- *Nominations Committee* - As permitted by the Israeli Companies Law, our board of directors selects director nominees subject to the terms of our articles of association which provide that incumbent directors are re-nominated for additional terms. Directors are not selected, or recommended for board of director selection, by independent directors constituting a majority of the board's independent directors or by a nominations committee comprised solely of independent directors as required by the Nasdaq Listing Rules.

Otherwise, we comply with the rules generally applicable to U.S. domestic companies listed on the Nasdaq Stock Market. We may in the future decide to use the foreign private issuer exemption with respect to some or all of the other Nasdaq Listing Rules related to corporate governance. We also comply with Israeli corporate governance requirements under the Israeli Companies Law as applicable to us.

ITEM 16H. MINE SAFETY DISCLOSURE

Not applicable.

ITEM 17. FINANCIAL STATEMENTS

Not applicable.

ITEM 18. FINANCIAL STATEMENTS

The financial statements required by this item are found at the end of this Annual Report, beginning on page F-1.

ITEM 19. EXHIBITS

See Exhibit Index on page 159.

Glossary of Terms

Certain standards and other terms that are used in this Annual Report are defined below:

H. pylori (*Helicobacter pylori****)*** **-** a Gram-negative bacterium found in the stomach. It was identified in 1982 by Dr. Barry Marshall and Dr. Robin Warren and is associated with peptic ulcer disease and the development of gastric cancer.

IND - Investigational New Drug - a status assigned by the FDA to a drug before allowing its use in humans, so that experimental clinical trials may be conducted.

IRB - Institutional Review Board - Under FDA regulations, an IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects.

ITT - intention-to-treat – intention-to-treat analysis means all of the patients who were enrolled and randomized into a clinical study are included in the analysis.

Mycobacterium avium subspecies paratuberculosis **(MAP) -** an obligate pathogenic bacterium in the genus Mycobacterium. MAP is the causative agent of Johne's disease, a chronic granulomatous ileitis occurring mainly in ruminants. MAP has been suspected as the cause of Crohn's disease in humans.

NDA - New Drug Application - an application by drug sponsors to the FDA for approval of a new pharmaceutical for sale and marketing in the U.S.

NTM - Nontuberculous Mycobacteria– a class of Mycobacteria also known as environmental mycobacteria, atypical mycobacteria and mycobacteria other than tuberculosis (MOTT).

Ondansetron - a drug in a class of medications called serotonin 5-HT_3 receptor antagonists. Ondansetron works by blocking the action of serotonin, a natural substance that may cause nausea and vomiting.

Orphan Drug Designation - the designation of orphan drug designation to drugs that are in the process of development for the treatment of rare diseases, affecting fewer than 200,000 people in the U.S. This status provides tax reductions and the exclusive rights to the cure for a specific condition for a period of seven years post-approval.

PK - pharmacokinetics - the study of the absorption, distribution, metabolism, and excretion of drugs in the body.

QIDP - Qualified Infectious Disease Product - designation granted under the FDA's Generating Antibiotic Incentives Now Act, which is intended to encourage the development of new antibiotic drugs for the treatment of serious or life-threatening infections that have the potential to pose a serious threat to public health**.**

Sphingosine kinase-2 (SK2) - an enzyme catalyzes the phosphorylation of sphingosine to generate sphingosine 1-phosphate. There are two isotypes of sphingosine enzyme, SK1 and SK2. Both isotypes have a key role in a variety of diseases, including the development of a range of solid tumors and are promising anti-cancer therapeutic targets.

TNFα - Tumor necrosis factor alpha is a cell-signaling protein (cytokine) involved in systemic inflammation.

REDHILL BIOPHARMA LTD

EXHIBIT INDEX

1.1	Articles of Association of the Registrant, as amended (unofficial English translation) (incorporated by reference to Exhibit 1.1 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 18, 2021).
2.1	Form of Deposit Agreement among the Registrant, the Bank of New York Mellon, as Depositary, and all Owners and Holders from time to time of American Depositary Shares issued hereunder (incorporated by reference to Exhibit 1 to the Registration Statement on Form F-6 filed by The Bank of New York Mellon with the Securities and Exchange Commission on December 6, 2012).
2.2	Form of American Depositary Receipt (incorporated by reference to Exhibit 1 to the Registration Statement on Form F-6 filed by The Bank of New York Mellon with the Securities and Exchange Commission on December 6, 2012).
2.3	Description of Share Capital (incorporated by reference to Exhibit 2.3 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 18, 2021).
4.1*	Asset Purchase Agreement, dated August 11, 2010, by and between the Registrant and Giaconda Limited (RHB-104, 105, 106) (incorporated by reference to Exhibit 4.4 to Draft Registration Statement on Form DRS disseminated with the Securities and Exchange Commission, dated December 3, 2012).
4.2	Amendment to Asset Purchase Agreement by and between the Registrant and Giaconda Limited (RHB-104, 105, 106) dated February 27, 2014 (incorporated by reference to Exhibit 4.2 of the Annual Report on Form 20 F filed with the Securities and Exchange Commission on February 26, 2019).
4.3*	Exclusive License Agreement, dated March 30, 2015, by and between the Registrant and Apogee Biotechnology Corp (incorporated by reference to Exhibit 4.7 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on February 25, 2016).
4.4†	Amendment #1 dated January 23, 2017, to the Exclusive License Agreement dated March 30, 2015, by and between the Registrant and Apogee Biotechnology Corp. (incorporated by reference to Exhibit 4.6 of the Annual Report on Form 20-F/A filed with the Securities and Exchange Commission on May 15, 2019).
4.5*	Amendment #2 dated June 22, 2017, to the Exclusive License Agreement dated March 30, 2015, by and between the Registrant and Apogee Biotechnology Corp. (incorporated by reference to Exhibit 4.5 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on February 22, 2018).
4.6*	Amendment #3 dated February 6, 2018, to the Exclusive License Agreement dated March 30, 2015, by and between the Registrant and Apogee Biotechnology Corp. (incorporated by reference to Exhibit 4.6 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on February 22, 2018).
4.7†	Amendment #4 dated January 3, 2019, to the Exclusive License Agreement dated March 30, 2015, by and between the Registrant and Apogee Biotechnology Corp. (incorporated by reference to Exhibit 4.9 of the Annual Report on Form 20-F/A filed with the Securities and Exchange Commission on May 15, 2019).
4.8	Amendment #5 dated January 23, 2019, to the Exclusive License Agreement dated March 30, 2015, by and between the Registrant and Apogee Biotechnology Corp. (incorporated by reference to Exhibit 4.10 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on February 26, 2019).
4.9	Form of Letter of Exemption and Indemnity adopted on July 26, 2021 (unofficial English translation).

4.10	Amended and Restated Award Plan (2010).
4.11	Compensation Policy, as amended.
4.12†	Subscription Agreement, dated October 17, 2019, by and between Registrant and Cosmo Pharmaceuticals N.V. and Cosmo Technologies Ltd (incorporated by reference to Exhibit 4.12 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 3, 2020).
4.13†	Exclusive License Agreement, dated October 17, 2019, by and between Registrant and Cosmo Technologies Ltd (incorporated by reference to Exhibit 4.13 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 3, 2020).
4.14†	Amendment #1 dated December 2, 2021, to the Exclusive License Agreement, dated October 17, 2019, by and between Registrant and Cosmo Technologies Ltd.
4.15^	Credit Agreement, dated February 23, 2020, by and among RedHill Biopharma Ltd., RedHill Biopharma Inc., HCR Collateral Management, LLC and the lenders from time to time party thereto (incorporated by reference to Exhibit 4.14 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 3, 2020).
4.16	First amendment dated March 31, 2020, to the Credit Agreement dated February 23, 2020, by and among RedHill Biopharma Ltd., RedHill Biopharma Inc., HCR Collateral Management, LLC and the lenders from time to time party thereto (incorporated by reference to Exhibit 4.15 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 18, 2021).
4.17	Second amendment dated August 12, 2020, to the Credit Agreement dated February 23, 2020, by and among RedHill Biopharma Ltd., RedHill Biopharma Inc., HCR Collateral Management, LLC and the lenders from time to time party thereto (incorporated by reference to Exhibit 4.16 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 18, 2021).
4.18	Third amendment dated January 28, 2021, to the Credit Agreement dated February 23, 2020, by and among RedHill Biopharma Ltd., RedHill Biopharma Inc., HCR Collateral Management, LLC and the lenders from time to time party thereto (incorporated by reference to Exhibit 4.15 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 18, 2021).
4.19	Fourth amendment dated July 22, 2021, to the Credit Agreement dated February 23, 2020, by and among RedHill Biopharma Ltd., RedHill Biopharma Inc., HCR Collateral Management, LLC and the lenders from time to time party thereto.
4.20^	Security Agreement, dated February 23, 2020, by and among RedHill Biopharma Ltd., RedHill Biopharma Inc., and HCR Collateral Management, LLC (incorporated by reference to Exhibit 4.15 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 3, 2020).
4.21^	Pledge Agreement, dated February 23, 2020, by and among RedHill Biopharma Ltd., RedHill Biopharma Inc., and HCR Collateral Management, LLC (incorporated by reference to Exhibit 4.16 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 3, 2020).
4.22†	License Agreement, dated February 23, 2020, by and between Registrant and AstraZeneca AB (incorporated by reference to Exhibit 4.17 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 3, 2020).
4.23†	Amendment #1 dated March 31, 2020, to the License Agreement, dated February 23, 2020, by and between Registrant and AstraZeneca AB (incorporated by reference to Exhibit 4.21 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 18, 2021).

4.24†	Amendment #2 dated July 14, 2020, to the License Agreement, dated February 23, 2020, by and between Registrant and AstraZeneca AB (incorporated by reference to Exhibit 4.22 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 18, 2021).
4.25†	Amendment #3 dated October 6, 2020, to the License Agreement, dated February 23, 2020, by and between Registrant and AstraZeneca AB (incorporated by reference to Exhibit 4.23 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 18, 2021).
4.26†	Amendment #4 dated March 11, 2021, to the License Agreement, dated February 23, 2020, by and between Registrant and AstraZeneca AB (incorporated by reference to Exhibit 4.24 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 18, 2021).
4.27†	Supply Agreement, dated February 23, 2020, by and between Registrant and AstraZeneca AB (incorporated by reference to Exhibit 4.18 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 3, 2020).
4.28†	Termination Agreement, dated August 3, 2020, by and between RedHill Biopharma Inc. and Daiichi Sankyo Inc (incorporated by reference to Exhibit 4.26 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 18, 2021).
4.29†	Securities Purchase Agreement, dated August 3, 2020, but effective as of July 1, 2020, by and between RedHill Biopharma Ltd., and Daiichi Sankyo, Inc (incorporated by reference to Exhibit 4.27 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on March 18, 2021).
8.1	Subsidiary List (incorporated by reference to Exhibit 8.1 of the Annual Report on Form 20-F filed with the Securities and Exchange Commission on February 22, 2018).
12.1	Certification by Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
12.2	Certification by Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
13	Certification by Chief Executive Officer and Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
15.1	Consent of Independent Registered Public Accounting Firm.
101	The following financial statements from the Company's 20-F for the fiscal year ended December 31, 2021, formatted in Inline XBRL: (i) Consolidated Statements of Comprehensive Loss, (ii) Consolidated Statements of Financial Position, (iii) Consolidated Statements of Changes in Equity, (iv) Consolidated Statements of Cash Flows, and (v) Notes to the Consolidated Financial Statements.
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).

* Confidential treatment granted with respect to certain portions of this Exhibit.

† Certain identified confidential information in this Exhibit has been omitted because such identified confidential information is (i) the type the Company treats as private or confidential and (ii) is not material.

^ Certain schedules and/or exhibits to this Exhibit have been omitted in accordance with the instructions to Item 19 of Form 20-F. A copy of any omitted schedule and/or exhibit will be furnished supplementally to the Securities and Exchange Commission or its staff upon request.

SIGNATURES

The Registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

REDHILL BIOPHARMA LTD

By: /s/ Dror Ben-Asher
Name: Dror Ben-Asher
Title: Chief Executive Officer and Chairman of the Board of Directors

By: /s/ Micha Ben-Chorin
Name: Micha Ben Chorin
Title: Chief Financial Officer

Date: March 17, 2022

REDHILL BIOPHARMA LTD.

2021 CONSOLIDATED FINANCIAL STATEMENTS

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Report of Independent Registered Public Accounting Firm

To the board of directors and shareholders of RedHill Biopharma Ltd.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated statements of financial position of RedHill Biopharma Ltd. and its subsidiary (the "Company") as of December 31, 2021 and 2020, and the related consolidated statements of comprehensive loss, of changes in equity and of cash flows for each of the three years in the period ended December 31, 2021, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2021, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021 in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2021, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Annual Report on Internal Control over Financial Reporting appearing under Item 15(b). Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall

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presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that (i) relate to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Recognition and measurement of allowance for certain rebates

As described in Note 2 to the consolidated financial statements, the Company offers various rebate and patient discount programs, which result in discounted prescriptions to qualified patients, of which the most significant are Managed Care (commercial rebates), Medicare Part D and Medicaid (and similar state programs). Rebates provided to patients under these arrangements are accounted for as variable consideration, and recognized as a reduction in revenue, for which unsettled amounts are accrued. The allowance for these rebates is calculated based on historical and estimated utilization of the rebate programs in accordance with the specific terms in the individual agreement, the estimated product in the channel and the estimated mix of programs in future prescriptions utilization. The allowance reported as of December 31, 2021 for revenue deductions amounted to $30.7 million, with a significant portion relating to Managed Care, Medicare Part D, and Medicaid.

The principal considerations for our determination that performing procedures related to recognition and measurement of the allowance for rebates is a critical audit matter are the significant estimations made by management due to the measurement uncertainty involved in developing the allowance, as the reserves are based on assumptions developed using contractual and mandated terms with payors and historical experience.

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This in turn led to a high degree of auditor judgment and subjectivity in applying procedures relating to these assumptions.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to the assumptions used to estimate the allowance for Managed Care (commercial rebates), Medicare Part D and Medicaid (and similar state programs). These procedures also included, among others, developing an independent expectation of the allowance using the terms of the specific rebates programs and the historical trend of actual rebates claims paid; comparing the independent estimate to management's estimate recorded by the Company; and testing rebates claims processed by the Company, including evaluating those claims for consistency with the contractual and mandated terms of the Company's arrangements.

Liquidity and capital resources

As discussed in Note 1 to the consolidated financial statements, the Company has an accumulated deficit and its activities have been funded primarily through offerings of the Company's securities and borrowing. There is no assurance that the Company's business will generate sustainable positive cash flows to fund its business. Management expects that the Company will incur additional losses as it continues to focus its resources on advancing the development of its therapeutic candidates, as well as advancing its commercial operations, based on a prioritized plan that will result in negative cash flows from operating activities. The Company believes its existing capital resources should be sufficient to fund its current and planned operations for at least the next 12 months.

The principal considerations for our determination that performing procedures related to liquidity and capital resources is a critical audit matter are the estimation and execution uncertainty regarding the Company's future cash flows and the risk of bias in management's judgments and assumptions in estimating these cash flows to conclude the Company would have sufficient liquidity to fund its operations for at least the next 12 months. This in turn led to a high degree of auditor subjectivity and judgment to evaluate the audit evidence supporting the liquidity conclusions.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with our overall opinion on the consolidated financial statements. Our audit procedures included, among others, testing the reasonableness of the forecasted revenue, operating expenses, and uses and sources of cash used in management's assessment of whether the Company has sufficient liquidity to fund operations for at least the next 12 months. This testing included testing the effectiveness of controls over management's liquidity assessment including the review of the inputs and assumptions used in this assessment. We assessed the appropriateness of forecast assumption by comparing prior period forecasts to actual results, comparing forecasted revenue to recent historical financial information, inquiring of management regarding the mitigating actions to reduce costs and manage cash flows and assessing whether the mitigating actions were within the Company's control, testing the underlying data generated to prepare the forecast scenarios and determined whether there was adequate support for the assumptions underlying the forecast, considering the terms of the Company's existing loans to obtain an understanding of the debt covenants, and evaluating management's analysis of the impact of the above assumptions on the forecasted cash flows.

We assessed the adequacy of the Company's liquidity disclosures included in Note 1 to the consolidated financial statements.

/s/ Kesselman & Kesselman
Certified Public Accountants (Isr.)
A member of PricewaterhouseCoopers International Limited

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Tel-Aviv, Israel
March 17, 2022
We have served as the Company's auditor since 2010.

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REDHILL BIOPHARMA LTD.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

	Note	Year Ended December 31,		
		2021	2020	2019
		U.S. dollars in thousands		
NET REVENUES	20	85,757	64,359	6,291
COST OF REVENUES		49,406	36,892	2,259
GROSS PROFIT		36,351	27,467	4,032
RESEARCH AND DEVELOPMENT EXPENSES	21	29,498	16,491	17,419
SELLING AND MARKETING EXPENSES	22	55,623	49,285	18,333
GENERAL AND ADMINISTRATIVE EXPENSES	23	32,365	25,375	11,481
OPERATING LOSS		81,135	63,684	43,201
FINANCIAL INCOME		51	270	1,335
FINANCIAL EXPENSES		16,660	12,759	438
FINANCIAL EXPENSES (INCOME), net	24	16,609	12,489	(897)
LOSS AND COMPREHENSIVE LOSS FOR THE YEAR		97,744	76,173	42,304
LOSS PER ORDINARY SHARE, basic and diluted (U.S. dollars)	26	0.21	0.21	0.14

The accompanying notes are an integral part of these consolidated financial statements.

REDHILL BIOPHARMA LTD.

CONSOLIDATED STATEMENTS OF FINANCIAL POSITION

	Note	December 31, 2021	December 31, 2020
		U.S. dollars in thousands	
CURRENT ASSETS:			
Cash and cash equivalents	5	29,474	29,295
Bank deposits		8,530	17
Financial assets at fair value through profit or loss	6	—	481
Trade receivables		31,677	28,655
Prepaid expenses and other receivables	7	4,661	5,521
Inventory	8	14,810	6,526
		89,152	70,495
NON-CURRENT ASSETS:			
Restricted cash	15	16,169	16,164
Fixed assets	9	572	511
Right-of-use assets	10	3,651	5,192
Intangible assets	11	71,644	87,879
		92,036	109,746
TOTAL ASSETS		181,188	180,241
CURRENT LIABILITIES:			
Account payable		11,664	11,553
Lease liabilities	10	1,618	1,710
Allowance for deductions from revenue	14	30,711	18,343
Accrued expenses and other current liabilities	13	20,896	24,082
Payable in respect of intangible assets purchase	16(5)(6)	16,581	17,547
		81,470	73,235
NON-CURRENT LIABILITIES:			
Borrowing	15	83,620	81,386
Payable in respect of intangible assets purchase	16(5)(6)	3,899	7,199
Lease liabilities	10	2,574	3,807
Royalty obligation	16(3)	750	750
		90,843	93,142
TOTAL LIABILITIES		172,313	166,377
EQUITY:	18		
Ordinary shares		1,495	1,054
Additional paid-in capital		375,246	293,144
Accumulated deficit		(367,866)	(280,334)
TOTAL EQUITY		8,875	13,864
TOTAL LIABILITIES AND EQUITY		181,188	180,241

The accompanying notes are an integral part of these consolidated financial statements.

REDHILL BIOPHARMA LTD.

CONSOLIDATED STATEMENTS OF CHANGES IN EQUITY

	Ordinary shares	Additional paid-in capital	Accumulated deficit	Total equity
	U.S. dollars in thousands			
BALANCE AT JANUARY 1, 2019	767	219,505	(169,086)	51,186
CHANGES DURING THE YEAR ENDED DECEMBER 31, 2019:				
Share-based compensation to employees and service providers	—	—	3,027	3,027
Issuance of ordinary shares to private investor	195	47,893	—	48,088
Exercise of options into ordinary shares	*	5	—	5
Comprehensive loss	—	—	(42,304)	(42,304)
BALANCE AT DECEMBER 31, 2019	962	267,403	(208,363)	60,002
BALANCE AT JANUARY 1, 2020	962	267,403	(208,363)	60,002
CHANGES DURING THE YEAR ENDED DECEMBER 31, 2020:				
Share-based compensation to employees and service providers	—	—	4,202	4,202
Issuance of ordinary shares, net of expenses	84	23,783	—	23,867
Exercise of options into ordinary shares	*	52	—	52
Share-based compensation in consideration for intangible assets	8	1,906	—	1,914
Comprehensive loss	—	—	(76,173)	(76,173)
BALANCE AT DECEMBER 31, 2020	1,054	293,144	(280,334)	13,864
BALANCE AT JANUARY 1, 2021	1,054	293,144	(280,334)	13,864
CHANGES DURING THE YEAR ENDED DECEMBER 31, 2021:				
Share-based compensation to employees and service providers	—	—	10,212	10,212
Issuance of ordinary shares, net of expenses	424	78,113	—	78,537
Exercise of options into ordinary shares	17	3,989	—	4,006
Comprehensive loss	—	—	(97,744)	(97,744)
BALANCE AT DECEMBER 31, 2021	1,495	375,246	(367,866)	8,875

*Less than a thousand

The accompanying notes are an integral part of these consolidated financial statements.

REDHILL BIOPHARMA LTD.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2021	2020	2019
	U.S. dollars in thousands		
OPERATING ACTIVITIES:			
Comprehensive loss	(97,744)	(76,173)	(42,304)
Adjustments in respect of income and expenses not involving cash flow:			
Share-based compensation to employees and service providers	10,212	4,202	3,027
Depreciation	1,914	1,710	997
Amortization and impairment of intangible assets	16,235	7,035	216
Non-cash interest expenses related to borrowing and payable in respect of intangible assets purchase	5,366	6,032	—
Fair value adjustments on derivative financial instruments	—	—	(344)
Fair value (gains) losses on financial assets at fair value through profit or loss	5	94	(27)
Exchange differences and revaluation of bank deposits	118	101	24
	33,850	19,174	3,893
Changes in assets and liability items:			
Increase in trade receivables	(3,021)	(27,439)	(258)
Decrease (increase) in prepaid expenses and other receivables	860	(3,277)	(368)
Increase in inventories	(8,285)	(4,644)	(1,113)
Increase in accounts payable	111	7,369	860
Increase (decrease) in accrued expenses and other liabilities	(3,186)	19,335	(2,726)
Increase in allowance for deductions from revenue	12,368	17,076	1,267
	(1,153)	8,420	(2,338)
Net cash used in operating activities	**(65,047)**	**(48,579)**	**(40,749)**
INVESTING ACTIVITIES:			
Purchase of fixed assets	(115)	(406)	(168)
Purchase of intangible assets	—	(53,368)	(35)
Change in investment in current bank deposits	(8,500)	10,200	(2,069)
Purchase of financial assets at fair value through profit or loss	—	—	(4,325)
Proceeds from sale of financial assets at fair value through profit or loss	475	7,925	11,761
Net cash provided by (used in) investing activities	**(8,140)**	**(35,649)**	**5,164**
FINANCING ACTIVITIES:			
Proceeds from long-term borrowings, net of transaction costs	—	78,061	—
Proceeds from issuance of ordinary shares, net of issuance costs	78,536	23,867	36,300
Exercise of options into ordinary shares	4,006	52	5
Repayment of payable in respect of intangible asset purchase	(7,397)	— —	—
Increase in restricted cash	—	(20,000) —	—
Decrease in restricted cash	—	4,000	—
Payment of principal with respect to lease liabilities	(1,683)	(1,610)	(796)
Net cash provided by financing activities	**73,462**	**84,370**	**35,509**
INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	275	142	(76)
EXCHANGE DIFFERENCES ON CASH AND CASH EQUIVALENTS	(96)	130	94
BALANCE OF CASH AND CASH EQUIVALENTS AT BEGINNING OF PERIOD	29,295	29,023	29,005
BALANCE OF CASH AND CASH EQUIVALENTS AT END OF PERIOD	29,474	29,295	29,023
SUPPLEMENTARY INFORMATION ON INTEREST RECEIVED IN CASH	47	414	753
SUPPLEMENTARY INFORMATION ON INTEREST PAID IN CASH	11,280	6,654	251
SUPPLEMENTARY INFORMATION ON NON-CASH INVESTING AND FINANCING ACTIVITIES:			
Acquisition of right-of-use assets by means of lease liabilities	303	2,930	2,805
Purchase of intangible assets posted as payable	—	24,619	—
Purchase of an intangible asset in consideration for issuance of shares	—	1,914	11,788

The accompanying notes are an integral part of these consolidated financial statements.

REDHILL BIOPHARMA LTD.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

NOTE 1 - GENERAL:

a. General:

1) RedHill Biopharma Ltd. (the "Company"), incorporated on August 3, 2009, together with its wholly-owned subsidiary, RedHill Biopharma Inc. ("RedHill Inc."), incorporated in Delaware, U.S. on January 19, 2017, is a specialty biopharmaceutical company primarily focused on gastrointestinal ("GI") diseases and infectious diseases.

The Company's ordinary shares were traded on the Tel-Aviv Stock Exchange ("TASE") from February 2011 to February 2020, after which the Company voluntarily delisted from trading on the TASE, effective February 13, 2020. The Company's American Depositary Shares ("ADSs") were traded on the Nasdaq Capital Market from December 27, 2012 and have been listed on the Nasdaq Global Market ("Nasdaq") since July 20, 2018.

The Company's registered address is 21 Ha'arba'a St, Tel-Aviv, Israel.

2) Since the Company established its commercial presence in the U.S. in 2017, it has promoted or commercialized various GI-related products that were either developed internally or acquired through in-licensing agreements. As of the date of approval of these financial statements, the Company commercializes in the U.S., mainly, Talicia®, for the treatment of *Helicobacter pylori* infection in adults, the first product approved by the U.S. Food and Drug Administration ("FDA") being developed primarily internally by the Company, and Movantik®, for the treatment of opioid-induced constipation.

Effective April 1, 2020, RedHill Inc. entered into an exclusive license agreement (the "License Agreement") with AstraZeneca AB ("AstraZeneca"), granting RedHill Inc. exclusive, worldwide (excluding Europe, Canada) commercialization and development rights to Movantik® (naloxegol). In addition, RedHill Inc. entered into certain related agreements, pursuant to which AstraZeneca provides RedHill Inc. transitional services for an agreed period.

3) Through December 31, 2021, the Company has an accumulated deficit and its activities have been funded primarily through public and private offerings of the Company's securities and borrowing. There is no assurance that the Company's business will generate sustainable positive cash flows to fund its business.

The Company plans to further fund its future operations through commercialization and out-licensing of its therapeutic candidates, commercialization of in-licensed or acquired products and raising additional capital through equity or debt financing or through non-dilutive financing. The Company's current cash resources are not sufficient to complete the research and development of all of its therapeutic candidates and to fully support its commercial operations until generation of sustainable positive cash flows. Management expects that the Company will incur additional losses as it continues to focus its resources on advancing the development of its therapeutic candidates, as well as advancing its commercial operations, based on a prioritized plan that will result in negative cash flows from operating activities. The Company believes its existing capital resources should be sufficient to fund its current and planned operations for at least the next 12 months.

If the Company is unable to out-license, sell or commercialize its therapeutic candidates, generate sufficient and sustainable revenues from its commercial operations, or obtain future financing, the Company may be forced to delay, reduce the scope of, or eliminate one or more of its research and development or commercialization programs, any of which may have a material adverse effect on the Company's business, financial condition or results of operations.

The current COVID-19 pandemic has presented substantial public health and economic challenges around the world and specifically in the Company's target markets in the U.S., affecting employees, patients,

medical clinics, medical diagnosis, communities and business operations. The full extent to which the COVID-19 pandemic will directly or indirectly impact the Company's business, results of operations and financial condition will depend on future developments that are highly uncertain and cannot be accurately predicted at this stage. The Company took actions designed to mitigate the potential impact of the COVID-19 pandemic on its business operations and to date, the COVID-19 pandemic has not caused significant disruptions to the supply chain and the Company has sufficient supply on hand to meet U.S. commercial demand and clinical studies' needs.

