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

FORM 20-F

☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR 12(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**

For the transition period from _____