A number of the Company's commercial activities have been impacted by the COVID-19 pandemic, including some launch sales and marketing activities for Talicia® for *H. pylori* infection and significant impact on sales of Aemcolo® for travelers' diarrhea. See note 11b regards to the impairment of Aemcolo® assets.

Although no major disruptions, other than manageable impact on its development and commercial activities, the Company continues to assess the potential impact of the COVID-19 pandemic on its business and operations, including on its sales, expenses, supply chain, financial resources, and clinical trials.

b. Approval of the financial statements:

The date of the approval of these financial statements by the Board of Directors (the "BoD") is March 17, 2022.

NOTE 2 - SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES:

a. Basis for presentation of the financial statements

The consolidated financial statements of the Company have been prepared in accordance with International Financial Reporting Standards ("IFRS"), as issued by the International Accounting Standards Board ("IASB").

The significant accounting policies described below have been applied consistently in relation to all the periods presented, unless otherwise stated.

The consolidated financial statements have been prepared under the historical cost convention, subject to adjustments in respect of revaluation of financial assets and financial liabilities at fair value through profit or loss.

The preparation of financial statements in conformity with IFRS requires the use of certain critical accounting estimates. It also requires management to exercise its judgment in applying the Company's accounting policies. The areas involving a higher degree of judgment or complexity, or areas where assumptions and estimates are significant to the financial statements, are disclosed in note 3. Actual results could differ significantly from those estimates and assumptions.

b. Translation of foreign currency transactions and balances

1) Functional and presentation currency

Items included in the consolidated financial statements are measured using the currency of the primary economic environment in which the Company and its subsidiary operate (the "Functional Currency"). The consolidated financial statements are presented in U.S. dollars ("$"), which is the Company's functional and presentation currency.

2) Transactions and balances

Foreign currency transactions in currencies different from the Functional Currency (hereafter foreign currency, mostly New Israeli Shekel ("NIS") and Euro are translated into the Functional Currency using the exchange rates at the dates of the transactions. Foreign exchange differences resulting from the settlement of such transactions and from the translation of period-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recorded in the Statements of Comprehensive Loss under financial income or financial expenses.

c. Principles of consolidation

The Company's consolidated financial statements include the accounts of the Company and its subsidiary. All intercompany balances and transactions have been eliminated in consolidation.

d. Cash and cash equivalents

Cash and cash equivalents include cash on hand and unrestricted short-term bank deposits with maturities of three months or less.

e. Trade receivables

Trade receivables are recognized initially at the amount of consideration that is unconditional. They are subsequently measured at amortized cost using the effective interest method, less expected loss allowance. See also note (i)(3).

f. Inventory

The Company's inventory represents items purchased by the Company and held for sale in the ordinary course of business, as well as inventory in the process of production for a sale in the ordinary course of business or materials or supplies to be used in the production process, to the extent they are recoverable. The inventory is stated at the lower of cost or net realizable value. Cost of inventory is determined using the first-in, first-out method.

The Company continually evaluates inventory for potential loss due to excess quantity or obsolete or slow-moving inventory by comparing sales history and sales projections to the inventory on hand. When evidence indicates that the carrying value of a product may not be recoverable, a charge is recorded to reduce the inventory to its current net realizable value.

g. Fixed assets

Fixed assets items are stated at cost less accumulated depreciation.

Depreciation is computed by the straight-line method, to reduce the cost of fixed assets to their residual value over their estimated useful lives as follows:

	%
Computer equipment	33
Office furniture and equipment	8-15

Leasehold improvements are depreciated by the straight-line method over the shorter of the term of the lease or the estimated useful life of the improvements.

h. Intangible assets

1) Licenses

The Company's intangible assets represent in-licenses of development-phase compounds acquired by the Company, where the Company continues or has the option to continue to do the development work ("R&D assets"), as well as commercialization rights for approved products ("Commercialization assets").

R&D assets that are available for use are stated at cost and amortized on a straight-line basis over their useful life from the time they are available for use. R&D assets that are not available for use are tested for impairment at least annually.

Commercialization assets are stated at cost and are amortized on a straight-line basis over their useful life when they are available for use. These assets are subsequently carried at cost less accumulated amortization and impairment losses.

In determining the useful life of a commercialization asset, the Company considered, among other factors, the duration of the license, patent and regulatory data exclusivities of the product, anticipated duration of sales of the product following loss of exclusivity, and competitors in the marketplace.

Amounts due for future payment based on contractual agreements are accrued upon reaching the relevant milestones.

All intangible assets are tested for impairment if any events have occurred or changes in circumstances have taken place which might indicate that their carrying amounts may not be recoverable. See also note 3 for key assumptions used in the determination of the recoverable amounts.

An impairment loss is recognized for the amount by which the asset's carrying amount exceeds its recoverable amount. The recoverable amount is the higher of an asset's fair value less costs to sell and value in use. For purposes of assessing impairment, assets are grouped at the lowest levels for which there are separately identifiable cash flows (cash-generating units).

2) Research and development

Research expenses are recognized as an expense as incurred. An intangible asset arising from the development of the Company's therapeutic candidates is recognized if all of the following conditions are met:

- it is technically feasible to complete the intangible asset so that it will be available for use;
- management intends to complete the intangible asset and use it or sell it;
- there is an ability to use or sell the intangible asset;
- it can be demonstrated how the intangible asset will generate probable future economic benefits; and
- adequate technical, financial and other resources to complete the development and to use or sell the intangible asset are available and costs associated with the intangible asset during development can be measured reliably.

Other development costs that do not meet the above criteria are recognized as expenses as incurred. Development costs previously recognized as an expense are not recognized as an asset in a subsequent period.

Research and development costs for the performance of pre-clinical trials, clinical trials, and manufacturing by subcontractors are recognized as expenses when incurred.

i. Financial assets

1) Classification

The financial assets of the Company are classified into the following categories: financial assets at fair value through profit or loss, and financial assets at amortized cost. The classification is done on the basis of the Company's business model for managing the financial asset and the contractual cash flow characteristics of the financial asset.

a) Financial assets at amortized cost

Financial assets at amortized cost are assets held within a business model whose objective is to hold assets in order to collect contractual cash flows and the contractual terms of the financial asset give rise on specified dates to cash flows that are solely payments of principal and interest on the principal amount outstanding.

Financial assets at amortized cost are included in current assets, except for those with maturities greater than 12 months after the Statements of Financial Position date (for which they are classified as noncurrent assets).

Financial assets at amortized cost of the Company are included in trade receivables, and other receivables and bank deposits in the Statements of Financial Position.

b) Financial assets at fair value through profit or loss

Financial assets at fair value through profit or loss of the Company are assets not measured at amortized cost in accordance with (1)(a) above. Assets in this category are classified as current assets if they are expected to be settled within 12 months; otherwise, they are classified as noncurrent.

2) Recognition and measurement

Regular purchases and sales of financial assets are recognized on the settlement date, which is the date on which the asset is delivered to the Company or delivered by the Company. Investments are initially recognized at fair value plus direct incremental transaction costs for all financial assets not recorded at fair value through profit or loss, except for trade receivables, that are recognized initially at the amount of consideration that is unconditional.

Financial assets measured at fair value through profit or loss are initially recognized at fair value, related transaction costs are expensed to profit or loss. Financial assets are derecognized when the rights to receive cash flows from the investments have expired or have been transferred and the Company has transferred substantially all risks and rewards of ownership. Financial assets at fair value through profit or loss are subsequently recorded at fair value. Financial assets at amortized cost are measured in subsequent periods at amortized cost using the effective interest method.

Gains or losses arising from changes in the fair value of financial assets at fair value through profit or loss are presented in the Statements of Comprehensive Loss under "Financial Expenses (Income), net."

3) Impairment

The Company recognizes a loss allowance for expected credit losses on financial assets at amortized cost.

At each reporting date, the Company assesses whether the credit risk on a financial instrument has increased significantly since initial recognition. If the financial instrument is determined to have a low credit risk at the reporting date, the Company assumes that the credit risk on a financial instrument has not increased significantly since initial recognition.

The Company measures the loss allowance for expected credit losses on trade receivables that are within the scope of IFRS 15 and on financial instruments for which the credit risk has increased significantly since initial recognition based on lifetime expected credit losses. Otherwise, the Company measures the loss allowance at an amount equal to 12-month expected credit losses at the current reporting date.

j. Financial liabilities

Financial liabilities are initially recognized at their fair value minus transaction costs that are directly attributable to the issue of the financial liability and are subsequently measured at amortized cost.

The Company's financial liabilities at amortized cost include: accounts payable, accrued expenses and other current liabilities, lease liabilities, borrowing, payable in respect of the intangible asset and royalty obligation.

k. Share capital

The Company's ordinary shares are classified as the Company's share capital. Incremental costs directly attributed to the issuance of new shares are presented under equity as a deduction from the proceeds of issuance.

l. Employee benefits

1) Pension and retirement benefit obligations

In any matter related to payment of pension and severance pay to employees in Israel to be dismissed or to retire from the Company, the Company operates in accordance with labor laws.

Labor laws and agreements in Israel, as well as the Company's practice, require the Company to pay severance pay and/or pensions to employees dismissed or retired, in certain circumstances.

The Company has a severance pay plan in accordance with Section 14 of the Israeli Severance Pay Law which is treated as a defined contribution plan. According to the plan, the Company regularly makes payments to severance pay or pension funds without having a legal or constructive obligation to pay further contributions if the fund does not hold sufficient assets to pay the related payments to employees' service in current and prior periods. Contributions for severance pay or pension are recognized as employee benefit expenses when they are due commensurate with receipt of work services from the employee, and no further provision is required in the financial statements.

The Company's subsidiary provides, at will, benefit contributions for its employees.

2) Vacation and recreation pay

Under Israeli law, each employee in Israel is entitled to vacation days and recreation pay, both computed on an annual basis. This entitlement is based on the period of employment. The Company records expenses and liability for vacation and recreation pay based on the benefit accumulated by each employee.

m. Share-based payments

The Company operates several equity-settled, share-based compensation plans to employees (as defined in IFRS 2 "Share-Based Payments") and service providers. As part of the plans, the Company grants employees and service providers, from time to time and at its discretion, options to purchase Company shares. The fair value of the employee and service provider services received in exchange for the grant of the options is recognized as an expense in profit or loss and is recorded as accumulated deficit within equity. For employees, the total amount recognized as an expense over the vesting period of the options (the period during which all vesting conditions are expected to be met) is determined by reference to the fair value of the options granted at the date of grant. For service providers (including equity instruments granted in consideration for intangible assets, see note 16(4), the Company measures the awards based on the fair value of the asset or service received.

Vesting conditions are included in the assumptions about the number of options that are expected to vest. The total expense is recognized over the vesting period, which is the period over which all of the specified vesting conditions are to be satisfied.

At the end of each reporting period, the Company revises its estimates of the number of options that are expected to vest based on non-market vesting conditions. The Company recognizes the impact of the revision to original estimates, if any, in profit or loss, with a corresponding adjustment to accumulated deficit.

When exercising options, the Company issues new shares. The proceeds, less directly attributable transaction costs, are recognized as share capital (par value) and share premium.

n. Revenue from contracts with customers

The Company generated revenue in the years presented in these financial statements from product sales, including in-licensed products, and from promotional services provided in relation to third-party products.

1) Revenue from the sale of products

The Company sells products mainly to wholesale distributors. Revenue is recognized at a point in time when control over the product is transferred to the customer (upon delivery), at the net selling price, which reflects reserves for variable consideration, including discounts and allowances.

The transaction price in these arrangements is the consideration to which the Company expects to be entitled from the customer. The consideration promised in a contract with the Company's customers may include fixed amounts and variable amounts. The Company estimates the variable consideration and includes it in the transaction price using the most likely outcome method, and only to the extent it is highly probable that a significant reversal of cumulative revenue recognized

will not occur when the uncertainty associated with the variable consideration is subsequently resolved.

The specific considerations the Company uses in estimating these amounts related to variable consideration are as follows:

Trade discounts and distribution fees. The Company offers discounts to its customers, as an incentive for prompt payment. The Company records these discounts as a reduction of revenue in the period the related revenue from the sale of products is recognized. In addition, distribution fees are paid to certain distributors based on contractually determined rates from the gross consideration. As the fee paid to the customer is not for a distinct good or service, it is recognized as a reduction of revenue in the period the related revenue from the sale of products is recognized.

Rebates and patient discount programs. The Company offers various rebate and patient discount programs, which result in discounted prescriptions to qualified patients. The Company estimates the allowance for these rebates and coupons based on historical and estimated utilization of the rebate and discount programs, at the time the revenues are recognized. These estimates are recognized as a reduction of revenue. See also notes 3 and 14.

Product returns. The Company offers customers a right of return of expired products. The Company estimates the amount of product sales that may be returned by its customers and records this estimate as a reduction of revenue at the time of sale, based on historical rates of return, or, if such historical data is not available, the Company estimates product returns based on its own sales information, its visibility into the inventory remaining in the distribution channel and product dating. At the end of each reporting period, the Company may decide to constrain revenue for product returns based on information from various sources.

Principal versus agent considerations. When a third party is involved in providing goods or services to a customer, the Company analyzes whether the Company acts as a principal or an agent in the transaction, based on whether the Company obtains control of the product before it is transferred to the customer, using the indicators provided in IFRS 15, including: primary responsibility for fulfilling the promise to provide the products to its customers, inventory risk before and after transfer to the customers and discretion in establishing the selling price of each product. When determined to be the principal in the arrangements, the Company recognizes revenues in the gross amount it expects to be entitled in exchange for the products transferred to the customers.

2) Revenue from promotional services

In 2020, the Company terminated the promotional agreements and recognized immaterial revenues from promotional services. In 2019 the Company recognized revenue from promotional services as it satisfied its performance obligation over time, in an amount equal to the consideration to which it expected to be entitled to, taking into consideration the constraint on variable considerations stipulated in IFRS 15.

3) Practical expedients and exemptions

The Company expenses sales commissions when incurred since the amortization period of the asset that the Company otherwise would have recognized would have been for less than one year. These costs are recorded as selling and marketing expenses.

o. Advertising and promotional expenses

Advertising and promotional costs include, among others, distribution of free samples of the commercialized products. These costs are recognized as an expense when incurred.

p. Loss per ordinary share

The computation of basic loss per share is based on the Company's loss divided by the weighted average number of ordinary shares outstanding during the period.

In calculating the diluted loss per share, the Company adds the weighted average of the number of shares to be issued to the average number of shares outstanding used to calculate the basic loss per share, assuming all shares that have a potentially dilutive effect have been exercised into shares.

q. Deferred taxes

Deferred income tax is recognized using the liability method for temporary differences arising between the tax bases of assets and liabilities and their carrying amounts in these financial statements.

Deferred income tax is determined using tax rates (and laws) that have been enacted or substantially enacted by the date of the Statements of Financial Position and are expected to apply when the related deferred income tax asset will be realized, or the deferred income tax liability will be settled. Deferred income tax assets are recognized only to the extent that it is probable that future taxable profit will be available against which the temporary differences can be utilized.

Since the Company is unable to assess whether it will have taxable income in the foreseeable future, no deferred tax assets were recorded in these financial statements.

r. Leases

From January 1, 2019, the leases are recognized as a right-of-use asset and a corresponding liability at the date at which the leased asset is available for use by the Company. Each lease payment is allocated between the liability and finance cost. The finance cost is charged to profit or loss over the lease period so as to produce a constant periodic rate of interest on the remaining balance of the liability for each period. The right-of-use asset is depreciated over the shorter of the asset's useful life and the lease term on a straight-line basis.

Assets and liabilities arising from a lease are initially measured on a present value basis. Lease liabilities include the net present value of the following lease payments: fixed payments (including in-substance fixed payments) and variable lease payments that are based on an index or a rate.

The lease payments are discounted using the lessee's incremental borrowing rate, being the rate that the lessee would have to pay to borrow the funds necessary to obtain an asset of similar value in a similar economic environment with similar terms and conditions.

Right-of-use assets are measured at cost being the amount of the initial measurement of the lease liability.

Payments associated with short-term leases and leases of low-value assets are not recognized as right-of-use assets or lease liabilities but are recognized on a straight-line basis as an expense in profit or loss. Short-term leases are leases with a lease term of 12 months or less. Low-value assets include IT-equipment and small items of office furniture.

Contracts may contain both lease and non-lease components. For leases of properties, the Company allocates the consideration in the contract to the lease and non-lease components based on their relative stand-alone prices. However, for leases of vehicles, for which the Company is a lessee, it has elected not to separate lease and non-lease components and instead accounts for these as a single lease component.

s. Recently issued accounting pronouncements:

1) Amendments to IAS 1 regarding classifying liabilities as current or non-current

In January 2020, the IASB issued amendment to IAS 1 to specify the requirements for classifying liabilities as current or non-current. The amendments clarify: the definition of a right to defer a settlement, that a right to defer must exist at the end of the reporting period, that classification is unaffected by the likelihood that an entity will exercise its deferral right, that only if an embedded derivative in a convertible liability is itself an equity instrument would the terms of a liability not impact its classification. The amendment is effective for annual periods beginning on or after January 1, 2023. At this stage the Company cannot evaluate the effect of the amendment on the financial statements.

2) Amendments to IFRS 9, IFRS 7, IFRS 16, IFRS 4 and IAS 39 regarding the IBOR reform

In August 2020, the IASB issued amendments to IFRS 9, “Financial Instruments”, IFRS 7, “Financial Instruments: Disclosures”, IAS 39, “Financial Instruments: Recognition and Measurement”, IFRS 4, “Insurance Contracts”, and IFRS 16, “Leases” (“IBOR Amendments”). The IBOR Amendments provide practical expedients when accounting for the effects of the replacement of benchmark InterBank Offered Rates (IBORs) by alternative Risk-Free Interest Rates (RFRs). Pursuant to one of the practical expedients, an entity will treat contractual changes or changes to cash flows that are directly required by the reform as changes to a floating interest rate. That is, an entity recognizes the changes in interest rates as an adjustment of the effective interest rate without adjusting the carrying amount of the financial instrument. The use of this practical expedient is subject to the condition that the transition from IBOR to RFR takes place on an economically equivalent basis. The IBOR Amendments include new disclosure requirements in connection with the expected effect of the reform on an entity’s financial statements, such as how the entity is managing the process to transition to the interest rate reform, the risks to which it is exposed due to the reform and quantitative information about IBOR-referenced financial instruments that are expected to change. The IBOR Amendments are effective for annual periods beginning on or after January 1, 2021. The IBOR Amendments are to be applied retrospectively. However, restatement of comparative periods is not required. Early application is permitted. The Company adopted the IBOR amendments as from January 1, 2021. The adoption of the IBOR Amendment does not have an effect on the Company’s financial statements.

REDHILL BIOPHARMA LTD.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

NOTE 3 - CRITICAL ACCOUNTING ESTIMATES AND JUDGMENTS:

The preparation of financial statements requires management to make estimates which, by definition, will seldom equal the actual results and will affect the reported amounts in the Company's consolidated financial statements and the accompanying notes. Some of the policies described in note 2 of the Company's consolidated financial statements involve a high degree of judgment or complexity. The Company believes that the most critical accounting policies and significant areas of judgment and estimation are in:

- Recognition and measurement of allowance for rebates and patient discount programs
- Impairment reviews of intangible R&D assets.
- Estimated recoverable amount of the Aemcolo® asset.
- Estimated useful life of the acquired assets in the Movantik® acquisition.

Recognition and measurement of allowance for rebates and patient discount programs

The Company offers various rebate and patient discount programs, which result in discounted prescriptions to qualified patients. Rebates and discounts provided to the wholesalers and to the patients under these arrangements are accounted for as variable consideration, and recognized as a reduction in revenue, for which unsettled amounts are accrued. The allowance for these rebates is calculated based on historical and estimated utilization of the rebate and discount programs at the time the revenues are recognized. The main estimates used in recognizing and measuring this allowance relate to the amount of products sold to customers not yet prescribed to patients (units "in the channel") and the mix of rebate and discount programs estimated for future prescription utilization. The Company periodically evaluates it estimates against actual results and, if necessary, updates the estimates accordingly. See also note14.

Impairment reviews of intangible R&D assets

The Company reviews annually or when events or changes in circumstances indicate the carrying value of the R&D assets may not be recoverable.

When and if necessary, an impairment loss is recognized for the amount by which the asset's carrying amount exceeds its recoverable amount. The recoverable amount is determined using discounted cash flow calculations where the asset's expected post-tax cash flows are risk-adjusted over their estimated remaining useful economic life. The risk-adjusted cash flows are discounted using the estimated Company's post-tax weighted average cost of capital ("WACC") which is 16%.

The main estimates used in calculating the recoverable amount include: outcome of the therapeutic candidates R&D activities; probability of success in gaining regulatory approval, size of the potential market and the Company's asset's specific share in it and amount and timing of projected future cash flows.

Estimated recoverable amount of the Aemcolo® asset

The Aemcolo® asset was acquired in October 2019 in exchange of the Company's ADSs and was recognized at fair value at the acquisition date. Following the outbreak of the COVID-19 pandemic and its significant impact on worldwide travel, the Company expects a continued decrease in U.S. outbound travel and the potential market for Aemcolo®, for traveler's diarrhea. Accordingly, during 2020 the Company had recognized an impairment of approximately $0.8 million. In addition, in 2021, in line with continued performance of the product, the Company has again reevaluated the recoverable amount of the intangible asset related to Aemcolo®. Based mainly on estimates of the asset's peak market share and the period in which it will be reached (including the likelihood of early termination of the license before it will be reached), the Company considered the Aemcolo® asset to be entirely impaired. See also note 11b.

Estimated useful life of the acquired assets in the Movantik® acquisition

In connection with the agreements mentioned in note 1a(2) above, the Company accounted for the acquisition of rights to Movantik® as an asset acquisition. Since all acquired assets are intended to generate revenues from sales of Movantik® and have a similar useful life, the Company attributed this consideration to a single intangible asset representing the acquired rights to Movantik®. The Company determined the asset's useful life, over which the asset will be amortized on a straight-line from its acquisition. The main estimate used in determining the useful life was the anticipated duration of sales of the product after its expected patent expiration. During 2021, as a result of reaching a litigation settlement related to Movantik IP, the Company has re-estimated the useful life of these assets to be 12.5 years from the date of acquisition.

NOTE 4 - FINANCIAL INSTRUMENTS AND FINANCIAL RISK MANAGEMENT:

Financial risk management:

1) Financial risk factors

The Company's activities expose it to a variety of financial risks: market risks (including foreign exchange risk and interest risk), credit risk and liquidity risk. The Company's overall risk management program focuses on the unpredictability of financial markets and seeks to minimize potential adverse effects on the Company's results of operations and financial position.

Risk management is performed by the Chief Financial Officer of the Company who identifies and evaluates financial risks in close cooperation with the Company's Chief Executive Officer.

The Company's finance department is responsible for carrying out financial risk management activities in accordance with policies approved by its BoD. The BoD provides general guidelines for overall financial risk management, as well as policies dealing with specific areas, such as exchange rate risk, interest rate risk, credit risk, use of financial instruments, and investment of excess cash. In order to minimize market risk and credit risk, the Company invests the majority of its cash balances in low-risk investments, such as (i) highly-rated bank deposits with terms of up to one-year term with exit points and (ii) a managed portfolio of select corporate bonds comprised of a diversified mix of highly-rated bonds. No more than 10% of the total value of the Company's corporate bonds portfolio is invested in a single bond issuer.

(a) Market risks

(i) The Company could be exposed to foreign exchange risk as a result of its payments to employees and service providers and investment of some liquidity in currencies other than the U.S. dollar (i.e., the Functional Currency). The Company manages the foreign exchange risk by aligning the currencies for holding liquidity with the currencies of expected expenses, based on the expected cash flows of the Company. Had the Functional Currency of the Company been stronger by 5% against the NIS, assuming all other variables remained constant, the Company would have recognized a negligible a reduction in expenses in all the years presented in these financial statements. The foreign exchange risks associated with these balances are immaterial.

(ii) The Company's main interest rate risk arises from long-term borrowing with interest on the outstanding loan computed as the 3-month USD LIBOR rate (hereinafter – the "LIBOR"), subject to a 1.75% floor rate, plus 8.2% fixed rate, which was decreased to 6.7%, starting April 1, 2021. The Company regularly monitors the LIBOR, as well as the LIBOR forward curve. Based on that, the Company estimates that the 1.75% floor rate will remain effective (i.e. – LIBOR will remain

below 1.75%) throughout the entire period of the borrowing and therefore the interest rate on this loan is effectively fixed.

In July 2017, the United Kingdom's Financial Conduct Authority ("FCA"), which regulates LIBOR, announced its intention to stop compelling the group of major banks that sustain LIBOR to submit rate quotations after the end of 2021 (the "LIBOR Reform"). ICE Benchmark Administration Limited (IBA), the administrator of the LIBOR, intends to cease the publication of the LIBOR settings immediately following the LIBOR publication on June 30, 2023. The IBA noted that any publication of the LIBOR settings based on panel bank submissions beyond December 31, 2021, will need to comply with applicable regulations, including as to representativeness. Based on current information from panel banks, IBA anticipates there being a representative panel for the continuation of these USD LIBOR settings through to June 30, 2023. As described above and in note 15, the Company's long-term borrowing, which matures in 2026, is linked to the LIBOR. It is unclear whether new methods of calculating LIBOR will be established or if alternative benchmark reference rates will be adopted. The borrowing agreement stipulates that if the administrator responsible for determining and publishing the LIBOR has made a public announcement identifying a date certain on or after which such rate shall no longer be provided or published, as the case may be, then the lender may, upon prior written notice to the Company, choose a reasonably comparable index or source to enable to preserve the current all-in yield (including interest rate margins, any interest rate floors and original issue discount, but without regard to future fluctuations of such alternative index). As mentioned above, and despite the LIBOR Reform, the Company estimates that the effective floor rate will remain 1.75% throughout the entire period of the borrowing.

(b) Credit risk

Credit risk arises mainly from cash and cash equivalents, bank deposits, restricted cash, and trade receivables. The Company estimates that since the liquid instruments are mainly invested with highly rated institutions, the credit and interest risks associated with these balances are low.

Credit risk of trade receivables is the risk that customers may fail to pay their debts. The Company manages credit risk by setting credit limits, performing controls and monitoring qualitative and quantitative indicators of trade receivable balances such as the period of credit taken and overdue payments. Customer credit risk also arises as a result of the concentration of the Company's revenues with its largest customers. See also note 25(b).

The Company's vast majority of sales is to three U.S.-based large wholesale customers, which their historical loss rate is practically zero. Based on the above information, as well as analyzing if there is any relevant forward-looking information related to the Company's customers, the Company did not record a loss allowance for trade receivables as of December 31, 2021, and December 31, 2020.

(c) Liquidity risk

Prudent liquidity risk management requires maintaining sufficient cash or the availability of funding through an adequate amount of committed credit facilities. Management monitors rolling forecasts of the Company's liquidity reserve (comprising of cash and cash equivalents and deposits). This is generally carried out based on the expected cash flow in accordance with practices and limits set by the management of the Company.

As of December 31, 2021, the Company has generated revenues from commercialization activities, however no sufficient revenue was generated to compensate for operating expenses and therefore the Company is exposed to liquidity risk.

REDHILL BIOPHARMA LTD.

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The tables below break down the Company's financial liabilities into relevant maturity groupings based on their contractual and estimated maturities. The amounts disclosed in the tables are the contractual and estimated undiscounted cash flows.

Contractual maturities of financial liabilities At 31 December 2021	Less than 1 year	2-5 years	More than 5 years	Total contractual cash flows	Carrying amount
			U.S. Dollars in Thousands		
Accounts payable	11,664			11,664	11,664
Lease liabilities	2,109	2,553		4,662	4,192
Accrued expenses and other current liabilities	20,896			20,896	20,896
Borrowing	9,159	107,213	9,000	125,371	83,620
Payable in respect of intangible assets purchase	17,600	5,000		22,600	20,480
Royalty obligation	-	1,011	1,351	2,362	750

Contractual maturities of financial liabilities At 31 December 2020	Less than 1 year	2-5 years	More than 5 years	Total contractual cash flows	Carrying amount
			U.S. Dollars in Thousands		
Accounts payable	11,553			11,553	11,553
Lease liabilities	1,985	4,210	—	6,195	5,517
Accrued expenses and other current liabilities	24,082			24,082	24,082
Borrowing	10,154	107,514	18,530	136,198	81,386
Payable in respect of intangible assets purchase	20,600	10,000		30,600	24,745
Royalty obligation	127	747	912	1,786	750

2) Capital risk management

The Company's objectives when managing capital are to safeguard the Company's ability to continue as a going concern in order to provide returns for shareholders, maintain optimal capital structure, and to reduce the cost of capital.

As discussed in note 15, the Credit Agreement contains a financial covenant requiring RedHill Inc. to maintain a minimum level of cash, as well as a covenant requiring it to maintain minimum net sales, beginning with the fiscal quarter ending June 30, 2022. As of December 31, 2021, and December 31, 2020, the minimum level of cash, which relates to the term loans is $16 million. This amount is presented as restricted cash on the statement of financial position.

3) Fair value estimation

As of December 31, 2020, the Company had an immaterial balance of assets measured at fair value through profit or loss, all based on quoted prices (unadjusted) in active markets for identical assets (level 1).

The carrying amount of cash equivalents, restricted cash, bank deposits, receivables, account payables and accrued expenses approximate their fair value due to their short-term characteristics.

The fair values of the Borrowing and the Payable in respect of intangible assets purchase balances as of December 31, 2021, are approximately $96 million and $23 million (as of December 31, 2020-$94 million and $26 million, respectively). These fair values are based on discounted cash flows using a current borrowing rate.

The fair value of the Royalty obligation balance is not materially different from its carrying amount.

REDHILL BIOPHARMA LTD.
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

NOTE 5 - CASH AND CASH EQUIVALENTS:

	December 31,	
	2021	2020
	U.S. dollars in thousands	
Cash in bank	28,890	14,265
Short-term bank deposits	584	15,030
	29,474	29,295

The carrying amounts of the cash and cash equivalents approximate their fair values.

NOTE 6 – FINANCIAL ASSETS AT FAIR VALUE THROUGH PROFIT OR LOSS

There are no financial assets as of December 31, 2021. The financial assets as of December 31, 2020, represent a portfolio of marketable debt securities.

The Company's business model regarding this portfolio is to realize cash flows through the sale of its assets, rather than hold these assets to collect their contractual cash flows or both to collect contractual cash flows and to sell these financial assets. The Company is primarily focused on fair value information and uses that information to assess the assets' performance and to make decisions. Therefore, this portfolio is classified as financial assets at fair value through profit or loss.

The fair value of the securities is based on their exchange market price at the end of each trading day and reporting period.

NOTE 7 - PREPAID EXPENSES AND OTHER RECEIVABLES:

	December 31,	
	2021	2020
	U.S. dollars in thousands	
Advance to suppliers	632	2,543
Government institutions	847	634
Prepaid expenses and others	3,182	2,344
	4,661	5,521

The fair value of other receivables, which constitute of financial assets, approximate their carrying amount.

NOTE 8 - INVENTORY:

	December 31,	
	2021	2020
	U.S. dollars in thousands	
Raw materials	3,012	1,792
Work in progress	5,195	—
Finished goods	6,603	4,734
	14,810	6,526

During the years ended December 31, 2021, and 2020, the Company recognized amounts of $7.7 million and $5.2 million, respectively, in inventory cost as part of cost of revenues.

Write-downs of inventories to net realizable value amounted to $0.3 million in 2021 and $0.4 million in 2020. These were recognized as an expense, included in cost of revenues in the consolidated statements of comprehensive loss.

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NOTE 9 - FIXED ASSETS:

The composition of assets and accumulated depreciation are grouped by major classifications:

	Cost		Accumulated depreciation		Depreciated balance	
	December 31		December 31		December 31	
	2021	2020	2021	2020	2021	2020
	U.S. dollars in thousands					
Office furniture and equipment (including computers)	1,024	753	677	479	347	274
Leasehold improvements	357	357	132	120	225	237
	1,381	1,110	809	599	572	511

NOTE 10 - LEASES:

Amounts recognized in the consolidated statements of financial position:

	Year Ended December 31,	
	2021	2020
	U.S dollars in thousands	
Right-of-use assets:		
Properties	1,986	2,593
Vehicles	1,665	2,599
	3,651	5,192
Lease liabilities:		
Current	1,618	1,710
Non-current	2,574	3,807
	4,192	5,517

Additions to the right-of-use assets and lease liabilities during the years ended 2021 and 2020 were 0.4 million and 2.9 respectively .

Amounts recognized in the consolidated statements of comprehensive loss:

	Year Ended December 31,	
	2021	2020
Depreciation charge of right-of-use assets		
Properties	608	607
Vehicles	1,282	948
	1,890	1,555
Interest expense (included in financial expenses)	397	574

Expenses relating to short-term leases and leases of low-value assets are immaterial.

The total cash outflow for leases in 2021 and 2020 was $1.9 million and $2 million respectively.

REDHILL BIOPHARMA LTD.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

NOTE 11 - INTANGIBLE ASSETS:

a. The Company's intangible assets represent in-licenses of R&D assets and Commercialization assets (rights related to Movantik® and Aemcolo®). The changes in those assets are as follows:

	Year Ended December 31,	
	2021	2020
	U.S. dollars in thousands	
R&D assets:		
Cost:		
Balance at beginning of year	5,757	5,355
Additions during the year	—	402
Balance at end of year	5,757	5,757
Accumulated amortization:		
Balance at beginning of year	(50)	—
Amortization charges	(66)	(50)
Balance at end of year	(116)	(50)
	5,641	5,707
Commercialization assets:		
Cost:		
Balance at beginning of year	89,373	11,788
Additions during the year see notes 16(4) - 16(6)	—	77,585
Balance at end of year	89,373	89,373
Accumulated impairments and amortization:		
Balance at beginning of year	(7,201)	(216)
Amortization and impairment charges see (b) below	(16,169)	(6,985)
Balance at end of year	(23,370)	(7,201)
	66,003	82,172
	71,644	87,879

The Company estimated the useful life of assets related to Movantik® at 10.5 years from the date of acquisition (April 2020). During 2021, as a result of reaching a litigation settlement related to Movntik's IP, the Company has re-estimated the useful life of these assets to be 12.5 years from the date of acquisition. Moreover, the Company estimated the useful life of the asset related to Talicia® and Aemcolo® at approximately 15 years from marketing approval date and approximately 11 years from the date of acquisition, respectively (November 2019 and October 2019, respectively). The amortization expenses are recognized under Cost of Revenues in the Consolidated Statements of Comprehensive Loss. For further details regarding the intangible assets, see notes 2h, 3, and 16.

b. Intangible assets impairment:

Following the prolongation of the COVID-19 pandemic and its significant impact on worldwide travel, the Company expects a continued decrease in U.S. outbound travel and the potential market for Aemcolo®, for traveler's diarrhea. Accordingly, the Company has reevaluated the recoverable amount of the intangible asset related to Aemcolo®. Based mainly on estimates of the asset's potential market, peak market share and the period in which it will be reached (including the likelihood of early termination of the license before it will be reached), the Company considered the Aemcolo® asset to be entirely impaired. Accordingly, as of December 31, 2021, the Company recognized an impairment loss of $8.9 million. The significant change in assumption is related to attributing a probability greater than zero to the possibility of early termination before the Company will generate meaningful revenues, that are greater than the

Company's investment in the asset. The impairment loss was recognized under Cost of Revenues in the Consolidated Statements of Comprehensive Loss.

As there were no indicators for impairment of any of the other amortized intangible assets, the Company did not specifically evaluate their recoverable amounts.

NOTE 12 - LIABILITY FOR EMPLOYEE RIGHTS UPON RETIREMENT:

a. Labor laws and agreements in Israel require the Company to pay severance pay and/or pensions to an employee dismissed or retiring from their employment in certain circumstances.

b. The Company's pension liability and the Company's liability for payment of severance pay for employees in Israel for whom the liability is within the scope of Section 14 of the Severance Pay Law, is covered by ongoing deposits with defined contribution plans. The amounts deposited are not included in the Statements of Financial Position.

The amounts charged as an expense with respect to defined contribution plans in 2021, 2020, and 2019 were $285,000, $214,000, and $184,000, respectively.

NOTE 13 - ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES:

	December 31,	
	2021	2020
	U.S. dollars in thousands	
Accrued expenses	17,234	18,972
Employees and related liabilities	3,496	4,963
Government institutions	167	147
	20,896	24,082

REDHILL BIOPHARMA LTD.
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

NOTE 14 - ALLOWANCE FOR DEDUCTIONS FROM REVENUES:

The following table shows the movement of the allowance for deductions from revenue:

	Rebates and patient discount programs	Product returns	Total
	U.S. dollars in thousands		
As of January 1, 2021	16,380	1,963	18,343
Increases	94,640	851	95,491
Decreases (utilized)	(80,633)	(2,179)	(82,812)
Adjustments	(645)	334	(311)
As of December 31, 2021	29,742	969	30,711

	Rebates and patient discount programs	Product returns	Total
	U.S. dollars in thousands		
As of January 1, 2020	1,001	266	1,267
Increases	56,669	2,469	59,138
Decreases (utilized)	(40,656)	(772)	(41,428)
Adjustments	(634)	-	(634)
As of December 31, 2020	16,380	1,963	18,343

	Rebates and patient discount programs	Product returns	Total
	U.S. dollars in thousands		
As of January 1, 2019	573	385	958
Increases	2,485	303	2,788
Decreases (utilized)	(2,057)	(72)	(2,129)
Adjustments	-	(350)	(350)
As of December 31, 2019	1,001	266	1,267

NOTE 15 – BORROWING:

a. General

On February 23, 2020 ("Closing Date") RedHill Inc. entered into a credit agreement and certain security documents (the "Credit Agreement") with HCR Collateral Management, LLC ("HCRM").

Under the terms of the Credit Agreement, RedHill Inc. received on March 12, 2020, a $30 million term loan to support its commercial operations. On March 31, 2020, RedHill Inc. received an additional $50 million term loan to fund the acquisition of rights to Movantik® from AstraZeneca.

For each quarter for the period from January 1, 2021, to December 31, 2029, HCRM will receive royalties of 4% of the Company's worldwide net revenues, subject to a $75 million cap per annum, as well as interest on the outstanding term loan to be computed as the 3-month LIBOR rate ("LIBOR"), subject to a 1.75% floor rate, plus 8.2% fixed rate, which was decreased to 6.7% starting April 1, 2021.

The term loans mature in six years with no principal payments required in the first three years. The term loans can be prepaid at RedHill Inc.'s discretion, subject to customary prepayment fees, which decrease over time. Upon the prepayment or repayment of all or any portion of the term loans, RedHill Inc. will pay HCRM 4% on the principal amount of the term loan being repaid or prepaid as an exit fee.

The borrowings under the Credit Agreement are secured by a first priority lien on substantially all of the current and future assets of RedHill Inc., all assets related in any material respect to Talicia®, and all of the equity interests in RedHill Inc. The Credit Agreement also restricts the ability of RedHill Inc. to make certain payments, including paying dividends, to the Company prior to the full repayment of the term loan facility.

The Credit Agreement contains certain customary affirmative and negative covenants, which were all met as of December 31, 2021. The Credit Agreement also contains a financial covenant requiring RedHill Inc. to maintain a minimum level of cash, as well as a covenant requiring it to maintain minimum net sales for the trailing four fiscal quarter periods, beginning with the fiscal quarter ending June 30, 2022. The minimum level of cash is relative to the amount borrowed under the term loan facility.

The Credit Agreement contains defined events of default, in certain cases subject to a grace period, following which the lenders may declare any outstanding principal and unpaid interest immediately due and payable.

As of December 31, 2021, the minimum level of cash, which relates to the term loans is $16 million. This amount is presented as restricted cash on the consolidated statement of financial position.

b. Accounting treatment

A financial liability is recognized for each tranche upon drawdown, at the amount drawn less transaction costs attributable to that tranche.

Upon initial recognition, the effective interest rate is calculated by estimating the future cash flows throughout the expected life of that tranche, taking into account the transaction costs allocated to each tranche. The Company determined that the basis of the royalty payments due to HCRM, the Company's worldwide net revenues, is a non-financial variable and specific to the Company.

Moreover, the royalty feature is an integral part of the terms and conditions of the term loans and cannot be transferred or settled separately from the term loan. Therefore, the royalties feature is not classified separately, does not meet the definition of a derivative, and is not measured separately. Instead, the royalty feature and other net revenues features are taken into account in estimating the effective interest rate.

Determining the weighted effective interest rate requires certain judgment related to the estimation of the timing and amounts of the Company's future worldwide net revenues.

The weighted effective interest rate on the Closing Date was approximately 16.5%.

Each tranche drawn down is subsequently measured at amortized cost. The effective interest rate is re-estimated at each interest rate determination date, as defined in the Credit Agreement, by updating per the LIBOR, if needed, taking into account the LIBOR floor (that is considered to be closely related to the host debt contract and is not separated from the host debt).

Furthermore, revisions to estimated amounts or timing of future cash flows, if needed, shall adjust the amortized cost of each tranche drawn down to reflect the present value of actual and revised estimated contractual cash flows, discounted using the original effective interest rate (adjusted for changes in the LIBOR, as described above). The adjustment will be recognized in profit or loss as a financial income or expense.

As described above, the Credit Agreement contains a financial covenant requiring the Company to maintain a level of cash liquidity, on any business day from the Closing Date to the maturity date, in

accounts that are subject to HCRM's control. Therefore, the amounts of minimum cash and cash equivalents are excluded from cash and cash equivalents in the Statements of Financial Position and the Statements of Cash Flows. Instead, these amounts are presented as restricted cash in the Statements of Financial Position and the movements in this restricted cash are presented as financing activities in the Statements of Cash Flows. The minimum cash amounts are restricted from being exchanged or used to settle a liability for at least twelve months after the reporting period and therefore are presented as non-current assets until 12 months prior to the term loan maturity dates.

Further details of the Company's exposure to risks arising from the Credit Agreement, as well as maturities and fair value information, are set out in note 4.

C. Reconciliation of liabilities arising from financing activities:

			Non-cash changes			
	U.S. dollars in thousands					
	January 1, 2021	Proceeds from borrowings	Principal and interest payments	Addition during the year	Interest expense	Foreign exchange movement	December 31, 2021
Borrowing	$81,386		($9,701)		$11,935		$83,620
Payable in respect of intangible assets purchase	$24,746		($8,500)		$4,234		$20,480
Lease liabilities	$5,517		($2,107)	$385	355	42	$4,192

			Non-cash changes			
	January 1, 2020	Proceeds from borrowings	Principal and interest payments	Addition during the year	Interest expense	Foreign exchange movement	December 31, 2020
Borrowing	-	$78,061	($6,246)		$9,571		$81,386
Payable in respect of intangible assets purchase	-			$22,288	$2,458		$24,746
Lease liabilities	$3,815		($1,802)	$2,930	$406	$168	$5,517

			Non-cash changes			
	January 1, 2019	Proceeds from borrowings	Principal and interest payments	Addition during the year	Interest expense	Foreign exchange movement	December 31, 2019
Lease liabilities	$1,667		($1,047)	$2,805	$251	$139	$3,815

NOTE 16 - COMMITMENTS:

Agreements to purchase intellectual property and commercial products:

1) On August 11, 2010, the Company entered into an agreement with a publicly-traded Australian company in an asset purchase agreement to acquire intellectual property relating to three therapeutic candidates for the treatment of gastrointestinal conditions. Pursuant to the asset purchase agreement, as amended, the Company paid the Australian company an initial amount of $500,000 and undertook to pay future payments in the range of 7% - 20% from the Company's revenues that may be generated from the sale and sublicense of the therapeutic candidates, less certain deductible amounts, as detailed in the agreement. Such potential payments are due until termination or

expiration of the last of the patents transferred to the Company pursuant to the agreement (each on a product-by-product basis).

Through December 31, 2021, the Company has paid the Australian company in total $1.5 million.

2) On June 30, 2014, the Company entered into an agreement with a German company that granted the Company the exclusive worldwide (excluding China, Hong Kong, Taiwan, and Macao) development and commercialization rights to all indications to a therapeutic candidate. Under the terms of the agreement, the Company paid the German company an upfront payment of $1 million and agreed to pay the German company potential tiered royalties, less certain deductible amounts, as detailed in the agreement, ranging from mid-teens and up to 30%. Such potential royalties are due until the later of (i) the expiration of the last to expire licensed patent that covers the product in the relevant country and (ii) the expiration of regulatory exclusivity in the relevant country. Through December 31, 2021, the Company has paid the German company only the initial amount mentioned above.

3) On March 30, 2015, the Company entered into an agreement with a U.S.-based private company that granted the Company the exclusive worldwide development and commercialization rights for all indications to a therapeutic candidate, and additional intellectual property rights, targeting multiple oncology, inflammatory and GI indications. Under the terms of the agreement, the Company undertook to pay the U.S. company an initial amount of $1.5 million and an additional amount of $2 million to be paid on a specific date. In addition, the Company undertook to pay up to $2 million in potential development milestone payments, and potential tiered royalties on revenues, less certain deductible amounts starting in the low double-digits, as detailed in the agreement. Such potential royalties are due until the later of (i) the expiration of the last to expire licensed patent that covers the product in the relevant country; and (ii) the expiration of regulatory exclusivity in the relevant country. Through December 31, 2021, the Company paid the U.S. company a total of $3 million.

Following an amendment to the agreement from February 2018, during December 2018, the Company elected to convert the current payment of the remaining $0.5 million into increased future potential royalty payments. As of December 31, 2021, and December 31, 2020, the Company recognized an amount of $0.75 million, as a non-current liability with respect to the increase in potential royalty payments.

4) On October 17, 2019, the Company entered into a strategic collaboration with Cosmo Pharmaceuticals N.V. (“Cosmo”), which includes an exclusive license agreement, as amended, for the U.S. rights to Aemcolo® and a simultaneous private investment by Cosmo.

Under the terms of the license agreement, Cosmo invested $36.3 million in cash and granted the Company the exclusive rights to commercialize Aemcolo® in the U.S. for travelers’ diarrhea.

The license agreement also grants the Company certain rights related to the potential development of additional indications for Aemcolo®, as well as arrangements related to other pipeline therapeutic candidates of Cosmo. Under the terms of the agreements, the Company issued 5,185,715 ADSs to Cosmo for the cash investment and 1,714,286 ADSs to Cosmo Technologies Ltd, a wholly-owned subsidiary of, as an upfront payment for the U.S commercialization rights granted under the license. In addition, the Company agreed to pay Cosmo a royalty percentage in the high twenties on net sales generated from the commercialization of Aemcolo® in the U.S. The license agreement further provides for potential regulatory and commercial milestone payments to Cosmo totaling up to $100 million.

With respect to this agreement, the Company measured the commercialization rights based on their fair value (approximately $11.8 million, as of the date of the acquisition) with a corresponding credit to equity. See also note 11(b).

5) **Movantik® acquisition:**

1. General

In connection with the agreements mentioned in note 1a(2), on April 1, 2020 (“Effective Date”), RedHill Inc. made an upfront payment of $52.5 million to AstraZeneca, and the AstraZeneca License Agreement, the Supply Agreement and the TSA became effective. Under the terms of the AstraZeneca License Agreement, as amended on July 14, 2020, RedHill Inc. agreed to pay a further non-contingent payment of $15.5 million in December 2021.

On March 11, 2021, RedHill Inc and AstraZeneca signed an amendment to the License Agreement, pursuant to which, the $15.5 million payment due in December 2021 was adjusted to gradual payments starting in March 2021 and ending in December 2022, totaling $16 million. The amendment is not considered a substantial modification of the terms and resulted in an adjustment of approximately $0.5 million in the carrying amount of the payable in respect of intangible assets purchase and a corresponding charge in the consolidated statements of comprehensive loss, under financial expenses.

RedHill Inc. will also assume responsibility for sales-based royalty, currently at a rate of 20%, as well as sales-based potential milestone payments that AstraZeneca is required to pay to Nektar Therapeutics (“Nektar”), the originator of Movantik®. The Company considers the likelihood of having to pay the milestone payments or increased royalties as negligible.

In addition, AstraZeneca transferred on the Effective Date to RedHill Inc. a co-commercialization agreement with Daiichi Sankyo, Inc. (“DSI”) for Movantik® in the U.S, according to which, RedHill Inc. would share costs and pay sales-based payments to DSI under that agreement. Effective July 1, 2020, RedHill Inc. and DSI replaced this agreement with a new royalty-bearing agreement. See note 16(6) below. On October 6, 2020, the parties amended the License Agreement to grant RedHill Inc. also the exclusive commercialization and development rights to Movantik® (naloxegol) in Israel.

Under its Supply Agreement with AstraZeneca used in connection with its commercialization of Movantik®, RedHill Inc. undertook an obligation for future purchase of API, bulk tables and finished goods. As of December 31, 2021, the total consideration for such purchase is approximately $22 million. RedHill Inc. expects to purchase the inventory, in the regular course of business, through 2025, as part of its ongoing commercialization of Movantik®.

On February 22, 2021, Aether Therapeutics Inc. (“Aether”), filed a complaint against RedHill Inc in the United States District Court for the District of Delaware ("Aether Litigation"). The complaint asserts that the Company's marketing of the Movantik® product infringes certain U.S. Patents held by Aether (the "Aether Patents"). Aether has asserted the Aether Patents against other entities previously involved in the marketing of Movantik®. The complaint requests customary remedies for patent infringement. Given the early stage of the Aether Litigation, the Company is unable to predict the likelihood of success of the claims of Aether or to quantify any risk of loss.

2. Accounting treatment

The Company, in accordance with IFRS 3 – Business Combinations and IAS 38 – Intangible Assets, accounted for the acquisition of rights to Movantik® as an asset acquisition, that does not constitute a business, for the following considerations:

(a) The Supply Agreement provides RedHill Inc. with the ability to purchase finished products and materials from AstraZeneca during a transition period at approximately fair value, without acquiring AstraZeneca's organized workforce or existing processes required to manufacture Movantik®. That is, RedHill Inc. does not purchase an in-place manufacturing process nor any specialized equipment required for the manufacturing process, but instead, the purpose of the Supply Agreement is to enable RedHill Inc. to establish its own manufacturing capabilities, whether directly or through a third party, that would also require obtaining relevant regulatory approvals, which presumably will take a significant period of time.

(b) The TSA is intended to allow a smooth transition of the different activities related to Movantik® for a relatively short period and is not intended for RedHill Inc. to acquire AstraZeneca's organized workforce, supply chain or distribution processes. The TSA had terminated on September 30, 2020.

(c) In addition, the Company determined that the concentration test under the new definition of a business is met, since substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets. (the rights to produce and sell Movantik®). Therefore, the Movantik® acquisition does not represent a business combination, rather than an asset acquisition.

The total acquisition consideration, including upfront payment, discounted present value of the deferred payment and directly attributable transaction costs amounted to approximately $65 million. Since all acquired assets are intended to generate revenues from sales of Movantik® and have a similar useful life, the Company attributed this consideration to a single intangible asset representing the acquired rights to Movantik®. The intangible asset shall be amortized commencing the Effective Date on a straight-line basis over its useful life, which was re-estimated at approximately 12.5 years from the Effective Date (see also note 11(a) with regards to change in estimation of the useful life).

With respect to sales-based royalties and milestone payments aforementioned, the Company applied an accounting policy, pursuant to which these variable payments shall not be included in the initial measurement of the cost of the intangible asset acquired, as they are not a present obligation of RedHill Inc. The sales-based royalties are expensed as incurred and recognized under Cost of Revenues.

Through September 30, 2020, AstraZeneca provided, among other services, Sales Order-To-Cash (SOTC) services. During this period, AstraZeneca remitted to RedHill Inc. the Sales Margin, as defined in the TSA, for the products sold and RedHill Inc. paid a fee of 4.5% of Net Revenues, as well as non-sales-based fees and out-of-pocket costs for the services rendered. During the SOTC period, the Company recognized revenues in the gross amount of consideration to which it expects to be entitled in exchange for the finished products transferred to the customers (the wholesalers). The fees and out-of-pocket costs were expensed as incurred. Starting October 1, 2020, AstraZeneca no longer provided the abovementioned services.

6) As described in note 16 (5) above, as part of the Movantik® transaction, the Company undertook the pre-existing co-commercialization agreement with DSI, under which the Company and DSI share certain costs while paying DSI a significant share from its sales volume of Movantik®.

Effective July 1, 2020, RedHill Inc. and DSI replaced the co-commercialization agreement with a new royalty-bearing agreement, under which RedHill Inc. bears all responsibilities and costs for commercializing Movantik® in the U.S. During the term of this new agreement, RedHill Inc. will pay DSI a mid-teen royalty rate on net sales of Movantik® in the U.S. in addition to $5.1 million paid in January 2022 and $5 million to be paid in July of each of the years 2022 and 2023. Concurrently, the Company also entered into a security purchase agreement, under which DSI received 283,387 ADSs as a partial consideration in relation to Movantik®.

The Company recognized an intangible asset in the amount of approximately $12.5 million. This amount includes approximately $10.5 million for the present value of the above-mentioned payments, recognized against a corresponding financial liability and approximately $2 million for the ADSs issued to DSI.

The intangible asset recognized has similar estimated useful life as the intangible asset discussed in note 16 (5) above and are amortized on a straight-line basis over its useful life.

7) As for an exclusive license agreement with Gaelan Medical Trade LLC for Talicia® in the United Arab Emirates (UAE) - see Note 28b.

NOTE 17 - INCOME TAX:

a. Taxation of the Company in Israel:

1) Measurement of results for tax purposes

The Company elected to compute its taxable income in accordance with Income Tax Regulations (Rules for Accounting for Foreign Investors Companies and Certain Partnerships and Setting their Taxable Income), 1986. Accordingly, the Company's taxable income or loss is calculated in U.S. dollars.

The results of the Company are measured for tax purposes in accordance with Accounting Principles Generally Accepted in Israel (Israeli GAAP). These financial statements are prepared in accordance with IFRS. The differences between IFRS and Israeli GAAP, both on an annual and a cumulative basis cause differences between taxable results and the results are reflected in these financial statements.

2) Tax rates

The net income of the Company is subject to the Israeli corporate tax rate. Israeli corporate tax rates is 23%.

b. U.S. subsidiary:

The Company's subsidiary is incorporated in the U.S. and is taxed under U.S. tax laws. The applicable corporate tax rate is 21%.

As a general rule, inter-company transactions between the Israel-resident Company and its U.S-resident subsidiary are subject to the reporting provisions of the Income Tax Regulations, section 85-A, 2006 of the Israeli Tax Ordinance of the Israeli Tax Ordinance.

c. Carryforward losses:

As of December 31, 2021, the Company had net operating loss ("NOLs") carried forward of approximately $265 million. Under Israeli tax laws, carryforward tax losses have no expiration date.

As of December 31, 2021, the U.S. subsidiary had a net operating loss carryforward of approximately $77 million, of which approximately $10 million expires in 2037, and approximately $67 million does not expire, but is limited to offset 80% of the net income in the year it is utilized.

Under U.S. tax laws, for NOLs arising after December 31, 2017, the 2017 Act limits a taxpayer's ability to utilize NOL carryforwards to 80% of taxable income. In addition, NOLs arising after 2017 can be carried forward indefinitely, but carryback is generally prohibited. NOLs generated in tax years beginning before January 1, 2018, will not be subject to the foregoing taxable income limitation and will continue to have a two-year carryback and twenty-year carryforward period. Furthermore, in accordance with Coronavirus Aid, Relief, and Economic Security Act (CARES Act) of 2020, losses from tax years beginning in 2018, 2019 or 2020 can be carried back 5 years.

Deferred tax assets on losses for tax purposes carried forward to subsequent years are recognized if utilization of the related tax benefit against a future taxable income is expected. The Company has not created deferred taxes on its carryforward losses since their utilization is not expected in the foreseeable future.

d. Deductible temporary differences:

The amount of cumulative deductible temporary differences, other than carryforward losses (as mentioned in c. above), for which deferred tax assets have not been recognized in the Statements of Financial Position as of December 31, 2021, and 2020, were $20 million and $12 million, respectively. These temporary differences have no expiration dates.

e. Tax assessments:

The Company has not been assessed for tax purposes since its incorporation. The Company's tax assessments for 2016 are therefore considered final.

NOTE 18 - SHARE CAPITAL:

a. Composition:

Company share capital is composed of shares of NIS 0.01 par value, as follows:

	Number of shares	
	December 31,	
	2021	2020
	In thousands	
Authorized ordinary shares	794,000	794,000
Authorized preferred shares (reserved)	6,000	6,000
Issued and paid ordinary shares	524,016	383,981

In May 2020, a general meeting of the Company's shareholders approved the increase of the authorized share capital of the Company to 800,000,000 shares. Consisting of 794,000,000 Ordinary Shares, NIS 0.01 par value per share and 6,000,000 preferred shares, NIS 0.01 par value per share.

b. During 2021, the Company issued 12,522,245 ADSs from underwritten offerings for gross proceeds of approximately $77 million. Net proceeds to the Company from the offerings, following underwriting commissions and other offering expenses, were approximately $72.7 million.

c. In October 2021, the Company has entered into an agreement with Kukbo Co. Ltd. ("Kukbo"), a South Korean corporation, for the sale of the Company's ADSs in a private placement of up to $10 million. Kukbo's investment in the Company is to be made in two tranches, with the first tranche of $5 million paid in October 2021 and the second tranche of $5 million to follow within six months, subject to satisfaction of certain conditions. As part of the first tranche, RedHill has issued 827,586 ADSs at a purchase price of $6.04, which represented a 20% premium over the 30-day weighted average price of the ADSs on the Nasdaq. The $5 million consideration for the first tranche was attributed in full to equity, Likewise, the number of ADSs to be issued in the second tranche will be calculated based on a price per ADS representing a 20% premium over the 30-day weighted average at the closing. In addition, under the terms of the agreement, the Company has agreed to grant Kukbo a right of first offer, for a period of six months, for a license with respect to one or more of the Company's late-stage clinical assets, Opaganib, RHB-107 (upamostat) and Talicia®, for one or more of the territories of South Korea, Japan, Indonesia, Vietnam, Thailand and Malaysia. Kukbo has the right to elect not to purchase the ADSs in the second tranche if no such license agreement is executed within six months of the closing of the first tranche. See also note 28(c).

d. During 2021, the Company sold 87,624 ADSs under an "at-the-market" equity offering program ("ATM program") at an average price of $9.03 per ADS. Net and gross proceeds to the Company were approximately $0.8 million. The sales are under the Company's sales agreements with SVB Leerink LLC and Cantor Fitzgerald & Co. Upon the terms and subject to the conditions and limitations in the sales agreements, the Company may elect from time to time, to offer and sell its ADSs having aggregate gross sales proceeds of up to $100 million through the ATM program, under which SVB Leerink LLC and Cantor Fitzgerald & Co act as the sales agents. During 2020, the Company sold 2,837,038 ADSs under an ATM program at an average price of $8.62 per ADS. Net proceeds to the Company, following issuance expenses of approximately $0.6 million, were approximately $23.8 million.

e. During 2021 and 2020, the Company issued 565,998 ADSs and 8,156 ADSs for $4 million and $52,000, respectively, resulting from exercises of options that had been issued to employees, of the Company.

f. In July 2020, as part of the transaction described in note 16 (6) above, the Company entered into a security purchase agreement with DSI and subsequently issued to DSI 283,387 ADSs for approximately $2 million.

g. In October 2019, the Company, under the strategic collaboration discussed in note 16(4), issued 5,185,715 ADSs to Cosmo for proceeds in cash of $36.3 million and 1,714,286 ADSs to Cosmo Technologies Ltd, a wholly-owned subsidiary of Cosmo, as an upfront payment for the U.S commercialization rights of Aemcolo®.

NOTE 19 - SHARE-BASED PAYMENTS:

On May 30, 2010, a general meeting of shareholders approved the option plan of the Company (the "Option Plan"), after being approved by the BoD. In 2017 the Option Plan was amended and restated as the 2010 Award Plan (the "Award Plan"). As of December 31, 2021, the Award Plan allows the Company to allocate up to 59,206,448 options to purchase ordinary shares to employees, consultants,

and directors and are reserved by the BoD for issuance under the Award Plan. The terms and conditions of the grants were determined by the BoD and are according to the Award Plan.

a. The following is information on options granted in 2021:

	Number of options granted				
	According to the Award Plan of the Company			Exercise price for 1 ADS ($)	Fair value of options on date of grant in U.S. dollars in thousands (1)(2)(3)
Date of Grant	Other than to directors (1)	To directors (1)(2)	Total		
March 2021	40,500	—	40,500	9.44	151
April 2021	2,036,440	—	2,036,440	7.08	8,274
May 2021	22,500	—	22,500	7.05	90
July 2021	17,000	310,341	327,341	6.9-7.08	1,377
August 2021	53,500		53,500	6.97-7.18	210
September 2021	12,000	—	12,000	4.56	31
November 2021	24,500	—	24,500	4.54	63
December 2021	17,000	—	17,000	2.65	26
	2,223,440	310,341	2,533,781		10,221

1) The options will vest as follows: for directors, employees and consultants of the Company and the Company's subsidiary who had provided services exceeding one year as of the grant date, options will vest in 16 equal quarterly installments over a four-year period. For directors, employees and consultants of the Company and the Company's subsidiary who had not provided services exceeding one year as of the grant date, the options will vest as follows: 1/4 of the options will vest one year following the grant date and the rest will vest over 12 equal quarterly installments. During the contractual term, the options will be exercisable, either in full or in part, from the vesting date until the end of 10 years from the date of grant.

   The options are exercisable into the Company's ADSs.

2) The general meeting of the Company's shareholders held on July 26, 2021 (the "July 2021 AGM"), subsequent to approval of the Company's BoD, approved the grant of 310,341 options under the Company's Award Plan, to directors and to the Company's Chief Executive Officer.

3) The fair value of the options was computed using the binomial model and the underlying data used was mainly the following: price of the Company's ADSs: $4.28 - $9.19, expected volatility: 64.05% - 66.65 %, risk-free interest rate: 1.26% - 1.73% and the expected term was derived based on the contractual term of the options, the expected exercise behavior and expected post-vesting forfeiture rates. the expected volatility assumption used in based on the historical volatility of the Company's ordinary share.

4) Exchange of options to purchase the Company's ADSs:

   a. On April 26, 2021, the Company made an offer (the "Exchange Offer") to eligible option holders (as defined in the offer), subject to specified conditions, to exchange some or all of their outstanding options to purchase ADSs (the "Exchanged Options") for new options to purchase ADSs (the "New Options"). On May 26, 2021, concurrently with the expiration of the Exchange Offer, the Company granted New Options to purchase 2,805,281 ADSs of the Company, pursuant to the terms of the Exchange Offer and the Company's Amended and Restated Award Plan (2010).

The New Options have lower exercise price per ADS than the Exchanged Options and subject to meeting certain performance conditions, specified in the Exchange Offer, may be further lowered. Other than the exercise price, each New Option has the same expiration date, vesting schedule and other terms as the Exchanged Options.

b. The incremental compensation expense recognized by the Company has been measured as the excess of the fair value of each New Option granted, as of the date the New Options were granted, over the fair value of the Exchanged Options, measured immediately prior to the exchange. The total incremental value measured by the Company is approximately $3.5 million, of which $3.3 million was recognized as an expense for the year ended December 31, 2021. The remaining incremental value will be recognized over the remaining vesting period of the New Options.

c. The incremental compensation expense was computed using the binomial model and the underlying data used was mainly the following: exercise price of the Company's ADS: $4.3 - $7.0 expected volatility: 58.8% - 65.28%, risk-free interest rate: 0.01% - 2.31% and the expected term was derived based on the contractual term of the options, the expected exercise behavior and expected post-vesting forfeiture rates.

b. The following is information on options granted in 2020:

	Number of options granted				
	According to the Award Plan of the Company			Exercise price for 1 Ads	Fair value of options on date of grant in U.S. dollars
Date of BoD	Other than to directors (1)	To directors (1) (2)	Total	($)	in thousands (3)
January 2020	95,000	—	95,000	6.60	243
February 2020	52,500	—	52,500	6.05	119
March 2020	285,000	—	285,000	4.87	683
May 2020	143,000	219,000	362,000	7.50	1,118
June 2020	767,500	—	767,500	7.72	2,671
July 2020	12,500	—	12,500	7.69	45
August 2020	55,500	—	55,500	8.72	264
November 2020	21,000	—	21,000	10.20	90
	1,432,000	219,000	1,651,000		5,233

1) The options vesting terms are as described in note 19(a)(1) above.

2) The general meeting of the Company's shareholders held on May 4, 2020, subsequent to approval of the Company's BoD, approved the grant of 219,000 options under the Company's Award Plan, to directors and to the Company's Chief Executive Officer.

3) The fair value of the options was computed using the binomial model and the underlying data used was mainly the following: price of the Company's ADSs: $4.28 - $9.19, expected volatility: 57.73% - 63.63%, risk-free interest rate: 0.64% - 1.51% and the expected term was derived based on the contractual term of the options, the expected exercise behavior and expected post-vesting forfeiture rates. the expected volatility assumption used in based on the historical volatility of the Company's ordinary share.

c. Changes in the number of options in ADSs and weighted averages of exercise prices are as follows:

	Year Ended December 31,			
	2021		2020	
	Number of options	Weighted average of exercise price ($)	Number of options	Weighted average of exercise price ($)
Outstanding at beginning of year	5,428,803	9.08	4,050,898	10.30
Exercised	(565,998)	7.08	(8,156)	6.38
Expired and forfeited	(575,095)	8.02	(264,939)	9.65
Granted	2,533,781	7.05	1,651,000	6.90
Outstanding at end of year	6,821,491	6.50	5,428,803	9.08
Exercisable at end of year	3,615,662	6.14	3,178,317	10.19

d. The following is information about the exercise price and remaining useful life of outstanding options at year-end:

Year Ended December 31,					
2021			2020		
Number of options outstanding at end of year	Exercise price range	Weighted average of remaining useful life	Number of options outstanding at end of year	Exercise price range	Weighted average of remaining useful life
6,821,491	$2.65-$15.6	6.8	5,428,803	$5.6-$16.1	5.9

e. Expenses recognized in profit or loss for the options are as follows:

Year Ended December 31,		
2021	2020	2019
U.S. dollars in thousands		
10,212	4,202	3,027

The remaining compensation expenses as of December 31, 2021, are $7.6 million and will be expensed in full by September 2025.

NOTE 20 - NET REVENUES:

	Year Ended December 31,		
	2021	2020	2019
	U.S dollars in thousands		
Movantik® revenues	76,767	59,356	—
Other products (1)	8,989	5,003	6,291
	85,757	64,359	6,291

1) During 2019 $3.1 million were attributed to the promotional services, and $3.2 million, were attributed to commercialization of products. In 2020, the Company terminated the promotional agreements and recognized immaterial revenues from promotional services.

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NOTE 21 - RESEARCH AND DEVELOPMENT EXPENSES:

	Year Ended December 31,		
	2021	2020	2019
	U.S. dollars in thousands		
Payroll and related expenses	839	636	623
Professional services	1,821	1,752	2,345
Share-based payments	1,910	883	671
Clinical and pre-clinical trials	23,905	12,569	12,840
Intellectual property development	349	298	317
Other	674	353	623
	29,498	16,491	17,419

NOTE 22 - SELLING AND MARKETING EXPENSES:

	Year Ended December 31,		
	2021	2020	2019
	U.S. dollars in thousands		
Payroll and related expenses	24,227	20,756	9,335
Share-based payments	2,570	1,464	941
Professional services	17,441	18,957	3,680
Samples	1,008	438	178
Travel, Fleet, meals and related expenses	7,305	5,729	2,193
Office-related expenses	1,285	957	789
Other	1,787	984	1,217
	55,623	49,285	18,333

NOTE 23 - GENERAL AND ADMINISTRATIVE EXPENSES:

	Year Ended December 31,		
	2021	2020	2019
	U.S. dollars in thousands		
Payroll and related expenses	11,974	11,159	4,903
Share-based payments	5,732	1,855	1,415
Professional services	11,040	9,132	3,479
Medical affairs	1,600	1,052	299
Office-related expenses	1,438	1,168	585
Other	581	1,009	800
	32,365	25,375	11,481

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NOTE 24 - FINANCIAL EXPENSES (INCOME), net:

	Year Ended December 31,		
	2021	2020	2019
	U.S dollars in thousands		
Financial income:			
Fair value gains on derivative financial instruments	—	—	344
Gains on financial assets at fair value through profit or loss	—	94	474
Gains from changes in exchange rates	—	—	74
Interest from bank deposits	51	176	443
	51	270	1,335
Financial expenses:			
Interest and finance charges for lease liabilities	395	405	390
Loss from changes in exchange rates	28	9	—
Interest expenses related to borrowing and payable in respect of intangible assets purchase	16,172	12,045	—
Other	65	300	48
	16,660	12,759	438
Financial expenses (income), net	16,609	12,489	(897)

NOTE 25 - SEGMENT INFORMATION:

The Chief Executive Officer is the Company's Chief Operating Decision Maker ("CODM"). The CODM allocates resources and assesses the Company's performance based on the following segmentation: Commercial Operations and Research & Development. The Commercial Operations segment covers all areas relating to the commercial sales and is being performed by the Company's U.S. subsidiary. The Research and Development segment includes all activities related of research and development and licensing of therapeutic candidates and is being performed by the Company.

Effective December 31, 2021, the Company changed its operating segments to reflect the manner in which the Company's CODM reviews and assesses performance. Accordingly, the Company reports on revenue and segment Adjusted EBITDA. Disclosures regarding the Company's reportable segments for prior periods have been adjusted to conform to the current period presentation. The CODM does not review assets by operating segment. Adjusted EBITDA represents net loss before depreciation, amortization, and financial expenses (income), adjusted to exclude share-based compensation and the Aemcolo® intangible asset impairment. (See also note 11b).

a. Segment information

1) **Revenues** - All revenues reported in these consolidated financial statements relate to the Commercial Operations segment and were generated in the U.S. (see also note 20).

2) **Adjusted EBITDA by segment:**

The following table presents segment profitability and a reconciliation to the consolidated net loss and comprehensive loss for the periods indicated:

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	Year Ended December 31,		
	2021	**2020**	**2019**
	U.S. dollars in thousands		
Commercial Operations Segment Adjusted EBITDA	(15,527)	(27,236)	(15,913)
Research And Development Adjusted EBITDA	(37,247)	(23,501)	(23,048)
Financial expenses (income), net	16,609	12,489	(897)
Share-based compensation to employees and service providers	10,212	4,202	3,027
Depreciation	1,914	1,710	997
Amortization and impairment of intangible assets	16,235	7,035	216
Consolidated Comprehensive loss	(97,744)	(76,173)	(42,304)

b. Major customers

The following table represent the percentages of total net revenues from the major customers:

	Year Ended December 31,		
	2021	2020	2019
Customer A	32%	35%	
Customer B	31%	28%	
Customer C	32%	35%	10%
Customer D			45%
Customer E			18%

The Company's revenues were entirely in the U.S. and the payment terms for all customers are 30 to 60 days.

c. Segment assets

The Company's non-current assets located in Israel as of December 31, 2021, amount to $7 million (mainly intangible assets- $5.6 million and right-of-use assets - $1.1 million). The remainder of the consolidated non-current assets as of December 31, 2021, amount to $84.9 million and are located in the U.S (consisting mainly of intangible assets- $66 million, restricted cash - $16 million and right-of-use assets - $2.5 million).

NOTE 26 - LOSS PER ORDINARY SHARE:

a. Basic

The basic loss per share is calculated by dividing the loss by the weighted average number of ordinary shares in issue during the period.

The following is data taken into account in the computation of basic loss per share:

REDHILL BIOPHARMA LTD.
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

	Year Ended December 31,		
	2021	2020	2019
Loss (U.S. dollars in thousands)	97,744	76,173	42,304
Weighted average number of ordinary shares outstanding during the period (in thousands)	465,273	364,276	296,922
Basic loss per share (U.S. dollars)	0.21	0.21	0.14

b. Diluted

Diluted loss per share is calculated by adjusting the weighted average number of ordinary shares outstanding, assuming conversion of all potentially dilutive ordinary shares, using the treasury stock method. The Company had two categories of potentially dilutive ordinary shares: warrants issued to investors and options issued to employees and service providers. The effect of these options and warrants for all reporting years is anti-dilutive.

NOTE 27 - RELATED PARTIES:

a. Key management in 2021 includes members of the Board of Directors, including the Company's Chief Commercial Officer and Chief Executive Officer:

	Year Ended December 31,		
	2021	2020	2019
	U.S. dollars in thousands		
Key management compensation:			
Salaries and other short-term employee benefits	1,668	1,526	876
Post-employment benefits	91	61	43
Share-based payments	1,611	661	468
Other long-term benefits	54	33	26

b. Balances with related parties:

	December 31,	
	2021	2020
	U.S. dollars in thousand	
Current liabilities -		
Credit balance in "accrued expenses and other current liabilities"	399	484

NOTE 28 - EVENTS SUBSEQUENT TO DECEMBER 31, 2021:

a. On January 20, 2022, the Company's BoD approved a grant of 1,920,500 Restricted Stock Units ("RSUs"), each one equal to one ADS of the Company, to officers, employees, and consultants of the Company and of RedHill Inc. and 140,000 RSUs to the Company's directors and Chief Executive Officer (subject to an approval by the Annual General Meeting of the Company's shareholders), under the Company's 2010 Award Plan. The estimated fair value of the RSUs as of the date of BoD approval date was $6 million.

b. In October 2021, the Company entered into an exclusive license agreement (the "License Agreement") with Gaelan Medical Trade LLC ("Gaelan") for Talicia® in the United Arab Emirates (UAE). Under the terms of the License Agreement, the Company will receive an upfront payment of $2 million. In addition, the Company is eligible for additional milestone payments as well as tiered royalties up to mid-teens on net sales of Talicia in the UAE. Gaelan will receive the exclusive rights to commercialize Talicia® in the UAE, as well as a right of first refusal to commercialize Talicia® in the Gulf Cooperation Council

region (Saudi Arabia, Kuwait, Qatar, Bahrain and Oman) for a pre-determined period. Gaelan shall be responsible for obtaining and maintaining regulatory approvals, as well as to conduct any and all required clinical and other studies. In addition, upon receipt of necessary regulatory approvals, Gaelan is to become "Medical Authorization Holder" in the UAE.

In connection with the License Agreement, the Company and Gaelan entered into a supply agreement, according to which, the Company will exclusively manufacture (by a third party CMO) and supply to Gaelan during the term of the agreement.

c. In March 2022 The company entered into an exclusive license agreement with Kukbo for oral opaganib for the treatment of COVID-19, in South Korea. Under the terms of the license agreement, which follows the strategic investment by Kukbo noted in note in note 18(c) above, RedHill will receive an upfront payment of $1.5 million and is eligible for up to $5.6 million in milestone payments as well as low double-digit royalties on net sales of oral opaganib in South Korea. Kukbo will receive the exclusive rights to commercialize opaganib in South Korea for COVID-19.

d. During February and March 2022, the Company sold 282,626 ADSs under the ATM program at an average price of $2.2 per ADS for aggregate net proceeds of approximately $0.6 million, net of an immaterial amount of issuance expenses.

Exhibit 4.9

This Letter of Exemption and Indemnification is an unofficial translation of a Letter of Exemption and Indemnification in Hebrew adopted by the Company.

RedHill Biopharma Ltd.

Public Co. Reg. No. 51-430400-5

21 Ha'arba'a Street, Tel Aviv, Israel

Telephone: 972-3-5413131; Fax: 972-3-5413144

To Mr/Ms.

Dear Sir;

Letter of Exemption and Indemnification

Whereas in accordance with its articles of association, the Company may exempt, in advance, an officer therein from all or any of his liability for damage due to a breach of the duty of care *vis-à-vis* the Company and to indemnify him in advance and/or retroactively, for any liability or expense as provided in the articles of association, imposed on him or incurred by him, due to any act performed by him by virtue of his being an officer in the Company; and

Whereas on January 16, 2011, the Company's Board of Directors, after having obtained the approval of the Company's audit committee to that effect, resolved to approve the Company's undertaking to exempt and indemnify officers in the Company, in accordance with the Companies Law, 5759 - 1999, the Company's Articles Of Association and the terms of exemption and indemnification set forth in this Letter; and

Whereas on January 27, 2011, the Company's general meeting also approved the said resolution of the board of directors in connection with directors in the Company; and

Whereas on February 15, 2012, the Company's general meeting approved the amendment of the Letter of Exemption and Indemnification; and

Whereas on July 31, 2013 and July 26, 2021, the Company's general meeting approved additional amendments of the Letter of Exemption and Indemnification to reflect increases in the Maximum Indemnity Amount; and

Chapter One: Interpretation

1. Definitions

In this Letter of Exemption and Indemnification, each of the terms below will have the meaning set out opposite it, unless expressly stated otherwise.

"**Means of control**"	- As defined in the Companies Law;
"**Financial liability *in lieu of* criminal proceedings**"	- Financial liability imposed by law *in lieu of* criminal proceedings, including an administrative penalty under the Administrative Offences Law, 5746 – 1985, penalty for an offence defined as a penalty offence under the provisions of the Criminal Procedure Law, financial sanction or forfeit;
"**Companies Law**"	- The Companies Law, 5759 -1999;
The "**Securities Law**"	- The Securities Law, 5728 – 1968;
The "**Criminal Procedure Law**"	- The Criminal Procedure Law [Combined Version], 5742 – 1982;
"**Administrative Proceeding**"	- A proceeding pursuant to Chapter H3 (Imposing Monetary Sanction by the ISA), H4 (Imposing Administrative Enforcement Measures by the Administrative Enforcement Committee) and/or I1 (Conditioned Arrangement for Avoidance of Taking Action of for Stopping Action) of the Securities Law, as amended from time to time
"**Distribution**"	- As defined in the Companies Law;
"**This Letter**"	- This Letter of Exemption and Indemnification, including the addendum hereto, constituting an inseparable part hereof;
"**Termination of proceeding without the filing of an indictment in a case in which a criminal investigation was instituted**"	- Closing the case pursuant to Section 62 of the Criminal Procedure Law, or a stay of proceedings by the Attorney General pursuant to Section 231 of the Criminal Procedure Law;
"**Act**" or "**Act in the capacity of officer**"	- A legal act, through any act or omission, of an officer in the capacity of an officer in the Company and/or as an officer and/or employee and/or observer at meetings of competent organs of a corporation in which the Company holds, directly or indirectly, the means of control (a "**Related Corporation**"), including such act which took place prior to the entry into force of this Letter of Exemption and Indemnification;

"**Third Party**"	- Any person who is not the Company and/or one of the shareholders of the Company and/or anyone acting on their behalf.

2. Interpretation

2.1 The Preamble to this Letter of Exemption and Indemnification constitutes an inseparable part hereof.

2.2 The section headings in this Letter of Exemption and Indemnification are for convenience only and shall not be used for the purpose of the interpretation hereof.

2.3 Words and terms defined in the singular will also include the plural and vice versa; words in the masculine gender will also include the feminine gender and vice versa.

2.4 To the extent not expressly defined in this Letter, the terms herein will be interpreted in accordance with the Companies Law and, where there is no definition in the Companies Law – in accordance with the Securities Law.

2.5 The Company's undertakings pursuant to this Letter shall be interpreted broadly, in a manner intended to fulfill them, to the maximum extent permitted under law, for the purpose for which they were designed

2.6 In the event of a conflict between any provision in this Letter and a provision of the law that cannot be contracted out of, and which may not be revised or supplemented, such provision of the law shall prevail, but same shall not prejudice or derogate from the force of the other provisions in this Letter. Furthermore, should it be determined that any provision in this Letter is unenforceable and/or lacks legal validity on any ground whatsoever, same shall not prejudice or derogate from the force of the other provisions in this Letter.

Chapter Two: Exemption

3. Exemption in Advance

Subject to the provisions of any law, the Company hereby exempts you in advance from any liability for any damage incurred by it, either directly or indirectly, due to the breach of your duty of care *vis-à-vis* the Company, by your acts in your capacity as an officer.

Without limitation to the generality of the foregoing, it is hereby clarified that so long as same is not permitted under law, the Company does not exempt you in advance from your liability to the Company for a breach of the duty of care upon Distribution, to the extent applicable to you, if any.

4. Exemption in Advance and Indemnification Have No Bearing on Each Other

Nothing in the Company's undertaking to exempt you in advance (as set forth in section 3 above) will derogate from the Company's undertaking to indemnify you in accordance with this Letter.

5. Retroactive Exemption

To the extent permitted by any law, the Company exempts you from any liability for any damage incurred by it, either directly or indirectly, due to the breach of your duty of care *vis-à-vis* the Company, by your acts in your capacity as an officer prior to the entry into force of this Letter of Exemption and Indemnification.

Chapter Three: Indemnification

6. Indemnification in Advance - General

6.1 Subject to the provisions of any law, the Company hereby undertakes to indemnify you in advance for any liability or expense as set forth in section 7 below, imposed on you or incurred by you in connection with acts performed by you in the capacity of an officer in the Company, to the extent that the liability or expense has not been actually paid by virtue of an insurance policy or by virtue of indemnification on behalf of a third party, provided that the Maximum Indemnity Amount will not exceed the amount set forth in subsection 8.1 below.

6.2 Subject to the provisions of subsection 8.3 of this Letter below, it is hereby clarified that nothing in the Company's undertaking to indemnify you in advance as set forth in subsection 6.1 of this Letter above, shall derogate from your right to receive, directly or via the Company, payments by virtue of an insurance policy or by virtue of indemnity on behalf of a third party, to the extent that you are entitled to such payments for any liability or expense as set forth in section 7 of this Letter below.

The Company's undertaking to indemnify you in advance as set forth in subsection 6.1 above, is conditioned on the fact that you have adopted all reasonable measures to receive payments by virtue of an insurance policy or by virtue of an indemnity undertaking and insurance by a Related Corporation in connection with your capacity as an officer in such corporation, if and to the extent that you are entitled to such payments, and they can be claimed under the circumstances of the case.

To remove any doubts, it should be clarified that the Company's undertaking to indemnify you will only apply with respect to the balance of your liabilities following the full utilization of your rights for insurance and indemnification in a Related Corporation in connection with your office in a Related Corporation and following the utilization in full of your rights for officers' insurance of the Company.

6.3 In the event that you have incurred excess insurance to receive payments pursuant to an insurance policy, the Company's undertaking to indemnify you in advance as set forth in subsection 6.1 of this Letter above shall also apply with respect to the amount of the self participation charged in accordance with the insurance policy.

7. Liabilities or Expenses to which the Indemnity Applies in Advance

The Company's undertaking to indemnify you in advance, as set forth in section 6 above, will apply due to any liability, payment or expense imposed on or incurred by you, as follows:

7.1 A financial liability imposed on you in favor of another person pursuant to a judgment, including a compromise judgment or an arbitrator's award, approved by the Court, due to acts performed by you in the capacity of an officer, and which pertain, directly or indirectly, to one or more of the events set forth in the addendum to this Letter (the "**Addendum**"), which, at the discretion of the Company's Board Of Directors, are anticipated in light of the Company's actual activity at the time of the issuance of the advance indemnity undertaking;

7.2 Reasonable litigation costs, including lawyer's fee, incurred by you pursuant to any investigation or proceeding conducted against you by any authority competent to conduct an investigation or proceeding, at the end of which, no indictment is filed against you and no financial liability is levied on you in lieu of criminal proceedings, or at the end of which, no indictment is filed against you but a financial liability is levied in lieu of criminal proceedings, in an offense not requiring proof of *mens rea* or in connection with a monetary sanction;

7.3 Reasonable litigation costs, including attorney's fees, incurred by you or with which you are charged by a Court, in a proceeding to be instituted against you by the Company or on its behalf or by another person, or in a criminal indictment from which you are acquitted, or in a criminal indictment in which you are convicted of an offense which does not require proof of *mens rea*.

7.4 A monetary liability imposed on you due to a payment for the party harmed by the breach in an Administrative Proceeding, as aforesaid in Section 52(54)(a)(1)(a) of the Securities Law.

7.5 Expenses incurred by you in connection with an Administrative Proceeding conducted in your matter, including reasonable litigation expenses, including legal fees.

7.6 Any liability or other expense which upon them the indemnification to an officer according to the law is allowed.

8. Amount of the Advance Indemnity

8.1 The amounts to be paid by the Company to all officers, in the aggregate, in any calendar year, in accordance with all letters of exemption and indemnification issued and/or to be issued to them by the Company for financial liabilities and reasonable litigation costs as set forth in subsection 7.1 above, will not exceed the higher of 25% (twenty five percent) of the Company's consolidated shareholders' equity as is in accordance with the Company's most recent consolidated annual financial statements, that existed as of the actual date of payment for the indemnification, or USD 10,000,000 (Ten million US Dollars) ("**Maximum Indemnity Amount**"). It should be clarified that the Company's Board Of Directors has determined that the Maximum Indemnity Amount, as defined in this Letter above, is reasonable under the circumstances.

8.2 If and to the extent that the total sum of all amounts which the Company is required to pay on any date, plus the sum of all amounts paid by the Company by such date, for financial liabilities and reasonable litigation costs as set forth in subsection 7.1 above, in accordance with all letters of exemption and indemnification issued and/or to be issued to all officers in the aggregate, exceeds the Maximum Indemnity Amount, the Maximum Indemnity Amount or the balance thereof, as the case may be, will be distributed among the officers entitled to such amounts in connection with demands submitted to the Company pursuant to the indemnity letters and which have not been paid to them before such date, so that the amount actually received by each of the said officers, will be calculated in the ratio of the amount payable to each of the officers from the sum payable to all the said officers in the aggregate, on such date, in connection with such demands. Should it turn out on a subsequent date, that amounts which the Company was required to pay become available, either in light of the contents of Section 10 below or due to the settlement of claims against officers without having to pay therefor all or any part of the amounts claimed by any officer, the balance of the amount for indemnification will increase by the amount of the sums becoming available, and all officers who have only received their pro rata share as aforesaid, will be entitled to their proportionate share, pro rata, out of the amounts that become available.

In order to clarify the calculation method detailed in this subsection 8.2, the following example is provided: assume that compensation payments were ruled against Officer A for the sum of $100. These payments are recoupable, and thus Officer A demands indemnification from the Company for these payments. Assume further that the maximum indemnification sum is 25% (twenty-five percent) from Company's consolidated shareholders' equity, which was set according to the last consolidated annual financial statements, that existed as of the actual date of payment for the indemnification, is $1,000. Therefore, the maximum indemnification sum is, as of the payment date of $100 to Officer A, is $250. Therefore, after payment for the indemnification or Officer A, and until the new consolidated annual financial statements, law suits are filed against Officers B, C and D, who demand repayment of $100, $200 and $300 – respectively. In such a case, since the latest claimed indemnification sum ($600) is higher than the balance maximum indemnification sum ($150), the balance shall be divided pro rata between the Officers as follows: Officer B shall receive 150*100/600, Officer C shall receive 150*200/600 and Officer D shall receive 150*300/600. In case after the specified above, and before the Company updates its consolidated annual financial statements the Company will learn that Officer A was not entitled to the Indemnification, the sum of $100 will become available and return to the general indemnification sum. The returned sum ($100) shall be divided pro rata between the Officers as follows: Officer B shall receive a further payment of 100*100/600, Officer C shall receive a further payment of 100*200/600 and Officer D shall receive a further payment of 100*300/600.

8.3 The indemnity amount paid to you by the Company, together with the amounts paid to you pursuant to an insurance policy and/or in accordance with an indemnity undertaking by any third party whatsoever, will in no event exceed the amount of the financial liability and/or the expenses as set forth in Section 7 above, which you have incurred or with which you have been charged. For this purpose, the amounts of the excess insurance in accordance with an insurance policy, if such have been

prescribed, will be deemed to be amounts not actually paid to you. Should the Company pay to you or in your place, amounts that you are entitled to receive in accordance with an insurance policy and/or an indemnity undertaking by any third party whatsoever, then you will assign to the Company your rights to receive the amounts in accordance with the insurance policy or the indemnity undertaking by any third party, to the extent that there is no impediment to the assignment of such rights, and you will authorize the Company to collect these amounts on your behalf, where required for the fulfillment of the provisions of this section, and, at the Company's request, you will sign any document for the purpose of assigning your rights and authorizing the Company to effect such collection. In the event that you have collected the aforesaid amounts directly from an insurance company or from any third party whatsoever, these amounts will be returned by you to the Company in accordance with the provisions of Section 10 below.

9. Realization of Advance indemnification

In any event in respect of which you are likely to be *prima facie* entitled to indemnity pursuant to this Letter, you and the Company will act as follows:

9.1 Subject to any law, you will give notice to the Company of any legal and/or administrative proceeding, investigation or proceeding by a competent authority instituted against you, and of any concern or threat that such proceeding or investigation will be instituted against you (in this section 9 and section 10.1 hereunder: "**Proceeding**"), with due expedition after you have first learned about it and not later than by the end of three (3) days after you first learned of it and on such date as will allow you and the Company a reasonable time to submit a response to such Proceeding, as required under law, and you will transfer to the Company or to anyone designated by it, without delay, a copy of any document relating to the Proceeding delivered to you by the initiator of the Proceeding (in this section: "**Duty to Give Notice and Deliver Documents**"). Subject to any law, in the event that the Company learns of such a Proceeding, the Duty to Give Notice and Deliver Documents will apply to the Company *vis-à-vis you*, *mutatis mutandis*.

It should be clarified that if you breach the Duty to Give Notice and Deliver Documents, this will not release the Company from its undertaking in accordance with this Exemption Letter, unless the breach committed by you as aforesaid, will have a material adverse effect on the Company's rights and/or its ability to defend in its name (in the event that the Company is also a party to the same Proceeding) and/or in your name against the Proceeding.

9.2 The Company will be entitled to assume the handling of your legal defense within the ambit of the same Proceeding and/or transfer such handling to a reputable attorney experienced in the relevant field, which the Company will select to this end, and who will act and will owe a fiduciary duty to you and to the Company. The Company will be entitled to appoint an attorney as aforesaid provided you give your prior approval, in writing, to the identity of the attorney. However, you will not unreasonably withhold such approval, including due to circumstances where, at your reasonable discretion, concern of a conflict of interests exists between your defense and the Company's defense or that of another officer. In the event of concern of a conflict of interests as aforesaid, a separate attorney will be appointed for you, who

will be acceptable to you, in order to protect your personal affairs, provided that such appointment is approved, in advance and in writing, by the Company. Subject to that stated heretofore and hereinafter, the Company and/or any such attorney will be entitled to act within the ambit of such handling of the Proceeding at their exclusive discretion subject to ongoing reporting to you and consultation with you from time to time.

The Company and/or such attorney will be entitled to terminate the Proceeding. However, the Company and/or the attorney will not agree to enter into a settlement in consequence of which you will be convicted of a criminal offense or required to pay an amount for which you would not be indemnified under this Indemnification Letter and would also not be paid to you pursuant to any insurance purchased by the Company or within the framework of any indemnity by a third party, other than with your prior written approval. The Company will not agree to decide the dispute by way of mediation or arbitration without first obtaining your prior written approval. However, you will not unreasonably withhold your approval as aforesaid.

At the Company's request, you will sign any document empowering the Company and/or any attorney as aforesaid, to handle your defense within such Proceeding on your behalf and to represent you in any matter pertaining thereto, as aforesaid.

9.3 You will collaborate with the Company and/or with any attorney as aforesaid and/or with any insurer in any reasonable manner as may be required of you by any of them as part of their handling in connection with such Proceeding, including the investment of all time required for dealing with the Proceeding, compliance with the provisions of the insurance policy, execution or delivery of applications, affidavits, powers of attorney and any other document, provided that the Company ensures the full coverage of all expenses relating thereto, in such manner as will not require you to pay or finance them in person, and all subject to the provisions of Sections 7 and 8 above.

9.4 The Company will not be obligated to indemnify you for any amount with which you are charged in the wake of a settlement arrangement, mediation or arbitration or in the event that, within the ambit of a criminal indictment, you confess to an offense not requiring proof of *mens rea*, unless the Company's approval has been given in advance and in writing for the settlement arrangement or the holding of such mediation proceeding or such arbitration or for your confession to such charge, as the case may be. It should be noted that the Company will not unreasonably withhold its approval as aforesaid.

9.5 Irrespective of whether or not the Company exercises its right under subsection 9.2 above, the Company will attend to the full coverage of all the litigation costs referred to in subsections 7.2, 7.3, 7.5 and 7.6 above, and, within this context, will also provide securities and/or sureties which it is charged to provide pursuant to an interim decision of a court or an arbitrator, including for the purpose of substituting attachments imposed on your assets, and will pay such costs so that you will not be required to pay or finance them in person, and all subject to the provisions of Section 7 above.

Subject to subsection 10.1 below, amounts paid by the Company as aforesaid will be credited as an advance payment on account of the indemnity amount to which you will be entitled under this Indemnification Letter.

9.6 Upon your request to effect a payment with respect to any event pursuant to this Indemnification Letter, the Company will adopt all measures required under law for the payment thereof and will act to procure any approval required to this end, if any. In the event that any approval whatsoever as aforesaid is required for such payment, and where such payment is not approved on any ground whatsoever, such payment or any part thereof which is not approved as aforesaid shall be subject to the court's approval (where relevant), and the Company will act to obtain same immediately, and will bear all costs and payments required to obtain same as aforesaid.

9.7 You may contact the Company secretary at any time, and receive information as to the balance of the Maximum Indemnification Amount, as at the date of such application, that has not yet been settled by virtue of the indemnification letters, as defined in subsection 8.2 above.

10 Refund of Amount Paid by virtue of the Advance Indemnity Undertaking

10.1 In the event that the Company has paid to you or on your behalf any amounts whatsoever under this Indemnification Letter, including amounts in accordance with subsection 9.5 above, and where subsequently it transpires that you are not entitled to indemnification from the Company for such amounts, these amounts will be deemed as a loan extended to you by the Company, which will bear interest at the minimum rate prescribed in accordance with subsection 3(i) of the Income Tax Ordinance, or any other law superseding same, as applicable from time to time, and which does not constitute a benefit with respect to your chargeable income (hereinafter in this subsection: the "**Loan**") . In such event you will repay the loan within three years from the date it became clear that the beneficiary is not entitled to indemnification from the company. and in accordance with such payments schedule as determined by the Company, with the approval of the Company's competent organs.

It should be clarified that in the event that the Company has paid litigation costs to you or on your behalf, including lawyer's fee, in connection with any investigation or proceeding conducted against you by a competent authority or in connection with a criminal proceeding instituted against you, such amounts will be deemed as a loan extended to you by the Company, under such terms as are set forth in this section. If and where it transpires that the Company may, by law, indemnify you for such amounts, these amounts will become indemnity amounts which have been paid to you by the Company pursuant to this Indemnification Letter, you will not be required to refund same to the Company, the interest thereon will be written off and the Company will bear the tax payments applicable to you in consequence thereof, if any.

10.2 It is clarified that amounts awarded in your favor within the framework of a legal proceeding, settlement, mediation or arbitration arrangement, in connection with any liability or expense paid to you or on your behalf theretofore by the Company in accordance with the Indemnification Letter, will be refunded by you to the Company

upon receipt thereof. In the event that such amounts were awarded in your favor and you have not yet received them, you will assign your rights to receive such amounts to the Company and/or authorize the Company to collect such amounts on your behalf.

11 Retroactive Indemnification

Subject to the provisions of the Company's Articles Of Association and to the resolution of the Company's competent organs, nothing in the foregoing in this Letter shall derogate from the Company's right to indemnify you retroactively.

Chapter Four: General Provisions

12 Exemption and Indemnification Exclusion

The Company does not exempt you in advance and will not indemnify you for any of the following:

12.1 Breach of fiduciary duty, other than in connection with indemnification, provided that you acted in good faith and had reasonable grounds to assume that your act would not adversely affect the best interests of the Company and/or a Related Corporation;

12.2 Breach of a duty of care committed intentionally or recklessly, other than if committed only by negligence;

12.3 A deliberate act to generate personal profit unlawfully;

12.4 Any fine, civil fine or ransom imposed upon you, provided that such fine or ransom have not been imposed pursuant to the conviction for a crime which does not require proof of criminal intent, or for a financial sanction levied on you.

13 Application subsequent to Termination of Office

The Company's obligations under this Letter of Exemption and Indemnification will be available to you and/or to your estate and/or to alternate directors duly appointed by you, without a time limitation, as well as subsequent to the termination of your capacity as officer in the Company and/or in a Related Corporation, as the case may be, provided that the acts forming the subject of this Letter of Exemption and Indemnification were committed in the course of your capacity as an officer in the Company and/or in a Related Corporation, as the case may be.

14 No Assignment

To remove any doubts, it should be clarified that this Letter may not be assigned. Notwithstanding the foregoing, in the event of your demise (G-d forbid), this Letter shall apply to you and to your estate.

15 Letter not in favor of Third Party

To remove any doubts, it should be clarified that this Letter will not be interpreted as intending to grant any right or benefit to any third party whatsoever, including any insurer.

16 Cancellation, Revision, Waiver and Refraining from Action

16.1 Nothing in this Letter of Exemption and Indemnification shall prejudice or derogate from future resolutions of the Company as to the grant of advance exemption and/or advance or retroactive indemnification in connection with any matter subject to any law, and same shall not compel the Company to grant you additional exemption and/or indemnification beyond that stated in this Letter of Exemption and Indemnification.

16.2 The Company will be entitled, at its exclusive discretion and at any time, to cancel its exemption and/or indemnification undertaking pursuant to this Letter, or to reduce the Maximum Indemnification Amount hereunder, or limit the events to which the indemnification applies, either in respect of all officers or in respect of only part of them, to the extent that such cancellation or revision refers to events taking place following the date of the cancellation or revision, provided you have been given a prior notice of its intention as aforesaid, in writing, not less than 30 days prior to the date on which its resolution takes effect. To remove any doubts, it is hereby clarified that any such resolution, likely to adversely affect the terms of or to revoke this Letter, will not have any retroactive applicability of any nature whatsoever and this Letter, prior to the revision or cancellation hereof, as the case may be, will continue to apply and be valid in all respects in connection with any event which occurred prior to the revision or the cancellation, even where the proceeding in connection therewith was instituted against the officer subsequent to the revision or cancellation of this Letter. In any other event, this Letter may not be revised unless signed by the Company and by you.

16.3 In the event that, in the future, the relevant law is modified so as to allow the Company to extend the scope of the exemption which it may grant an officer from his liability for breach of the duty of care and/or allowing the Company to extend its undertaking to indemnify an officer, then such modification will also be deemed to apply to you by law, and this Letter of Exemption and Indemnification will be deemed to have been modified so as to include such modification.

16.4 A delay, postponement, grant of extension or failure on your part or on the part of the Company to exercise or enforce any of the rights in accordance with this Letter, will not be deemed as a waiver or impediment, on your part or on the part of the Company, of the exercise of the rights under this Letter and pursuant to any law in the future, and will not prevent you or the Company from instituting all legal and other measures required to exercise such rights.

17 Law and Jurisdiction

Israeli Law shall exclusively apply to this Letter, and to any dispute arising with respect to this Letter. The exclusive jurisdiction in respect of everything related to and arising from

this Letter, including with respect to its validity, breach and interpretation hereof, will vest in the competent courts in the district of Tel – Aviv only.

18 Entry into Force; Previous Letters of Exemption and Indemnification

18.1 This Letter of Exemption and Indemnification will take effect only upon your execution of a copy hereof, in the place designated therefor, and upon the delivery of the signed copy to the Company. Upon its entry into force, this Letter of Exemption and Indemnification revokes any previous undertaking for exemption and/or indemnification, if and insofar as offered and granted to you by the Company. Without derogating from the generality of the foregoing, if and insofar as this Letter of Exemption and Indemnification is declared or found to be void by the competent courts, then any exemption and/or indemnification undertaking preceding the date of the entry into force of this Letter of Exemption and Indemnification, and which this Letter of Exemption and Indemnification was intended to replace, will remain in full force and effect.

18.2 Nothing in this Letter of Exemption and Indemnification will derogate from any other exemption or indemnification granted to you by any third party and/or to which you are entitled from any other source under law.

19 Addresses And Notices

The Parties' addresses are as follows:

	Address	Electronic mail
RedHill Biopharma Ltd.	21 Ha'arba'a St., Tel Aviv 6473921, Israel	micha@redhillbio.com
Name		

Any notice forwarded by one Party to the other in accordance or in connection with this Letter will be sent by registered mail and by electronic mail or hand delivered. A notice to be delivered to the Company should be delivered, as aforesaid, to two addresses. A notice which is hand delivered will be deemed to have reached its addressee on the actual date of delivery, provided that it is a business day and if it is not a business day, then on the first business day subsequently. A notice sent by registered mail will be deemed to have reached its addressee within three (3) business days from its dispatch, and a notice transmitted via electronic mail will be deemed to have reached its addressee on the date of transmitting the notice, subject to receipt of an electronic confirmation of the transmission thereof.

In Witness Whereof the Company Has Signed, via its duly authorized signatories.

RedHill Biopharma Ltd.

By:		By:	
Position:		Position:	
Date:		Date:	
Signature:		Signature:	

I have read this Letter of Exemption and Indemnification thoroughly, I have fully understood its contents, and I confirm receipt of this Letter of Exemption and Indemnification and confirm my consent to all its provisions. I am aware that in respect of this Letter of Exemption and Indemnification, the Company's legal advice does not represent me and that I cannot rely thereon.

Name

Date:	
Signature:	

Addendum

1. To remove any doubt, all definitions, terms and expression in this Addendum, will have the same meaning imparted to them in the Letter of Exemption and Indemnification to which this Addendum is attached, unless expressly stated otherwise.

2. Subject to the provisions of any law, you will be entitled to indemnity for any liability or expense imposed on you in favor of another person pursuant to a judgment, including a compromise judgment or an arbitrator's award approved by a Court, due to any act committed by you in the capacity of an officer in the Company, and/or any derivation of such act, in connection with the following events which at the discretion of the Company's Board Of Directors are anticipated in view of the Company's actual activity at the time of the issuance of the advance indemnity undertaking:

   2.1 Issue of securities and/or listing them for trading on a stock exchange in Israel or abroad, including, without limitation to the foregoing, offering securities to the public under a prospectus, a private offering, an offer for sale, issue of bonus shares or offering of securities in any other manner whatsoever.

   2.2 An event arising from the Company being a public company or arising from the fact that its shares were offered to the public or arising from the fact that the Company's shares are traded on a stock exchange in Israel or abroad.

   2.3 A transaction within the meaning of Section 1 of the Companies Law, including negotiations to enter into a transaction or act, transfer, sale, lease, purchase or encumbrance of assets or liabilities (including securities) or granting or receiving any interest in any of the foregoing, obtaining credit and provision of securities, as well as any act directly or indirectly connected to such transaction, including disclosure of information and documents.

   2.4 Resolutions and/or acts relating to approval of transactions with stakeholders, as such transactions are defined in Chapter 5 of Part VI of the Companies Law.

   2.5 A report or notice submitted under the corporate laws, the securities laws, communications laws, tax laws, antitrust laws, labor laws or any other law compelling the Company to submit a report or a notice, including in accordance with rules or guidelines prevailing in a stock exchange in Israel or abroad, or in accordance with any law of another country regulating similar matters and/or refraining from submitting any report or notice as aforesaid.

   2.6 Adoption of the findings of external opinions for the purpose of the issuance of an immediate report, prospectus, financial statements or any other disclosure document.

   2.7 Discussion and passing resolutions and discovery and disclosure in the Company's reports, including an evaluation with respect to the effectiveness of internal control and other issues incorporated in the report of the Company's Board Of Directors, as well as the issuance of statements and reference to the financial statements.

2.8 Preparation, editing, approval and execution of the financial statements, including the passing of resolutions as to the application of accounting principles and restatement in the financial statements.

2.9 Adoption of financial reporting in accordance with International Financial Reporting Standards (IFRS), and any act in connection therewith.

2.10 Events relating to the effecting of investments on the part of the Company in any corporations whatsoever.

2.11 A resolution as to distribution, as defined in the Companies Law, including a distribution with the court's approval.

2.12 A change in the Company's structure, a change in the Company's ownership, the Company's reorganization, the liquidation thereof, the sale of its assets or businesses (in whole or in part), or any resolution in respect thereof, including, without limitation to the generality of the aforesaid, a merger, spin off, a change in the Company's capital, establishment of subsidiaries, winding up or selling them, allocation or distribution.

2.13 Consolidation, change or revision of arrangements between the Company and the shareholders and/or holders of bonds and/or banks and/or creditors of the Company or of Related Corporations, including the preparation or revision of the trust deeds, bonds and outline and arrangement documents in general.

2.14 Acts relating to the issuance of licenses, permits or approvals, including approvals and/or exemptions in respect of restrictive trade practices.

2.15 Participation in and preparation of tenders.

2.16 A statement, declaration, including the expression of a position or opinion, vote and/or abstaining from voting, made in good faith by you as an officer in the course and by virtue of your capacity, such as in negotiations and contractual engagements with suppliers or customers, including within the framework of meetings of management, board of directors or any of its committees.

2.17 Any act in contravention of the Company's articles of association.

2.18 Any act or resolution with respect to an employer-employee relationship including negotiations, contracting and implementation of personal or collective employment agreements, employees' benefits, including allocation of securities to employees.

2.19 Any act or resolution relating to safety at work and/or to terms of employment.

2.20 Acts in connection with conducting medical trials and/or product trials and/or the sale, distribution, licensing or use of such products.

2.21 Negotiations, contractual engagements and activation of insurance policies.

2.22 Consolidation of work plans, including pricing, marketing, distribution, guidelines to employees, to customers and to suppliers and collaboration with competitors.

2.23 Resolutions and/or acts relating to the environment and to public health, including hazardous materials.

2.24 Resolutions and/or acts relating to the Consumer Protection Law, 5741 – 1981 and/or orders and/or regulations by virtue thereof.

2.25 Acts relating to the Company's intellectual property and the protection thereof, including the registration or enforcement of intellectual property rights and their protection within claims in connection therewith.

2.26 Infringement of intellectual property rights of third parties, including, without limitation, patents, designs, breeders' rights, trademarks, copyright, and so forth.

2.27 Negotiations, execution and implementation of contracts of any nature or type with suppliers, distributors, agents, franchisers, marketers, importers, exporters, customers, etc. of the products or the services marketed and/or sold and/or supplied by the Company or used by it.

2.28 Negotiations, execution and implementation of contracts with manpower contractors, service contractors, construction contractors, refurbishing contractors, etc.

2.29 Reports, notices and submission of an application to State and other authorities.

2.30 Investigations on the part of State authorities.

2.31 Management of the bank accounts which the Company operates at banks and performance of transactions in such bank accounts, including with respect to transactions in foreign currency (including foreign currency deposits), securities (including resale transactions in securities and lending and borrowing of securities), loans and credit facilities, debit cards, bank guarantees, letters of credit, consultation agreements concerning investments including with portfolio managers, hedging transactions, options, futures contracts, derivatives, swap transactions, and so forth.

2.32 Realization of personal guarantees provided by the officer to the Company, as security for the Company's obligations and/or declarations.

2.33 Failure to maintain complete and/or proper due diligence procedures over the Company's investments, resulting in a loss of the investments in whole or in part and/or an adverse effect to the Company's businesses and/or breach of an undertaking *vis-à-vis* a third party.

2.34 Events and acts in connection with investments performed by the Company in various corporations, before or after effecting the investment, including for the purpose of entering into a transaction, its implementation, development, follow up and supervision.

2.35 Financial liability imposed on an officer in connection with acts in which he took part on behalf of the Company, *vis-à-vis* the various State institutions.

2.36 Financial liability imposed on an officer in connection with a claim by third parties against the officer due to deficient or misleading disclosure, in writing or verbally, to existing and/or potential investors in the Company, including in the event of the merger of the Company with another company.

2.37 Covering the excess insurance in the event of the activation of officers' liability insurance.

2.38 Breach of the provisions of any agreement whatsoever to which the Company is a party.

2.39 An act relating to a tax liability of the Company and/or a subsidiary and/or shareholders of any of them.

2.40 Any of the foregoing events, in connection with the capacity of the officer in the Company by virtue of his capacity as an officer and/or employee and/or observer at meetings of competent organs of a Related Corporation.

2.41 Acts and omissions not covered by a Product insurance policy

2.42 Acts and omissions in connection with bodily injuries or property damage attributed to the Company and/or to an officer who has acted on its behalf.

2.43 Acts and omissions arising from failure to purchase appropriate insurance and/or to take sufficiently secure measures and/or negligence in risk management.

2.44 Any event and/or act that in respect of which indemnification may be made pursuant to the Improvement of Enforcement Proceedings in the ISA law (Legislative Amendments), 5771-2011.

* * *

Exhibit 4.10

RedHill Biopharma Ltd.
(the "Company")

AMENDED AND RESTATED AWARD PLAN (2010)

As most recently amended by the Board of Directors on January 6, 2022

TABLE OF CONTENTS

1. **PREAMBLE**

1.1 This plan, as amended from time to time, shall be known as the RedHill Biopharma Ltd. Amended and Restated Award Plan (2010) (the "**Plan**"). The purpose and intent of the Plan is to provide incentives to employees, directors and/or service providers including advisors of the Company and/or of subsidiaries and/or affiliated companies of the Company (each a "**Related Company**" and collectively, "**Related Companies**") by providing them with the opportunity to purchase a proprietary interest in the Company by the issuance of ordinary shares of the Company ("**Shares**") and/or American Depositary Shares, and by the grant of options and awards of restricted shares ("**Restricted Shares**"), Restricted Share Units ("**RSUs**") and other share-based awards pursuant to the Plan , determined pursuant to the Plan, and such other securities as may be substituted for such shares pursuant to this Plan (collectively, "**Awards**").

1.2 The Plan is intended to enable the Company to grant Awards under various and different tax regimes, including, without limitation: (i) pursuant and subject to Section 102 of the Israeli Income Tax Ordinance (New Version), 1961 (the "**Income Tax Ordinance**") or any provision which may amend or replace it and any regulations, rules, orders or procedures promulgated thereunder (collectively, "**Section 102**") and to designate them as either grants made through a trustee or not through a trustee; (ii) pursuant and subject to Section 3(i) of the Income Tax Ordinance; (iii) as "incentive stock options" within the meaning of Section 422 of the United States Internal Revenue Code of 1986, as amended ("**Incentive Stock Options**" and the "**Code**", respectively) to Employees (as defined below) of the Company or any subsidiary of the Company which qualifies as a Corporation (as defined below); (iv) as options to U.S. residents, which would not qualify as Incentive Stock Options ("**Non-Qualified Stock Options**"); and (v) to grantees in jurisdictions other than Israel and the United States.

The Company, however, does not warrant that the Plan will be recognized by the income tax authorities in any jurisdiction or that future changes will not be made to the provisions of applicable laws, or rules or regulations which are promulgated from time to time thereunder, or that any exemption or benefit currently available, whether pursuant to Section 102 or otherwise, will not be abolished.

For purposes of the Plan, (i) the term "**Employee**" means a common law employee (as defined in accordance with the regulations and revenue rulings then applicable under Section 3401(c) of the Code) of the Company or any subsidiary of the Company; provided, however, in the case of individuals whose employment status, by virtue of their employer or residence, is not determined under Section 3401(c) of the Code, Employee means an individual treated as an employee for local payroll tax or employment purposes by the applicable employer under applicable law; and (ii) the term "**Corporation**" means any entity that is defined as a corporation under Section 7701 of the Code and is the Company or is in an unbroken chain of corporations (other than the Company) beginning with the Company, if each of the corporations other than the last corporation in the unbroken chain owns stock possessing a majority of the total combined voting power of all classes of stock in one of the other corporations in the chain.

1.3 The Board of Directors of the Company (the "**Board**") shall have the authority to make any requisite adjustments in the Plan and determine the relevant terms in any Agreement (as defined in Section 7 below) in order to comply with the requirements of any relevant tax regime. Furthermore, should any provision of Section 102 be amended, such

amendment shall be deemed included in the Plan with respect to Awards granted in the context of Section 102. Where a conflict arises between any section of the Plan, the Agreement or their application, and the provisions of any relevant tax law, rule or regulation, whether relied upon for tax relief or otherwise, the Board in its sole discretion shall determine the necessary changes to be made to the Plan and its determination regarding this matter shall be final and binding.

1.4 The Plan contemplates the grant of Awards by the Company both as a private company and as a company whose securities are publicly-traded. In the event the Company's securities should be registered for trading on the Nasdaq Stock Exchange, the New York Stock Exchange, any other stock exchange or an electronic quotation system, whether in the USA or elsewhere, the Awards allotted in accordance with the Plan may be made conditional to any requirement or instruction of the stock exchange authorities or of any other relevant authority acting pursuant to applicable law as shall exist from time to time. In such case, by means of a Board resolution, the Plan and the Agreements prepared pursuant hereto, may be amended as necessary to meet such requirements. In the event of a contradiction between any such amendment and the Plan's provisions, the amendment shall prevail.

2. ADMINISTRATION OF THE PLAN

2.1 The Plan shall be administered by the Board and/or by any committee of the Board so designated by the Board. Any subsequent references herein to the Board shall also mean any such committee, if appointed and, unless the powers of the committee have been specifically limited by law or otherwise, such committee shall have all of the powers of the Board granted herein. Without derogating from the generality of the foregoing, the Board shall have the authority to designate grants made pursuant to Section 102 as either grants made through a trustee or not through a trustee and to determine (and from time to time change, subject to Section 102) the tax route applicable to Awards granted through a trustee pursuant to Section 102 (e.g., the capital gains route or the employment income route) and to make any other elections with respect to the Plan pursuant to applicable law. Subject to Sections 4 and 15, the Board shall have plenary authority to determine the terms and conditions of all Awards (which need not be identical), including, without limitation, whether the Awards will be exercisable into ordinary shares of the Company or into American Depositary Shares, the purchase price of the Shares covered by each Award, the identity of those to whom, and the time or times at which, Awards shall be granted, the number of Shares to be subject to each Award, whether an Award shall be granted pursuant to Section 102 or otherwise and when an Award can be exercised and whether in whole or in installments. Subject to Section 15, the Board shall have plenary authority to construe and interpret the Plan, to prescribe, amend and rescind the rules and regulations relating to it and to make all other determinations deemed necessary or advisable for the administration of the Plan. All determinations and decisions of the Board pursuant to the provisions of the Plan and all related orders and resolutions of the Board shall be final, conclusive and binding on all persons, including the Company, its shareholders, grantees and their estates and beneficiaries.

2.2 Any directive or notice signed by a member of the Board shall constitute conclusive proof and authority for every act or decision of the Company.

2.3 No director or officer of the Company shall be personally liable or obligated to any grantee as a result of any decision made and/or action taken with respect to the Plan or its execution.

3. **SHARES SUBJECT TO THE PLAN**

The maximum number of Shares that may be issued under the Plan is 97,662,810 Shares and shall automatically be increased on January 1, April 1, July 1 and October 1 of each year such that immediately following such increase the maximum number of Shares that may be issued under the Plan will be equal to sixteen and a half percent (16.5%) of the number of outstanding Shares on a fully-diluted basis on the last day of immediately preceding fiscal quarter, one hundred percent (100%) of which may be granted pursuant to Incentive Stock Options. The Board may from time to time increase or decrease the maximum number of ordinary shares that may be issued under the Plan.

4. **OPTION EXERCISE PRICES**

The consideration to be paid by a grantee for each Share purchased by exercising an option (the "**Option Exercise Price**") shall be as determined by the Board on the date of grant, provided that the Option Exercise Price shall not be less than the nominal value of the Shares subject to the option, and if on the date of grant the Company's Shares are listed on any established stock exchange or a national market or quotation system, then except as otherwise determined by the Board, the Option Exercise Price shall not be less than the closing price on the date of grant on such established stock exchange or a national market or quotation system. The Option Exercise Price shall be denominated in the currency of the primary economic environment of, either the Company or the grantee (that is the functional currency of the Company or the currency in which the grantee is paid) as determined by the Company.

The Board may, in its discretion, grant to the holder of an outstanding option, in exchange for the surrender and cancellation of such option, a new option having an Option Exercise Price lower than provided in the option so surrendered and canceled, and containing such other terms and conditions as the Board may prescribe in accordance with the provisions of this Plan provided that such new Option Exercise Price shall not be less than the nominal value of the Shares subject to the new option.

Notwithstanding anything herein to the contrary, with respect to the grant of a Non-Qualified Stock Option or an Incentive Stock Option, the Option Exercise Price shall be no less than the Fair Market Value (as defined below) of a Share on the date of grant of such Non-Qualified Stock Option or Incentive Stock Option; provided, however, if an Incentive Stock Option is granted to an Employee who owns or is deemed to own (by reason of the attribution rules of Section 424(d) of the Code) more than ten percent (10%) of the combined voting power of all classes of stock of the Company (or any Related Company), the Option Exercise Price shall be at least one hundred ten percent (110%) of the Fair Market Value of a Share on the date of grant of such Incentive Stock Option.

For purposes hereof, the "**Fair Market Value**" of the Shares shall mean, as of any date, the last reported sale price, on that date, of the Shares of the Company on the principal securities exchange on which such Shares are then traded, or, in the event that no sales of such Shares took place on such date, the last reported sale price of such Shares on such principal securities exchange on the most recent prior date on which a sale of Shares took place; provided, however, that if such Shares are not publicly traded on the date as of which Fair Market Value is to be determined, "Fair Market Value" of the Shares shall mean the value as determined in good faith by the Board. The determination of Fair Market Value shall, where applicable, be in compliance with Section 409A of the Code.

5. **EXCLUSIVITY OF THE PLAN**

Unless otherwise determined by the Board in any particular instance as part of the Agreement, each grantee hereunder will be required to declare and agree that all prior agreements, arrangements and/or understandings with respect to Awards and options to purchase Shares of the Company which have not actually been granted prior to execution of the Agreement shall be null and void and that only the provisions of the Plan and/or the Agreement shall apply.

Notwithstanding the above, the adoption of this Plan, by itself, shall not be construed as amending, modifying or rescinding any incentive arrangement previously approved by the Board or as creating any limitations on the power of the Board to adopt such other incentive arrangements as it may deem desirable, including, without limitation, the granting of Awards otherwise than under this Plan, and such arrangements may be either applicable generally or only in specific cases.

6. **GRANT OF THE AWARDS TO THE TRUSTEE; VOTING OF SHARES**

6.1 The Board shall appoint a trustee for the purposes of this Plan, which trustee shall be approved, with respect to grants designated as grants made through a trustee pursuant to Section 102, in accordance with Section 102 (the "**Trustee**"). The Trustee shall have all the powers provided by law, Section 102 and the Plan and shall act pursuant to the provisions thereof, as they shall apply from time to time. The Company shall pay the Trustee a fee as shall be agreed between the Trustee and the Company.

6.2 Unless otherwise determined by the Board, all Awards shall be issued by the Company in the name of the Trustee and the Share certificates representing any Shares issued pursuant to options exercised hereunder or Shares vested under other Awards granted hereunder, and any and all other or additional rights deriving in connection therewith, if any, such as, but not limited to, bonus Shares (Share dividends) ("**Additional Rights**"), shall be issued by the Company in the name of the Trustee in trust for the designated grantee and shall be deposited with the Trustee, held by him or her and registered in his or her name in the register of members of the Company for such period as determined by the Board but, in the case of grants designated as grants made through a trustee pursuant to Section 102, not less than the period required, or approved, with respect thereto pursuant to Section 102, as shall be in effect from time to time (the "**Required Holding Period**").

Furthermore, and without derogating from the aforesaid or any other provision hereof, with respect to Awards granted which were designated as made through a trustee pursuant to Section 102: (i) they may not be sold until the end of the Required Holding Period, unless otherwise allowed or determined by the Israeli tax authorities; and (ii) all Additional Rights will be subject to the same tax route applicable to the original Award.

6.3 Awards granted and designated as grants made through a trustee pursuant to Section 102 will be held by the Trustee and registered in his name in trust for the designated grantee, for not less than the Required Holding Period.

6.4 Awards granted hereunder shall not confer upon the holder thereof any of the rights of a shareholder of the Company with respect to the Shares subject to such Awards until such Shares are issued and registered in the name of the holder upon exercise of the options.

6.5 For as long as any Shares are held by the Trustee or registered in his name or for as long as the certificates representing any Shares are held by the Trustee, the Trustee alone shall

be entitled to receive every notice to which a shareholder is entitled, or to demand any information, and any financial and/or other report to which a shareholder is entitled from the Company, and only he or whomever he shall designate pursuant to the Proxy and Power of Attorney referred to and as defined in Section 10.2 below (the "**Attorney**"), shall be entitled to exercise every other right of the shareholders vis-a-vis the Company including the right to participate in and to vote at all shareholders' meetings. No grantee shall be entitled to exercise any of these rights as shareholder nor make any demand or request of the Trustee and/or of the Attorney in this regard.

6.6 Shares registered in the Trustee's name shall be represented at all meetings of shareholders of the Company and shall be voted by the Trustee or the Attorney in the same manner, proportionately, as the other shareholders of the Company voting on such matter.

6.7 Nothing in the foregoing provisions shall derogate from the power of the Board to grant options to the Trustee otherwise than under the provisions of Section 102 or to grant options to grantees directly otherwise than through the Trustee or on terms which differ from those specified above or to approve the transfer of Shares from the Trustee to the name of any grantee(s) upon such conditions as shall be determined by the Board.

7. AWARD AGREEMENT; TERMINATION OF EMPLOYMENT

Unless otherwise determined by the Board, every grantee shall be required to sign grant letter or other documents as shall be determined by the Board, in the form approved by the Board (the "**Agreement**").

The Agreement shall specify the type of Award granted and whether it constitutes an Award pursuant to Section 102, and if so, under which regime, an Award pursuant to Section 3(i) of the Income Tax Ordinance, an Incentive Stock Option, a Non-Qualified Stock Option or otherwise. The Agreement need not be identical with respect to each grantee. The following terms, however, shall apply to all Awards, unless expressly otherwise decided in respect of a particular Award:

7.1 The Option Exercise Price shall be paid by the grantee to the Company no later than the date of exercise of the option unless otherwise determined in the Agreement.

7.2 The grantee shall have no right of first refusal to purchase Shares of the Company which may be offered for sale by shareholders of the Company, and shall have no pre-emptive rights to purchase Shares which are being allotted or shall in the future be allotted by the Company, to the extent any such rights otherwise exist.

7.3 The Award and/or the right to the Award are personal and except insofar as is specified in this Plan, and, where applicable, subject to Section 102, may not be transferred, assigned, pledged, withheld, attached or otherwise charged either voluntarily or pursuant to any law, except by way of transfer pursuant to the laws of inheritance, and no power of attorney or deed of transfer, whether the same has immediate effect or shall take effect on a future date, shall be given with respect thereto. During the lifetime of the grantee the Award may only be exercised by the designated grantee or, if granted to the Trustee, by the Trustee on behalf of the designated grantee. A note as to the provisions of this sub-section or a legend may appear on any document which grants the Award and in particular in the Agreement, and also on any Share certificate.

7.4 The right to exercise an option is granted to the Trustee on behalf of the grantee. Unless otherwise provided in the Agreement, vesting shall be in installments, gradually over a period of four (4) years from the date of grant of the option or such other period or periods as determined by the Board. Unless otherwise determined, at the conclusion of each period for the exercise of the option as determined in the Agreement ("**Vesting Periods**"), the option may, from time to time, be exercised in relation to part or all the Shares allocated for that period in such manner that at the end of each year following the granting of the option the Trustee shall, in the absence of a contrary determination in the Agreement, be entitled to exercise on behalf of the grantee and at his or her request up to one third (1/4) of the Shares subject to the option.

In addition, during each of the Vesting Periods, the option may be exercised in relation to all or part of the Shares allocated for any previous Vesting Period in which the option was not fully exercised, provided, subject to the provisions of Section 7.7 hereof, that at the time of the exercise of the option the grantee has continued to be employed by or to serve as a director of or provide services to, the Company or a Related Company on a continual basis from the date of the grant thereof until the date of their exercise. After the end of the Vesting Periods and during the balance of the option period, the option may be exercised, from time to time, in relation to all or part of the Shares which have not at that time been exercised and which remain subject to the option, subject to the provisions of Section 7.7 hereof and to any condition in the Agreement, if such exists, which provides a minimum number of Shares with respect to which the option may be exercised and any provision which determines the number of times that the Trustee may send the Company notice of exercise on behalf of the grantee in respect of the option. The Board shall be entitled at any time to shorten the vesting schedule or any Vesting Period.

7.5 The Board may determine at its sole discretion, that any grantee shall be entitled to receive the Awards, through the Trustee, pursuant to the provisions of this Plan or, subject to the provisions of Section 102 as relevant, directly in the name of the grantee, immediately upon execution of the Agreement or on such other date or dates as the Company has undertaken towards such grantee. In the event that a grantee is exempt from the Vesting Periods (pursuant to the provisions of Section 7.4), the Board shall be entitled, subject to the provisions of Section 102 as relevant, to determine that where the grantee does not comply with the conditions determined by the Board or ceases to be an employee of the Company or a Related Company, the Trustee, the Company or a Related Company shall have the right to repurchase the Shares from the grantee for nominal or any other consideration paid by the grantee or as otherwise determined by the Board at the time of grant. The Board may set additional conditions to this right of repurchase, including the provision of appropriate arrangements for the monies which shall be available to the Trustee or a Related Company or others for the purpose of the repurchase and may set conditions with respect to the voting rights of the grantee, rights of first refusal or pre-emptive rights to purchase Shares in the Company, to the extent such rights exist, the grantees right to receive reports or information from the Company, and the grantee's right to a dividend in respect of Shares which are subject to a right of reacquisition as aforesaid. For as long as the foregoing conditions of the Board (including a minimum period of employment as a condition for the lapse of the right to reacquisition) have not been complied with, the grantee shall not be entitled to sell or charge or transfer in any other manner the Shares which are subject to the right of reacquisition. As security for the compliance with this undertaking the Share certificate will be deposited with the Trustee who will release the same to the grantee only after the grantee becomes entitled to the Shares and the same are not subject to any other restrictive condition.

7.6 With respect to the grant of Incentive Stock Options, the Board may not grant Incentive Stock Options to any Employee which would permit the aggregate Fair Market Value (determined on the date of grant) of the Shares with respect to which Incentive Stock Options (under this and any other plan of the Company and its subsidiaries) are exercisable for the first time by such Employee during any calendar year to exceed $100,000 (U.S.). To the extent any option granted under this Plan which is designated as an Incentive Stock Option exceeds this limit or otherwise fails to qualify as an Incentive Stock Option, such option (or any such portion thereof) shall be a Non-Qualified Stock Option. If Shares acquired upon exercise of an Incentive Stock Option are disposed of by the grantee prior to the expiration of either two (2) years from the date of grant of such Incentive Stock Option or one (1) year from the transfer of Shares to the grantee pursuant to the exercise of such Incentive Stock Option, or in any other "disqualifying disposition" within the meaning of Section 422 of the Code, such grantee shall be required to notify the Company in writing of the date and terms of such disposition. A disqualifying disposition by a grantee shall not affect the status of any other option granted under the Plan as an Incentive Stock Option.

7.7 Termination of Employment/Cause Events

7.7.1 If a grantee ceases to be an employee, director or service provider (or, if relevant, an employee of a service provider) of the Company or a Related Company, other than: (i) by reason of death, disability (as determined by the Board in its absolute discretion) or retirement as provided in Section 7.7.3 below; or (ii) for Cause (as defined in Section 8.2 below); the options that shall have vested prior thereto shall remain exercisable for a period of ninety (90) days (or three (3) months in the case of an Incentive Stock Option) following the earlier of such cessation or notice of cessation (but only to the extent exercisable at termination of employment and not beyond the scheduled expiration date), unless the Agreement provides otherwise. If (i) a grantee ceases to be an employee, director or service provider (or, if relevant, an employee of a service provider) of the Company or a Related Company for Cause (as defined in Section 8.2 below) ("**Termination for Cause**") or (ii) a Cause Event (as defined in Section 8.2 below) occurs with respect to a grantee who is a former employee, director or service provider (or, if relevant, an employee of a service provider) of the Company or a Related Company, then immediately upon the Termination for Cause or notice of Termination for Cause in the case of clause (i) or the occurrence of a Cause Event in the case of clause (ii), the grantee shall not be entitled to exercise any Options, whether vested or unvested, and all such Awards granted to the grantee shall return to the pool of ordinary shares available for future grants under this Plan.

7.7.2 If the employment or the director or service-provider relationship of a grantee is terminated by reason of death, disability (as determined by the Board in its absolute discretion) or retirement after age 60 with the approval of the Board, the option shall remain exercisable for a period of twenty four (24) months following such termination (but only to the extent exercisable at termination of employment and not beyond the scheduled expiration date); provided, however, in the case of an Incentive Stock Option, with respect to a termination of employment as a result of death or disability (within the meaning of Section 22(e) of the Code), the period shall be twelve (12) months, and in the case of retirement, the period shall be three

(3) months (in each case, only to the extent exercisable at termination of employment and not beyond the scheduled expiration date).

7.7.3 The Board may determine whether any given leave of absence constitutes a termination of employment. Options awarded under this Plan shall not be affected by any change of employment so long as the grantee continues to be an employee, director or service-provider, as applicable, of the Company or a Related Company.

7.7.4 Notwithstanding the foregoing, the Board may in its absolute discretion, extend the period of exercise of the option by a grantee or grantees for such time as it shall determine either with or without conditions.

8. **ACCELERATION OF AN AWARD; LIQUIDATION**

8.1 Acceleration in the Event of Sale of Assets, Certain Mergers. In the event of: (i) a sale of all or substantially all of the assets of the Company; or (ii) a consolidation or merger of the Company in which the Company is not the continuing or surviving corporation and the continuing or surviving corporation (or, if such transaction is effected through a subsidiary, the parent of such continuing or surviving corporation), does not assume the Award or substitute it with an appropriate award in the continuing or surviving corporation (or in the parent as aforesaid), then, notwithstanding any contrary Vesting Periods in any Agreement or in this Plan, and unless in each case: (A) the applicable Agreement provides otherwise; or (B) the Board determines otherwise, all of the outstanding Awards held by or for the benefit of any grantee whose vesting dates fall within the first twelve (12) months thereafter shall be accelerated and become vested and exercisable immediately prior to the consummation or closing of such proposed action.

8.2 Acceleration in the Event of a Significant Event. If a "Significant Event", as defined below, shall occur, and following which the employment of a grantee with the Company or a Related Company is terminated by the Company or a Related Company, other than for "Cause" as defined below; and unless the applicable Agreement provides otherwise, all of the outstanding Awards held by or for the benefit of any grantee shall be accelerated and become immediately vested and exercisable.

Each of the following shall be a "**Significant Event**": a consolidation or merger of the Company with or into another corporation approved by the Board of the Company in which the Company is the continuing or surviving corporation or in which, if the Company is not the continuing or surviving corporation, the continuing or surviving corporation (or, if such transaction is effected through a subsidiary, the parent of such continuing or surviving corporation) assumes the Award or substitutes it with an appropriate award in the surviving corporation (or in the parent as aforesaid).

The term "**Cause**" shall mean, for the purposes hereof, any of the following: (a) the definition ascribed to Cause in the individual employment agreement or services agreement between the Company and/or its Related Party and the grantee; (b) any one of the following: dishonesty towards the Company or Related Party, substantial malfeasance or nonfeasance of duty, unauthorized disclosure of confidential information, and conduct substantially prejudicial to the business of the Company or Related Party; or, any substantial breach by the Participant of (i) his or her employment or service agreement or (ii) any other obligations toward Company or a Related Party; and (c) without limiting the foregoing clauses (a) and (b), a conviction (whether following trial, by plea of guilty or

failure to contest prosecution) in a criminal proceeding of (i) a misdemeanor involving fraud, false statements or misleading omissions, embezzlement, bribery, forgery or extortion; or (ii) a felony; or (iii) an equivalent charge to those in (i) and (ii) above in jurisdictions which do not use those designations.

The term "**Cause Event**" with respect to a former employee, director or service provider (or, if relevant, an employee of a service provider) of the Company or a Related Company shall mean, for the purposes hereof, any of the following: (a) the definition ascribed to Cause in the individual employment agreement or services agreement between the Company and/or its Related Party and the grantee in effect at the time such grantee ceases to be such an employee, director or service provider; (b) any one of the following: dishonesty towards the Company or Related Party, unauthorized disclosure of confidential information, and conduct substantially prejudicial to the business of the Company or Related Party; or, any substantial breach by the Participant of his or her obligations toward Company or a Related Party; and (c) without limiting the foregoing clauses (a) and (b), a conviction (whether following trial, by plea of guilty or failure to contest prosecution) in a criminal proceeding of (i) a misdemeanor involving fraud, false statements or misleading omissions, embezzlement, bribery, forgery or extortion; or (ii) a felony; or (iii) an equivalent charge to those in (i) and (ii) above in jurisdictions which do not use those designations.

8.3 Acceleration in the Event of a Hostile Takeover. Notwithstanding the provisions of Sections 8.1 and 8.2 above, if a "Hostile Takeover", as defined below, shall occur, and unless the applicable Agreement provides otherwise, all of the outstanding options held by or for the benefit of any grantee shall be accelerated and become immediately vested and exercisable.

Each of the following shall be a "**Hostile Takeover**": an occurrence where a person, entity or group that was not an interested party, as defined under the Israeli Securities Law 1968 on the date of the initial public offering of the Company's ordinary shares, becomes a "controlling shareholder," as defined in the Israeli Securities Law 1968, or a "holder," as defined in the Israel Securities Law 1968, of 25% or more of the voting rights in the Company or any merger or consolidation involving the Company, in each case without a resolution by the Board supporting the transaction.

8.4 Liquidation; Merger. Unless otherwise determined by the Board, in the event of: (i) the proposed liquidation or dissolution of the Company; or (ii) a consolidation or merger as described in Section 8.1 (ii) above; all outstanding Awards (including, without limitation, any Awards accelerated pursuant to Section 8.1 above) will terminate and expire immediately upon to the consummation or closing of such proposed action. Without derogating from any other right or authority of the Board hereunder, the Board may, in connection with any proposed liquidation or dissolution, or in connection with any merger or consolidation as aforesaid, determine any other date and time upon which any outstanding Awards will terminate and may also provide for the acceleration and vesting of, and right to exercise, any option which would not otherwise be exercisable.

9. TERM OF AWARDS; EXERCISE

9.1 The term of each Award shall be for such period as the Board shall determine, but not more than ten (10) years from the date of grant thereof or such shorter period as is prescribed in Section 7.7 or 8.3 hereof; provided, however, with respect to Incentive Stock Options, if

an Employee owns or is deemed to own (by reason of the attribution rules of Section 424(d) of the Code) more than ten percent (10%) of the combined voting power of all classes of stock of the Company (or any Related Company) and an Incentive Stock Option is granted to such Employee, the term of such Incentive Stock Option (to the extent required by the Code at the time of grant) shall be no more than five (5) years from the date of grant thereof.

9.2 A grantee who desires that the Trustee exercise an option granted to the Trustee on his or her behalf shall so instruct the Trustee in writing in the form annexed hereto as **Appendix A** or in such other form as shall be approved by the Board from time to time. The notice shall be accompanied by, or specify the arrangements for, payment of the full Option Exercise Price of such Shares as provided in the Agreement. The Company may require as a condition to the exercise of an option that the grantee pay or otherwise make arrangements to the Company's satisfaction, for the payment of the tax and other obligatory payments applicable to him or her (including all sums payable arising out of or in connection with the Company's obligation to deduct tax and other obligatory payments at source) pursuant to applicable law and the provisions of the Plan. The Company may also require that the grantee provide or make such representations and agreements as to grantee's investment intent and such other matters as the Company may deem necessary, advisable or appropriate at such time. Upon receipt of all the requisite documents, approvals and payments from the grantee, including sufficient proof of payment or other arrangement with respect to the payment of any applicable taxes in form satisfactory to the Company and the Trustee, the Trustee shall deliver a notice to the Company in the form annexed hereto as **Appendix B** or in such other form as shall be approved by the Board from time to time, whereupon the Company shall allot the Shares in the name of the Trustee.

9.3 A grantee who desires to exercise an option granted directly to him or her (and not through the Trustee) shall so notify the Company in writing in such form as shall be prescribed by the Board from time to time. As a condition for the exercise of the option, the grantee shall pay or otherwise make arrangements, to the Company's and Trustee's satisfaction, for the payment of the tax and other obligatory payments applicable to him or her (including all sums payable by the Company arising out of its obligation to deduct tax and other obligatory payments at source) pursuant to applicable law and the provisions of the Plan. Upon receipt of all the requisite documents, approvals and payments from the grantee, including sufficient proof of payment or other arrangement with respect to the payment of any applicable taxes in form satisfactory to the Company and the Trustee, the Company shall allot the Shares in the name of the grantee.

9.4 Without limiting the foregoing, the Board may, with the consent of the grantee, from time to time cancel all or any portion of any option then subject to exercise, and the Company's obligation in respect of such option may be discharged by: (i) payment to the grantee or to the Trustee on behalf of the grantee of an amount in cash equal to the excess, if any, of the Fair Market Value of the relevant Shares at the date of such cancellation subject to the portion of the option so canceled over the aggregate Option Exercise Price of such Shares; (ii) the issuance or transfer to the grantee or to the Trustee on behalf of the grantee of Shares of the Company with a Fair Market Value at the date of such transfer equal to any such excess; or (iii) a combination of cash and Shares with a combined value equal to any such excess, all as determined by the Board in its sole discretion.

Without derogating from the above, solely for the purpose of determining the tax liability pursuant to Section 102(b)(3) of the Income Tax Ordinance, if at the date of grant the Company's Shares are listed on any established stock exchange or a national market or

quotation system, the Fair Market Value of an Share at the date of grant shall be determined in accordance with the average value of the Company's Shares during the thirty (30) trading days preceding the date of grant, or in the thirty (30) trading days following the date of registration for trading, as the case may be.

9.5 Exercise of options will not be permitted on the effective date for distribution of bonus Shares, rights offering, distribution of a dividend, capital consolidation, capital split or capital reduction (all of the above will be: "**Effective Date**" and "**Company Event**", respectively).

If the Ex Date of a Company Event precedes the Effective Date of a Company Event, the exercise of options will not be permitted on the Ex Date as mentioned.

Ex Date - the first trading day, in which the securities are traded without the right to any payment under a Company Events.

10. **RESTRICTED SHARES**

10.1 General

Restricted Shares may be granted to a grantee in such form and having such terms and conditions as the Board shall deem appropriate. The provisions of separate Awards of Restricted Shares shall be set forth in separate Restricted Share Agreements ("**Restricted Share Agreements**"), which need not be identical. Subject to the restrictions set forth in Section 10.2 hereof, and except as otherwise set forth in the applicable Restricted Share Agreement, the grantee shall generally have the rights and privileges of a shareholder as to such Restricted Shares, including the right to vote such Restricted Shares. Unless otherwise set forth in a grantee's Restricted Share Agreement, cash dividends and share dividends, if any, with respect to the Restricted Share shall be withheld by the Company for the grantee's account. Except as otherwise determined by the Board, no interest will accrue or be paid on the amount of any cash dividends withheld.

10.2 Vesting and Restrictions on Transfer

Restricted Shares shall vest in such manner, on such date or dates, or upon the achievement of performance or other conditions, in each case as may be determined by the Board and set forth in a Restricted Share Agreement; *provided, however*, that notwithstanding any such vesting dates, the Board may in its sole discretion accelerate the vesting of any Award of Restricted Shares at any time and for any reason. Unless otherwise specifically determined by the Board, the vesting of an Award of Restricted Shares shall occur only while the grantee is employed by or rendering services to the Company or a Related Company, and all vesting shall cease upon the termination of the employment or service of a grantee for any reason. In addition to any other restrictions set forth in a grantee's Restricted Share Agreement, the grantee shall not be permitted to sell, transfer, pledge, or otherwise encumber the Restricted Shares prior to the time the Restricted Shares have vested pursuant to the terms of the Restricted Share Agreement or for such other period as the Board shall determine (the "**Restricted Period**"). Certificates for Shares issued pursuant to Restricted Share Awards shall bear an appropriate legend referring to such restrictions, and any attempt to dispose of any such Shares in contravention of such restrictions shall be null and void and without effect. Such certificates may, if so determined by the Board, be held in escrow by an escrow agent appointed by the Board,

or, if a Restricted Share Award is made pursuant to Section 102, by the Trustee. In determining the Restricted Period of an Award the Board may provide that the foregoing restrictions shall lapse with respect to specified percentages of the awarded Restricted Shares on successive anniversaries of the date of such Award. To the extent required by the Income Tax Ordinance or the Israeli Tax Authority, the Restricted Shares issued pursuant to Section 102 of the Income Tax Ordinance shall be issued to the Trustee in accordance with the provisions of the Income Tax Ordinance and the Restricted Shares shall be held by the Trustee for the benefit of the grantee for such period as may be required by the Income Tax Ordinance.

10.3 Forfeiture

Subject to such exceptions as may be determined by the Board, if the grantee's continuous employment or other service with the Company and/or any Related Company shall terminate for any reason prior to the time that such grantee's Restricted Shares have vested, any such Restricted Shares remaining subject to vesting or restrictions or with respect to which the purchase price has not been paid in full, shall thereupon be forfeited and shall be deemed transferred to, and reacquired by, or cancelled by, as the case may be, the Company and/or a Related Company at no cost to the Company and/or any Related Company, subject to all applicable laws. Upon forfeiture of Restricted Shares, the grantee shall have no further rights with respect to such Restricted Shares.

10.4 Other Share-Based Awards

The Board is authorized, subject to limitations under applicable law, to grant to grantee such other Awards that may be denominated or payable in, valued in whole or in part by reference to, or otherwise based upon, or related to, Shares, as deemed by the Board to be consistent with the purposes of the Plan. The Board may also grant Shares as a bonus (whether or not subject to any vesting requirements or other restrictions on transfer), and may grant other Awards in lieu of obligations of any member of the Company and/or any Related Company to pay cash or deliver other property under the Plan or under other plans or compensatory arrangements, subject to such terms as shall be determined by the Board. The terms and conditions applicable to such Awards shall be determined by the Board and evidenced by Award Agreements, which agreements need not be identical.

11. TAXATION

11.1 General

The grantee shall be liable for all taxes, duties, fines and other payments which may be imposed by the tax authorities (whether in Israel or abroad) and for every obligatory payment of whatever source (including, but not limited to, social security, health tax, etc., as may be applicable) in respect of the Awards (including, without limitation, upon the grant of the Awards, the exercise of the options, or the registration of the Shares in the grantee's name) or dividends or any other benefit in respect thereof and/or for all charges which shall accrue to the grantee, the Company, any Related Company and/or to the Trustee in connection with the Plan, the Awards, or any act or omission by the grantee or the Company in connection therewith or pursuant to any determination by the applicable tax or other authorities, including, without limitation, any such payments required to be made by the Company as the result of any sale by the grantee of Shares which were

designated as made through a trustee pursuant to Section 102 prior to the end of the Required Holding Period. Notwithstanding the foregoing, if the Company elects the "employment income" route for Awards granted through a trustee pursuant to Section 102, the Company or the Related Company, as applicable, shall pay, at its expense, any social security payments payable by the employer with respect to Awards so granted to the extent required as a result of such choice.

11.2 Deduction at Source

The Company (including any Related Company) and/or the Trustee shall have the right to withhold or to require the grantee to pay an amount in cash or to retain or sell without notice, Shares in value sufficient to cover any tax or obligatory payment required by any governmental or administrative authority to be withheld or otherwise deducted and paid with respect to the Awards or the Shares subject thereto (including, without limitation, upon their grant, exercise, issuance or sale or the registration of the Shares in the grantee's name) or with respect to dividends or any other benefits in respect thereof ("**Withholding Tax**"), and to make payment (or to reimburse itself or himself for payment made) to the appropriate tax or other authority of an amount in cash equal to the amount of such Withholding Tax. Notwithstanding the foregoing, the grantee shall be entitled to satisfy the obligation to pay any Withholding Tax, in whole or in part, by providing the Company and/or the Trustee with funds sufficient to enable the Company and/or the Trustee to pay such Withholding Tax.

11.3 Certificate of Authorization of Assessing Officer

The Company (including any Related Company) or the Trustee shall at any time be entitled to apply to the Assessing Officer, and in the case of a grantee abroad, to any foreign tax authority, and to any other governmental or administrative authority for receipt of their certificate of authorization as to the amount of tax or other obligatory payments which the Company or any Related Company or the grantee or the Trustee is to pay to the tax or other authorities resulting from granting the Awards, or regarding any other question with respect to the application of the Plan.

11.4 Security for Payment of Taxes

Without derogating from the above, the Company (including any Related Company) and/or the Trustee shall have the right to require that any grantee provide guarantees or other security to the Company's satisfaction to guarantee the payment of any taxes or other obligatory payments which may be payable as a result of or in connection with the grant of an Award, the exercise thereof, the registration of any Awards in the grantee's name (including any sum payable arising out of or in connection with the Company's obligations to deduct tax and other obligatory payments at source); and, with respect to Awards granted pursuant to Section 102 which were not designated as made through a trustee, if the grantee's employment with the Company or any Related Company is terminated for any reason, the grantee will be obligated to provide the Company with a guarantee or other security to its satisfaction and at its discretion, to cover any tax obligations which may arise thereafter in connection with the disposition of the Shares.

12. **DIVIDENDS**

The Shares issued as a result of the vesting or the exercise of the Awards shall participate equally with the Company's other Shares in every cash dividend that shall be declared and distributed subject to the following provisions:

12.1 A cash dividend shall be distributed only to persons registered in the register of members as shareholders on the record date fixed for the distribution of the dividend.

12.2 A dividend with regard to Shares that are registered in the name of the Trustee shall be paid to the Trustee, subject to any lawful deduction of tax, whether such rate is at the usual rate applicable to a dividend or at a higher rate. The Trustee shall transfer the dividend to the grantees in accordance with instructions that he shall receive from the Company. Alternatively, the Company shall be entitled to pay the dividend directly to the grantee subject to the deduction of the applicable tax.

12.3 Without derogating from the provisions of Sections 11.2 and 12.2 hereof, the Company or the Trustee shall be entitled to set off and deduct at source from any dividend any sum that the grantee owes to the Company (including any Related Company) or the Trustee, whether under the Plan or otherwise, and/or any sum that the grantee owes to the tax or other authorities.

13. **RIGHTS AND/OR BENEFITS ARISING OUT OF THE EMPLOYEE/ EMPLOYER RELATIONSHIP AND THE ABSENCE OF AN OBLIGATION TO EMPLOY**

13.1 No income or gain which shall be credited to or which purports to be credited to the grantee as a result of the Plan, shall in any manner be taken into account in the calculation of the basis of the grantee's entitlements from the Company or any Related Company or in the calculation of any social welfare right or other rights or benefits arising out of the employee/employer relationship. If, pursuant to any law, the Company or any Related Company, shall be obliged for the purposes of calculation of the said items to take into account income or gain actually or theoretically credited to the grantee, the grantee shall indemnify the Company or any Related Company, against any expense caused to it in this regard.

13.2 Nothing in the Plan shall be interpreted as obliging the Company or any Related Company to employ the grantee and nothing in the Plan or any Award granted pursuant thereto shall confer upon any grantee any right to continue in the employment of the Company or any Related Company or restrict the right of the Company or any Related Company to terminate such employment at any time. The grantee shall have no claim whatsoever against the Company or any Related Company as a result of the termination of his or her employment, including, without limitation, any claim that such termination causes any Awards to expire and/or prevents the grantee from exercising the options and/or from receiving or retaining any Shares pursuant to any agreement between him or her and the Company, or results in any loss due to an imposition, or earlier than anticipated imposition, of tax or other liability pursuant to applicable law.

14. **ADJUSTMENTS UPON CHANGES IN CAPITALIZATION**

Upon the occurrence of any of the following described events, a grantee's rights to purchase Shares under the Plan shall be adjusted as hereinafter provided:

14.1 In the event that the Company distributes a **cash dividend**, the effective date for the distribution thereof, will take place after the date of the allocation of the Awards to the Trustee for a grantee, but before the exercise or expiry of the Option Exercise Price shall be decreased in respect of each option by the amount of the dividend per Share. For the avoidance of doubt, under no circumstances will the Option Exercise Price be decreased to a price which is less than the nominal value of an ordinary share of the Company.

14.2 In the event that the Company distributes **bonus Shares**, the effective date for the distribution of which takes place after the date of the allocation of the Awards to the Trustee for the grantee, but before the exercise or vesting or expiry of the Awards, the number of Shares to which the grantee is entitled upon the exercise or upon vesting of the Awards shall increase by the number of the Shares that the grantee would have been entitled to as bonus Shares, had he exercised the options prior to the effective date for the distribution of the bonus Shares. The Option Exercise Price shall not vary as a result of the increase in the number of Shares to which the grantee is entitled in the wake of the distribution of bonus Shares.

14.3 If rights to acquire any securities whatsoever are offered to Company shareholders by way of **rights**, the Company shall act with a view that the number of Shares that each grantee is entitled to upon the exercise or vesting of the Awards, as applicable, will be adjusted by multiplying the relevant number of Shares by the Benefit Ratio.

Benefit Ratio - the closing price of the stock exchange on the last trading day before the Ex Date divided by the base price of the ex-rights stock.

14.4 In any event of **division or consolidation** of the Company's share capital, or any other corporate capitalization event of a significantly similar nature, the Company shall effect such changes or adjustments as are required to prevent dilution or increase in a grantee's rights, pursuant to the Plan with respect to the number and class of the Shares in relation to the Awards not yet vested in accordance with their terms or exercised by the grantee and/or the Option Exercise Price of each option.

14.5 In any event of a **merger**, spin-off and/or any other structural change, Awards which have been granted under this Plan, shall be replaced by, or converted to, an alternative Award in the Company after such structural change, all at the absolute discretion of the Company's Board.

14.6 Notwithstanding anything herein to the contrary, no adjustment shall be made or authorized to the extent that such adjustment would cause the Plan or any option to violate Section 422 of the Code or Section 409A of the Code, and to the extent any adjustments are made, such adjustments shall be made in accordance with the requirements of Section 422 of the Code or Section 409A of the Code, and the rules of any securities exchange, stock market, or stock quotation system to which the Company is subject, as applicable.

15. TERM, TERMINATION AND AMENDMENT

Unless the Plan shall theretofore have been terminated as hereinafter provided, the Plan shall terminate on, and no Award shall be granted after, the tenth anniversary of the date the Plan is adopted by the Board. The Board may at any time terminate, modify or amend the Plan in such respects as it shall deem advisable. Awards granted prior to termination of the Plan may, subject to

the terms of the Plan and any Agreement or Restricted Share Agreement, be exercised thereafter. No amendment or modification of the Plan may, without the consent of the grantee to whom any Award shall theretofore have been granted, adversely affect the rights of such grantee under such Award.

16. AWARD MODIFICATIONS

Subject to the terms, conditions and limitations of the Plan, the Board at any time and from time to time in its discretion: (i) may select (by price, expiration or other relevant term or otherwise) one or more outstanding Awards granted under the Plan; (ii) may modify, extend or renew those Awards; (iii) may authorize the Company to accept the surrender of outstanding Awards and grant new or replacement Awards pursuant to the Plan in substitution therefor; and (iv) may provide that such modified, extended, renewed or substituted Awards have one or more of the following (in any combination) (A) a lower exercise price or similar component than the surrendered Award or Awards, (B) a higher number of Shares covered by such Award than the number of Shares covered by the surrendered Award or Awards, (C) a longer term than the surrendered Award or Awards, (D) more rapid vesting and exercise ability than the surrendered Award or Awards, (E) a different market or intrinsic value than the surrendered Award or Awards, and (F) other modifications and additional provisions that are authorized by the Plan and more favorable to the grantee than the surrendered Award or Awards. Notwithstanding the foregoing, however: (1) if the exercise price or similar component of the original Award was originally set at the Fair Market Value or a specified fraction or multiple thereof, such exercise price or similar component shall not be lowered in any such modification, extension, renewal or substitution to an amount that is less than the full Fair Market Value or such specified fraction or multiple thereof, as applicable, on the date of such modification, extension, renewal or substitution; and (2) no modification of an Award granted under this Plan shall adversely affect the rights or obligations of a grantee under such Award without such grantee's consent.

17. **EFFECTIVENESS OF THE PLAN; APPROVALS**

The Plan shall become effective as of the date determined by the Board. Notwithstanding the foregoing and Sections 3 and 15 above, in the event that approval of the Plan or any modification or amendment thereto by the shareholders of the Company is required under applicable law or pursuant to applicable stock exchange rules or regulations, such approval shall, to the extent possible, be obtained within the time required under the applicable law, rule or regulation. If such shareholder approval is required in connection with the application of specified tax treatments, the Company shall make reasonable efforts to obtain such approval within the required time.

18. **RELEASE OF THE TRUSTEE AND THE ATTORNEY FROM LIABILITY**

In no event shall the Trustee or the Attorney be liable to any grantee under the Plan, or to a purchaser of Shares from any grantee with respect to any act which has been or will be carried out in relation to the Plan, its execution and any matter connected thereto or arising therefrom. The grantee will be required to covenant upon signing the Agreement that he or she will not make any claim against the Trustee or the Attorney in any manner whatsoever and on any ground whatsoever and that he or she will expressly agree that if the Trustee or the Attorney are sued by them, then the Trustee or the Attorney shall be entitled by virtue of this Section alone to apply to the court for dismissal of the action against them with costs.

19. **GOVERNING LAWS**

The Plan and all instruments issued thereunder shall be governed by and construed in accordance with the laws of the State of Israel, subject to the provisions of the Code with respect to Incentive Stock Options and, in the event of any ambiguity or conflict, the provisions hereof shall be so construed and applied as to give effect to the intention that any Incentive Stock Option granted will qualify as such under Section 422 of the Code.

* * *

RedHill Biopharma Ltd.
Appendix A
to
RedHill Biopharma Ltd. Amended and Restated Award Plan (2010)
(Section 9.2)

NOTICE OF EXERCISE

Date: _____

To: Meitav Dash Trusts Ltd. (the "**Trustee**"), By Fax: 972-3-6960255 or benefits@altshul.co.il

To: RedHill Biopharma Ltd. ("**RedHill**"), Fax: 972-3-5413144 or Email: einav@redhillbio.com

Dear Sir/Madam:

Re: **Notice of Exercise**

I hereby wish to inform you that it is my desire to exercise _____ options ("**Options**") out of the _____ options which were granted on my name on _____ [Date] under the RedHill Biopharma Ltd. Award Plan (2010), as amended ("**Plan**"), and tenders herewith payment of the purchase price for such shares in full.

The exercise price of said Options is USD _____ per share, all in accordance with the Plan and the Israeli Securities Law of 1968 or any state securities laws.

The total amount for the exercise of the Options of USD _____ was paid to RedHill by me on the date of _____. I am aware that the exercise of the Options will be done only after RedHill will transfer to you written confirmation that the exercise amount was paid in full.

I am aware that all the shares will be allotted to you, registered in your name and that you will hold all the share certificates representing such shares. Likewise, I am aware of and agree to all the other provisions of the Plan and applicable laws.

Yours sincerely,

Signature: _____
Name: _____

The receipt of this form by the Trustee must be verified by phone (No. 972-3-7903444).

.RedHill Biopharma Ltd

Appendix B
to
(RedHill Biopharma Ltd. Amended and Restated Award Plan (2010
(Section 9.2)

NOTICE OF EXERCISE

Date: _____

To: RedHill Biopharma Ltd.

Dear Sirs:

Re: **Notice of Exercise**

Please be advised that on the date of _____ we received instruction from _____ ("the Grantee") to exercise _____ options ("**Options**") out of the _____ options which were granted in his/her name on _____ [Date] under the RedHill Biopharma Ltd. Award Plan (2010), as amended ("**Plan**").

The exercise price of said Options is USD _____ per share, all in accordance with the Plan and the Israeli Securities Law of 1968 or any state securities laws.

The total amount for the exercise of the Options of USD _____ should have been paid to you in full by the Grantee. Upon reception of a written confirmation from you that you received this amount in full, we will exercise the Options for shares and register these shares under our name.

Attached to this notice is the exercise notice sent to us by the Grantee.

Yours sincerely,

Meitav Dash Trusts Ltd.

Signature: _____
Name: _____

Exhibit 4.11

RedHill Biopharma Ltd.

(The "Company")

Compensation Policy

(the "Policy" or "Compensation Policy")

As last amended by the Company's Shareholders on July 26, 2021

1. Definitions

"Board of Directors" or "Board"	- The Company's board of directors;
"Committee" or "Compensation Committee"	- The Company's compensation committee;
"Company"	- RedHill Biopharma Ltd.;
"Companies Law"	- The Companies Law, 1999, Israel;
"Securities Law"	- The Securities Law, 1968, Israel;
"Retirement Bonus"	- Bonus, payment, compensation or any other benefit awarded to an officer with regard to conclusion of their office with the Company;
"Officer"	- As defined in the Companies Law;
"Stock Option Plan"	- Amended and Restated Award Plan (2010), as it may be amended from time to time, or such other equity incentive plan, including an employee stock purchase plan, adopted by the Company from time to time;
"Base Salary"	- A fixed amount paid by the Company to its Officers in return for work performed. Base salary does not include benefits, bonuses or any other potential compensation;
"Cost"	- Cost to the employing entity.

2. Overview

The principles of the Compensation Policy were set forth in accordance with the requirements of the Companies Law and after discussions by the Compensation Committee and the Board. Policy principles were designed to grant proper, fair and well-considered compensation to Officers, in alignment with the Company's long-term best interests and organizational strategy. Part of the rationale is that the Policy should encourage a sense of identification with the Company and its objectives on the part of its Officers. An increase in Officer satisfaction and motivation should retain the employment of high-quality Officers in the Company's service over the long term.

The Compensation Policy considers, *inter alia*, the Company's risk management parameters, size and nature of its operations and, with regard to terms of office and employment which include variable components, the Officer's long-term contribution to achieving the Company's objectives and to maximizing shareholders value, taking into account the scope and reach of the Officer's role.

The Compensation Policy was prepared with due consideration to the nature of the Company's operations in the biopharmaceutical sector, territories where the Company operates, market capitalization on the applicable stock exchange or trading platforms on which the Company's ordinary shares and American Depository Shares ("ADS") are then listed or traded, as well as other criteria.

The compensation principles, targets and benchmarks are derived, *inter alia*, form the Company's annual work plan and from long-term plans as determined by the Board of Directors from time to time.

In the process of drafting this Policy, the Board and the Compensation Committee have examined the ratio between employer cost (as defined in the Companies Law) associated with the engagement of the Officer and the average and median employer cost associated with the engagement of the other employees of the Company (the "**Ratio**"). The Compensation Committee and Board believe that the current Ratio does not adversely impact the work environment in the Company.

Compensation Policy components will include each of the following:

a. Base Salary;

b. Benefits;

c. Cash bonuses;

d. Equity based compensation;

e. Retirement and termination of service arrangements; and

f. Exemption, Indemnification and Insurance.

While the Company's employment agreements and/or consulting agreements may be in NIS or in USD, the Company's compensation costs (including salaries, benefits and consulting) are reported in the Company's financial statements in USD. Thus, all compensation components are presented in this policy in USD.

The language of this Compensation Policy uses the male pronoun only as a measure of comfort. This Policy applies to both male and female Officers.

This Policy aims to balance the mix of "Fixed Component" (comprised of Base Salary and benefits) and "Variable Component" (comprised of cash bonuses and equity-based compensation) in order to, among other things, appropriately incentivize Officers to meet the Company's short and long term goals, while taking into consideration the Company's need to manage a variety of business risks.

The total Variable Component of each Officer shall not exceed 80% of the total compensation package of such Officer on an annual basis. The Compensation Committee and Board believe that such ratio expresses the appropriate compensation mix in the event that all performance objectives are achieved and assumes that all compensation elements are granted with respect to a given year.

3. Officers' areas of responsibility, education and experience

The compensation package to the Officers is individually determined by the Compensation Committee and the Board (unless other approvals are required under any applicable law) according to the educational background, prior vocational experience, qualifications, role, business responsibilities, past performance and previous compensation arrangements of such Officer.

4. Base Salary and Benefits

4.1. Position: Chairman of the Board of Directors (the "Chairman")

4.1.1. The annual Base Salary of the Chairman, consisting of a fixed annual payment and additional fixed payment per meeting, shall not exceed two times the annual Base Salary of other Board members. If the Chairman is also an Officer, no additional compensation will be payable to the Chairman for his role as Chairman.

4.1.2. The Chairman will be entitled to reimbursement of reasonable expenses incurred in the course of discharging his office, including expenses with respect to attending meetings, travel and entertainment expenses, against provision of receipts. The policy for overseas travel expense reimbursement will be the same as for the Company CEO.

4.2. Position: Company CEO

4.2.1. The annual Base Salary for the Company CEO shall be up to USD 750,000[1] for a full time position. Such amount may be linked to increases in the Israeli Consumer Price Index or to increases in the representative rate of exchange of the US dollar, as the case may be.

4.2.2. The Company CEO will be entitled to reimbursement of reasonable per diem expenses incurred in the course of discharging his office, including expenses with respect to attending meetings, travel and entertainment expenses, against provision of receipts. The Company may pay the CEO's expenses by credit card. Expense reimbursement for overseas travel will be in conformity with Company's policy.

The following benefits will be granted to the CEO in order, among other things, to comply with legal requirements:

- Vacation days in accordance with market practice and applicable law, including redemption thereof;
- Sick days in accordance with market practice and applicable law;
- Convalescence pay according to applicable law;

[1] In accordance with the USD-NIS representative rate of exchange of the Bank of Israel as of the date of approval of the Policy by the Company shareholders

- Monthly remuneration for a study fund with reference to the Company's practice and common market practice;
- Contribution by the Company on behalf of the Officer to an insurance policy or a pension fund, as allowed by applicable law and with reference to the Company's policies and procedures and common market practice; and
- Contribution by the Company on behalf of the Officer towards work disability insurance, as allowed by applicable law and with reference to the Company's policies and procedures and common market practice.

The Company may offer additional benefits to the CEO, including but not limited to: communication, company car and travel benefits, insurances, other benefits (such as newspaper subscriptions, academic and professional studies), etc., including their gross up.

4.3. Position: Officers (other than Board member or CEO)

4.3.1. The annual Base Salary for each Officer (other than a Board member, in his capacity as a Board member only, or the CEO) shall not exceed 90% of the annual Base Salary for the CEO.

4.3.2. In addition, each Officer (other than a Board member, in his capacity as a Board member only, or the CEO) will be entitled to reimbursement of reasonable per diem expenses incurred in the course of discharging his office, including expenses with respect to attending meetings, travel and entertainment expenses, against provision of receipts. The Company may pay the Officer's expenses by credit card. Expense reimbursement for overseas travel will be in conformity with Company policy.

The following benefits may be granted to Officers in order, among other things, to comply with legal requirements:

- Vacation days in accordance with market practice and applicable law, including redemption thereof;
- Sick days in accordance with market practice and applicable law;
- Convalescence pay according to applicable law;

- Monthly remuneration for a study fund, as allowed by applicable law and with reference to the Company's practice and common market practice;
- Contribution by the Company on behalf of the Officer to an insurance policy or a pension fund, as allowed by applicable law and with reference to the Company's policies and procedures and common market practice; and
- Contribution by the Company on behalf of the Officer towards work disability insurance, as allowed by applicable law and with reference to the Company's policies and procedures and common market practice.

The Company may offer additional benefits to the Officers, including but not limited to: communication, company car and travel benefits, insurances, other benefits (such as newspaper subscriptions, academic and professional studies), etc., including their gross up.

4.4. Position: Board member

4.4.1. The following benefits may be provided as compensation to Redhill's Board members:

4.4.1.1. All Redhill's Board members, excluding the chairman of the Board may be entitled to an annual cash fee retainer of up to USD 50,000, committee members may be entitled to an additional annual cash fee retainer of up to USD 15,000, and committee chairpersons may be entitled to an additional annual cash fee retainer of up to USD 20,000 (not to be paid both as committee member and chairperson).

4.4.1.2. The fair market value of equity-based compensation awarded to each non-management director in a given year, as calculated at grant date, shall not exceed 400% of the annual cash fee retainer of such director, as the case may be.

4.4.1.3. To the extent the Company has external directors, the compensation of such directors, if any, shall be in accordance with the Companies Regulations (Rules Regarding the Compensation and Expenses of an External Director), 5760-

2000, including the relative compensation provisions in such regulations as determined by the Company, as amended by the Companies Regulations (Relief for Public Companies Traded in Stock Exchange Outside of Israel), 5760-2000, as such regulations may be amended from time to time.

4.4.1.4. It is hereby clarified that the compensation (and limitations) stated under Section 4.4.1. will not apply to directors who serve as Officers.

4.4.2. Board members will be entitled to reimbursement of reasonable expenses incurred in the course of their duty, including expenses with respect to attending meetings, travel and entertainment expenses, against provision of receipts. Expense reimbursement for overseas travel will be in accordance with Company policies.

4.5. According to section 1B3 to the Companies Regulations (Relief in Transactions With Related Parties), 2000, non-material changes in the terms of employment of an officer who is subject to the CEO, will not require compensation committee approval, as stated in section 272(C) to the Companies Law. For these purposes, a change shall be considered to be non-material so long as the change in the compensation does not exceed 15% of the fixed compensation and has been approved by the CEO, and all within the framework of the Policy.

4.6. Signing Bonus

At the Compensation Committee's and Board's discretion, the Company may grant a signing bonus to a newly recruited Officer. The signing bonus shall not exceed six (6) monthly Base Salaries of such Officer.

4.7. Work overseas

4.7.1. The maximum Base Salary for an Officer who works in the US may exceed the maximum Base Salary for the Officer pursuant to this Policy, by up to 50%.

4.7.2. Conditioned only upon continued employment with the Company, the Company may reimburse an Officer for his actual reasonable relocation expenses when relocating, outside or inside the US, and when returning.

4.7.3. Conditioned only upon continued employment with the Company, the Company may grant a one-time relocation bonus of up to six (6) monthly Base Salaries to an Officer, when relocating, outside or inside the US.

5. Cash Bonuses

5.1. Annual bonus

The Company may award an annual bonus to an Officer based on the following guidelines:

5.1.1. The payment of annual bonuses for any particular fiscal year shall be subject to the satisfaction (in addition to the satisfaction of the applicable objectives set forth below in Section 5.1.2 below) of one or more of the following criteria:

5.1.1.1. For the Company to recognize minimum revenues of US $80 million in the relevant year;

5.1.1.2. For the Company to reduce its negative cash from operations to less than $25 million per annum;

5.1.1.3. A market cap of at least USD 300 million;

5.1.1.4. Increase in the share price of 15% or more in the relevant fiscal year;

5.1.1.5. A significant positive event in the Company's business, affecting the Company's overall positioning and prospect in the medium or the long term.

5.1.2. The annual bonus to the Chairman and the CEO will be based on measurable criteria. The measurable criteria and their relative weight shall be determined by the Compensation Committee and the Board in respect of each calendar year. These measurable criteria may include, inter alia,

objectives relating to the development of clinical trials, significant progress of pipeline products, operational and financial targets achieved, significant business development progress and any additional significant objectives determined by the Board.

5.1.3. In addition, the Company may grant the CEO a bonus of up to three (3) monthly Base Salaries or up to 25% of the total variable compensation, at the sole discretion of the Compensation Committee and Board, based on the CEO's contribution to the Company.

5.1.4. The Company may also grant, subject to the approval of the Compensation Committee and the Board, an annual bonus to its Officers (other than the CEO) for their contribution to the Company. Such grants may be based in whole or in part on discretion of the Compensation Committee and the Board, provided that they do not exceed the ceiling specified in Section 5.4 below.

5.2. Special Annual Bonus

In addition to the Annual Bonus, each Officer of the Company may be awarded once a year a special annual bonus (the "**Special Annual Bonus**") regardless of a specified target and regardless of a bonus plan. Such Special Annual Bonus shall be approved by the Compensation Committee and the Board of Directors, which shall consider the CEO's recommendation (based on recognition of special and extraordinary contribution by the Officer in the course of Company business, such as a special effort and achievements related to financing raised, merger, acquisition, sale or license of rights, achievement of major corporate goal in R&D or in commercial operations, business and corporate development or other significant general corporate goal, intellectual property protection of the Company's products, etc.). Such Special Annual Bonus shall not exceed three (3) monthly Base Salaries for each Officer of the Company, except for the CEO as provided in Section 5.1.3 above.

5.3. Bonus calculation upon termination of employment: Should the employment or service of the Officer terminate prior to the end of a fiscal year, the Company may pay the Officer the pro rata share of that fiscal year's bonus, based on the

period such Officer was employed by the Company or has served in the Company.

5.4. Maximum bonus: the combined Annual Bonus and Special Annual Bonus amount shall not exceed 200% of the Officer's annual Base Salary.

5.5. The Company's Compensation Committee and Board of Directors may reduce the bonus awarded to an Officer at their discretion, including under the following circumstances: material deterioration of the Company's position or such material deterioration anticipated by the Board of Directors, deterioration in the state of the economy, deterioration in the performance of the Officer or inappropriate conduct by the Officer.

5.6. Compensation Recovery ("Clawback"):

5.6.1. In the event of an accounting restatement, the Company shall be entitled to recover from its Officers the bonus compensation in the amount in which such bonus exceeded what would have been paid under the financial statements, as restated, provided that a claim is made by the Company prior to the third anniversary of fiscal year end of the restated financial statements.

5.6.2. Notwithstanding the aforesaid, subject to compliance with applicable law, the compensation recovery will not be triggered in the following events:

- The financial restatement is required due to changes in the applicable financial reporting standards; or
- The Compensation Committee has determined that Clawback proceedings in the specific case would be impossible, impractical or not commercially or legally efficient; or
- The amount to be paid under the Clawback proceedings is less than 10% of the relevant bonus received by the Officer.

5.6.3. Nothing in this Section limits the Company's obligation to comply with any "Clawback" or similar provisions regarding disgorging of profits imposed on Officers by virtue of applicable securities laws.

6. Equity-Based Compensation

6.1. The Compensation Committee and the Board shall review from time to time the overall equity-based grant for all Officers. When doing so, the Compensation Committee and the Board shall take into consideration: (1) each Officer's (including Board members) contribution to the Company including expected contribution; and (2) creating an effective long-term incentive to harness and motivate Officers.

6.2. The equity-based compensation offered by the Company may be in the form of share options, restricted shares and/or other equity-based awards, such as RSUs, in accordance with the Stock Option Plan.

6.3. Subject to any applicable law and at the Compensation Committee and the Board's discretion, as applicable, the Company may determine the tax regime under which equity-based compensation may be granted, including a tax regime which will maximize the benefit to the Officers.

6.4. The fair market value of equity-based compensation awarded to each Officer in a given year, as calculated at grant date, shall not exceed 200% of the annual Base Salary of such Officer, as the case may be.

6.5. The exercise price for each option shall be no less than the closing Company share price on Nasdaq on the date of the approval of the award by the Board of Directors (or in the case of grants to Officers who are subject to U.S. taxation and which require shareholder approval, on the date of approval by the shareholders of the Company)

6.6. All other terms of the equity awards shall be in accordance with the Stock Option Plan and other related practices and policies.

6.7. Subject to the terms of the Stock Option Plan, the Compensation Committee and Board of Directors shall not reduce the amount of unexercised options of an Officer, nor will they limit the exercise value of such unexercised options.

7. Retirement and Termination of Service Arrangements

7.1. Severance pay: in the case of termination (other than termination of an Officer for cause), the Officer will be eligible to receive severance pay in full.

7.2. Notice period:

- The Company may give an Officer a notice period of up to twelve (12) months.
- The Company may waive the Officer's services to the Company during the notice period and pay the amount payable in lieu of notice, plus the value of benefits, even in case of immediate termination.
- During the notice period, the Officer would be eligible to receive bonuses with respect to this period and would also continue to accrue vesting of options awarded.

7.3. Non-compete bonus: the Company may grant an Officer a bonus upon termination of employment in return for a commitment by the Officer not to compete with Company business. The extent of the non-compete commitment would be determined by the Company's Compensation Committee and Board of Directors. Such bonus shall be calculated according to a key of up to two (2) monthly Base Salaries for each three (3) months of non-compete period and shall not exceed a total of twelve (12) monthly Base Salaries.

7.4. Retirement bonus: the Company may grant an Officer a retirement bonus upon termination of employment. The retirement bonus shall not exceed twelve (12) monthly Base Salaries for Officers that engaged with the Company for over three (3) years and six (6) monthly Base Salaries for an Officer that was engaged with the Company for less than three (3) years**,** except in the case of termination of employment upon "change of control" in which case the limitations of Section 7.5 shall apply.

Such retirement bonus, if applicable, shall be awarded based on the Officer's tenure, the Company's achievements during the relevant period and the Officer's contribution to such achievements, and the circumstances of such Officer's retirement from the Company.

7.5. Creation/Change of Control: the Company may grant an Officers a bonus upon a "change of control" (as defined in a plan approved by the Compensation Committee and the Board) upon such conditions determined by the Compensation Committee and the Board. The bonus shall not exceed twelve

(12) monthly Base Salaries for each Officer who served the Company for over three (3) years and six (6) monthly Base Salaries for each Officer who served in the Company for less than three (3) years.

The Company may also grant the CEO a bonus upon a "change of control" upon such conditions determined by the Compensation Committee and the Board. The bonus to the CEO shall not exceed eighteen (18) monthly Base Salaries.

8. Exemption, Indemnification and Insurance

8.1. Board member and Officer liability insurance (claims made): the Company may obtain a liability insurance policy for Board members and Officers, which would apply to Officers of the Company and/or of its subsidiaries, as they may be, from time to time, subject to the following terms and conditions: (a) the total insurance coverage under the insurance policy shall not exceed US $100 million; and (b) the purchase of such policy shall be approved by the Compensation Committee (and, if required by law, by the Board) which shall determine that such policy reflects the current market conditions, and it shall not materially affect the Company's profitability, assets or liabilities.

8.2. Board member and Officer's liability insurance (run-off): should the Company sell its operations (in whole or in part) and/or in case of merger, spin-off or any other significant business combination involving the Company and/or part or all of its assets, the Company may obtain a Board member and Officer's liability insurance policy (run-off) for Board members and Officers in office with regard to the relevant operations, subject to the following terms and conditions: (a) the insurance term shall not exceed 7 years; (b) the coverage amount shall not exceed US $100 million; and (c) the purchase of such policy shall be approved by the Compensation Committee (and, if required by law, by the Board) which shall determine that such policy reflects the current market conditions, and it shall not materially affect the Company's profitability, assets or liabilities.

8.3. Waiver of liability: the Company may, subject to statutory provisions, waive the Officer's liability for any damage incurred by the Company, directly or indirectly, due to any breach of the Officer's due care duty towards the Company and/or any affiliated entity by his action and pursuant to his position as an Officer.

8.4. Advance indemnification: the Company may provide a commitment to indemnify in advance any Officer of the Company in the course of his position as Officer of the Company and its subsidiaries thereof, all subject to the letter of indemnification, as approved by the Company's shareholders from time to time and in accordance with the Company's Articles of Association.

8.5. Retroactive indemnification: the Company may provide retroactive indemnification to any Officer to the extent allowed by the Companies Law.

9. Engagement as a contractor or through a management company

The Company may engage an Officer as an independent contractor rather than as a salaried employee. In such a case, the maximum cost of employment would be calculated based on the maximum cost for a salaried employee in a similar position, and guidelines of the Compensation Policy would apply to such an officer, *mutatis mutandis*.

10. Miscellaneous

10.1. The identity of the Officers is subject to the discretion of the Company's CEO. Changes may occur in the identity of Officers from year to year, and persons who served as Officers in one year and whose terms of employment or office were subject to this Compensation Policy may not necessarily continue to serve as Officers in subsequent years, and thus, their terms of employment or office would not be subject to this Compensation Policy, and vice versa. Moreover, the Company may revise the terms of employment or office of any Officer at any time, and is under no obligation to apply the same terms of employment or office to any Officer applied to them in previous years.

10.2. This Policy shall not confer any right on Officers to whom this Compensation Policy applies, nor on any other third party, to receive any compensation whatsoever.

10.3. Note, for the sake of clarification, that the content of this policy does not detract from provisions of the Companies Law with regard to the manner of approval of contracting between the Company and any Officer with regard to terms of employment or office, and the provisions of this Policy do not detract from any

mandatory reporting with regard to Officer compensation pursuant to the Securities Law and regulations based there upon.

10.4. For the avoidance of doubt, it is clarified that in case of any amendment made to provisions of the Companies Law and any other relevant rules and regulations in a manner that will facilitate the Company with respect to its action with regard to Officer compensation, the Company may be entitled to follow these provisions even if they contradict the principles of this Policy.

10.5. Any payment made to Officers pursuant to compensation plans, in addition to the fixed compensation component, is not and shall not be deemed part of the Officer's regular pay for all intents and purposes, and shall not form basis for calculation and/or eligibility and/or accrual of any benefits and will not, notwithstanding the foregoing, be a component included in payment of paid leave, severance pay, contributions to provident funds, etc.

10.6. As part of the approval process of each annual plan, with its various components, changes to Company objectives, market conditions, the Company's position, etc. would be reviewed annually by the Board of Directors. Consequently, the targets, benchmarks and compensation targets for each plan would be reviewed annually, and their actual application would be subject to change based on decisions made by the Board of Directors from time to time.

10.7. The Board of Directors shall review from time to time the Compensation Policy and the need to revise it in case of any material change in circumstances prevailing upon setting said Policy, or for any other reasons.

10.8. Any change in compensation of an Officer related to his or her fixed component that will change the composition of the compensation without affecting the total employer cost to the Company will not require approval of the compensation committee nor the Board of Directors, if it is approved by the CEO or the CFO of the Company and provided that such changed compensation is otherwise in accordance with the terms of the Compensation Policy.

* * * * *

Exhibit 4.14

CERTAIN IDENTIFIED INFORMATION MARKED [***] HAS BEEN EXCLUDED FROM THE EXHIBIT BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.

AMENDMENT TO EXCLUSIVE LICENSE AGREEMENT

This Amendment (the "Amendment") is entered into as of December 2, 2021 (the "Amendment Effective Date") by and between Cosmo Technologies Ltd., a company duly incorporated and existing under the laws of Ireland, with registered offices at Riverside II, Sir John Rogerson's Quay, Dublin 2, Ireland **("Cosmo")** and RedHill Biopharma, Inc. a Delaware corporation, having an address at 8045 Arco Corporate Drive, Suite 120, Raleigh, North Carolina 27617 and all Affiliates thereof **("RedHill").** Cosmo and RedHill each may be referred to herein individually as a "Party," or collectively as the "Parties".

RECITALS

WHEREAS, the Parties entered into an exclusive license agreement on October 17,2019 for AEMCOLO (the "Exclusive License Agreement").

WHEREAS, the Parties seek to modify the terms of the Exclusive License Agreement.

NOW, THEREFORE, In consideration of the foregoing and other good and valuable consideration, the receipt and legal sufficiency of which Is hereby acknowledged, the Parties agree to modify the Agreement as set forth below.

AGREEMENT

It is herein agreed that Section 18.2.2 of the Exclusive License Agreement is now entirely replaced with the following new section:

1. 18.2.2 Voluntary Termination. Each Party shall be entitled, in its sole discretion, to terminate this Agreement at any time on [***] written notice to the other Party following the Effective Date. Neither Party will be required to pay the other Party any compensation in respect of such termination. Upon termination of this Agreement, the License granted under this Agreement shall immediately terminate and, except as permitted in Section 18.3.1, RedHill will immediately cease any and all development and other activities regarding the Product.

2. No Other Changes. Except as modified herein by the Amendment, all other terms and conditions set forth in the Exclusive License Agreement will continue in full force and effect.

IN WITNESS WHEREOF, the Parties hereto have caused this Agreement to be executed by their duly authorized representatives as of the Amendment Effective Date.

Cosmo Technologies Ltd.
RedHill Biopharma Inc.

Signature: */s/ [***]*
Name: [***]
Title: [***]

Signature: */s/ Micha Ben Chorin*
Name: Micha Ben Chorin
Title: Director

Signature: */s/ Todd Krzyzaniak*
Name: Todd Krzyzaniak
Title: US Finance

Signature: */s/ Rick Scruggs*
Name: Rick Scruggs
Title: Chief operating officer

Exhibit 4.19

FOURTH AMENDMENT

TO

CREDIT AGREEMENT

THIS FOURTH AMENDMENT (this "Amendment") to the Credit Agreement, dated July 22, 2021 (the "Credit Agreement"), among REDHILL BIOPHARMA INC., a Delaware corporation (the "Borrower"), REDHILL BIOPHARMA LTD., a company incorporated under the laws of the State of Israel, as Guarantor ("Parent"), the Lenders (defined therein), HCR Collateral Management, LLC ("Agent" and together with the Borrower, Parent, the Lenders and Agent, the "Parties"), as Administrative Agent and those additional entities that hereafter become parties hereto in accordance with the terms hereof by executing a Joinder Agreement, is executed as of January 28, 2021 (the "Effective Date"). Capitalized terms not otherwise defined herein have the same meaning as in the Credit Agreement (and all rules governing terminology or interpretation set forth in the Credit Agreement are hereby incorporated by reference).

WHEREAS, the Borrower wishes to amend the Credit Agreement to modify the provisions requiring a certain number of salespeople on and after a certain date pursuant to Section 7.21(b) (the "Salespeople Requirement").and

NOW, THEREFORE, in accordance with and pursuant to Section 11.01 of the Credit Agreement, the Lenders and the Borrower hereby agree as follows:

1. ***Amendments***

(a) Section 7.21(b) of the Credit Agreement shall be deleted in its entirety and the following shall be inserted in place thereof:

> "The Loan Parties shall Exploit or engage in the Exploitation of (i) Talicia and the Talicia Assets in accordance with the plan provided to the Administrative Agent prior to the Closing Date and attached hereto as Exhibit I; provided, that, for the avoidance of doubt, the number of sales representatives exclusively responsible for Talicia, the Acquired Assets and Aemcolo being below (a) 76 sales representatives on or after the Effective Date through September 30, 2020, (b) 100 sales representatives from and after September 30, 2020, and (c) 119 sales representatives from and after January 1, 2022, in each case for 30 consecutive days shall be a failure to perform and observe this Section 7.21, and (ii) the Acquired Assets in accordance with the plan to be provided to the Administrative Agent prior to the Tranche B Funding Date pursuant to Section 5.03(a)(ii)."

2. ***Waiver.*** The Agent and each Lender hereby waive any Default or Event of Default which resulted, or would have resulted, from a failure to meet the Salesperson Requirement, provided, that such waiver shall be retroactive, and from and after the date hereof, the Borrower shall be required to comply with the terms and conditions of the Credit Agreement as amended by this Amendment.

3. ***Representations and Warranties.*** The Borrower hereby represents and warrants to the Agent and each Lender (before and after giving effect to this Amendment) that:

(a) The Borrower has the corporate power and authority, and the legal right, to execute, deliver and perform this Amendment and to obtain extensions of credit under the Credit Agreement as amended by this Amendment (the "Amended Credit Agreement");

(b) The Borrower has taken all necessary corporate action to authorize the execution, delivery and performance of this Amendment;

(c) No consent or authorization of, filing with, notice to or other act by, or in respect of, any Governmental Authority or any other Person is required in connection with this Amendment, the extensions of credit under the Amended Credit Agreement or the execution, delivery, performance, validity or enforceability of this Amendment, or the performance, validity or enforceability of the Amended Credit Agreement, except consents, authorizations, filings and notices which have been obtained or made and are in full force and effect;

(d) This Amendment has been duly executed and delivered on behalf of the Borrower. This Amendment and the Amended Credit Agreement constitute the legal, valid and binding obligations of the Borrower and the other Loan Parties party thereto and are enforceable against the Borrower and the other Loan Parties party thereto in accordance with their terms except as enforceability may be limited by applicable bankruptcy, insolvency, reorganization, moratorium or similar laws affecting the enforcement of creditors' rights generally and by general equitable principles (whether enforcement is sought by proceedings in equity or at law);

(e) Each of the representations and warranties made by the Borrower herein or in or pursuant to the Loan Documents is true and correct in all material respects on and as of the Effective Date as if made on and as of such date (except that any representation or warranty which by its terms is made as of an earlier date shall be true and correct in all material respects as of such earlier date);

(f) No Default or Event of Default has occurred and is continuing, or will result from this Amendment or any extension of credit under the Amended Credit Agreement.

4. ***Miscellaneous.***

(a) **Loan Documents Otherwise Not Affected; Reaffirmation**. Except as expressly amended pursuant hereto or referenced herein, the Credit Agreement and the other Loan

Documents shall remain unchanged and in full force and effect and are hereby ratified and confirmed in all respects. The Lenders' and Agent's execution and delivery of, or acceptance of, this Amendment shall not be deemed to create a course of dealing or otherwise create any express or implied duty by any of them to provide any other or further amendments, consents or waivers in the future. The Borrower and Parent hereby reaffirms the grant of security under the Collateral Documents and hereby reaffirms that such grant of security in the Collateral secures all Obligations under the Credit Agreement, including without limitation any Loans funded on or after the Effective Date, as of the date hereof.

(b) **Release**. In consideration of the agreements of Agent and each Lender contained herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Borrower and Parent, each on behalf of itself and its successors, assigns, and other legal representatives, hereby fully, absolutely, unconditionally and irrevocably releases, remises and forever discharges Agent and each Lender, and its successors and assigns, and its present and former shareholders, affiliates, subsidiaries, divisions, predecessors, directors, officers, attorneys, employees, agents and other representatives (Agent, Lenders and all such other persons being hereinafter referred to collectively as the "Releasees" and individually as a "Releasee"), of and from all demands, actions, causes of action, suits, covenants, controversies, agreements, promises, sums of money, accounts, bills, reckonings, damages and any and all other claims, counterclaims, defenses, rights of set-off, demands and liabilities whatsoever of every name and nature, known or unknown, suspected or unsuspected, both at law and in equity, which Borrower and Parent, or any of their successors, assigns, or other legal representatives may now own, hold, have or claim to have against the Releasees or any of them for, upon, or by reason of any circumstance, action, cause or thing whatsoever which arises at any time on or prior to the day and date of this Amendment, including, without limitation, for or on account of, or in relation to, or in any way in connection with, the Credit Agreement, or any of the other Loan Documents or transactions thereunder or related thereto. Borrower and Parent understand, acknowledge and agree that the release set forth above may be pleaded as a full and complete defense and may be used as a basis for an injunction against any action, suit or other proceeding which may be instituted, prosecuted or attempted in breach of the provisions of such release. Borrower and Parent agree that no fact, event, circumstance, evidence or transaction which could now be asserted or which may hereafter be discovered shall affect in any manner the final, absolute and unconditional nature of the release set forth above.

(c) **No Reliance**. Borrower and Parent hereby acknowledge and confirm to Agent and the Lenders that the Borrower and Parent are executing this Amendment on the basis of their own investigation and for their own reasons without reliance upon any agreement, representation, understanding or communication by or on behalf of any other Person.

(d) **Costs and Expenses**. The Borrower agrees to pay to Agent within ten (10) days of its receipt of an invoice, the reasonable and documented out-of-pocket costs and expenses of Agent and the Lenders party hereto, and the reasonable fees and disbursements of counsel to Agent and the Lenders party hereto (including allocated costs of internal counsel), in connection with the negotiation, preparation, execution and delivery of this Amendment and any other documents to be delivered in connection herewith on the Effective Date or after such date.

(e) **Binding Effect**. This Amendment binds and is for the benefit of the successors and permitted assigns of each party.

(f) **Governing Law**. **THIS AMENDMENT AND ANY CLAIMS, CONTROVERSY, DISPUTE OR CAUSE OF ACTION (WHETHER IN CONTRACT OR TORT OR OTHERWISE) BASED UPON, ARISING OUT OF OR RELATING TO THIS AMENDMENT AND THE TRANSACTIONS CONTEMPLATED HEREBY AND THEREBY SHALL BE GOVERNED BY, AND CONSTRUED IN ACCORDANCE WITH, THE LAW OF THE STATE OF NEW YORK.**

(g) **Complete Agreement; Amendments**. This Amendment and the Loan Documents represent the entire agreement about this subject matter and supersede prior negotiations or agreements with respect to such subject matter. All prior agreements, understandings, representations, warranties, and negotiations between the parties about the subject matter of this Amendment and the Loan Documents merge into this Amendment and the Loan Documents.

(h) **Severability of Provisions.** Each provision of this Amendment is severable from every other provision in determining the enforceability of any provision.

(i) **Counterparts**. This Amendment may be executed in any number of counterparts and by different parties on separate counterparts, each of which, when executed and delivered, is an original, and all taken together, constitute one Amendment. Delivery of an executed counterpart of a signature page of this Amendment by facsimile, portable document format (.pdf) or other electronic transmission will be as effective as delivery of a manually executed counterpart hereof.

(j) **Loan Documents**. This Amendment and the documents related thereto shall constitute Loan Documents.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the parties hereto have executed this Amendment as of the date first above written.

BORROWER:

REDHILL BIOPHARMA INC.

By:	/s/ Dror Ben-Asher	/s/ Micha Ben Chorin
	Name: Dror Ben-Asher	Micha Ben Chorin
	Title: CEO	CFO

GUARANTOR:

REDHILL BIOPHARMA LTD

By:	/s/ Dror Ben-Asher	/s/ Micha Ben Chorin
	Name: Dror Ben-Asher	Micha Ben Chorin
	Title: CEO	CFO

AGENT:

HCR Collateral Management, LLC.

By: /s/ Paul J. Haden
Name: Paul J. Haden
Title: Authorized Signatory

Lenders:

HCR Stafford Fund, L.P.
By: HCR Stafford Fund GP, LLC, its general partner

By: /s/ Paul J. Haden
Name: Paul J. Haden
Title: Authorized Signatory

HCR Stafford Fund, L.P.
By: HCR Stafford Fund GP, LLC, its general partner

By: /s/ Paul J. Haden
Name: Paul J. Haden
Title: Authorized Signatory

HCR Molag Fund, L.P.
By: HCR Molag Fund GP, LLC, its general partner

By: /s/ Paul J. Haden
Name: Paul J. Haden
Title: Authorized Signatory

HCR Overflow Fund, L.P.
By: HCR Overflow Fund GP, LLC, its general partner

By: /s/ Paul J. Haden
Name: Paul J. Haden
Title: Authorized Signatory

HealthCare Royalty Partners IV, L.P.
By: HealthCare Royalty Partners IV, LLC, its general partner

By: /s/ Paul J. Haden
Name: Paul J. Haden
Title: Authorized Signatory

HCR Stafford Fund, L.P.
By: HCR Stafford Fund GP, LLC, its general partner

By: /s/ Paul J. Haden
Name: Paul J. Haden
Title: Authorized Signatory

Exhibit 12.1

CERTIFICATION BY CHIEF EXECUTIVE OFFICER PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Dror Ben-Asher, certify that:

1. I have reviewed this annual report on Form 20-F of RedHill Biopharma Ltd.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

    a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting;

5. The company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

    a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

    b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: March 17, 2022

/s/ Dror Ben-Asher

Dror Ben-Asher
Chief Executive Officer

Exhibit 12.2

CERTIFICATION BY CHIEF FINANCIAL OFFICER PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Micha Ben Chorin certify that:

1. I have reviewed this annual report on Form 20-F of RedHill Biopharma Ltd.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the company and have:

    a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

    b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    c) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

    d) Disclosed in this report any change in the company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting;

5. The company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):

    a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and

    b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: March 17, 2022

/s/ Micha Ben Chorin

Micha Ben Chorin
Chief Financial Officer

Exhibit 13

CERTIFICATION BY CHIEF EXECUTIVE OFFICER AND CHIEF FINANCIAL OFFICER PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of RedHill Biopharma Ltd. (the "Company") on Form 20-F for the period ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company certifies, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that to such officer's knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company

Dated: March 17, 2022

/s/ Dror Ben-Asher
Dror Ben-Asher
Chief Executive Officer

/s/ Micha Ben Chorin
Micha Ben Chorin
Chief Financial Officer

Exhibit 15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form F-3 (file No. 333-258259, file No. 333-254848 and file No. 333-232777) and the Registration Statements on Form S-8 (file No. 333-262099, file No. 333-255710, file No. 333-254692, file No. 333-232776, file No. 333-225122, file No. 333-219441, file No. 333-207654 and file No. 333-188286) of RedHill Biopharma Ltd. of our report dated March 17, 2022 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 20-F.

/s/ Kesselman & Kesselman
Certified Public Accountants (Isr.)
A member firm of PricewaterhouseCoopers International Limited

Tel-Aviv, Israel
March 17, 2022

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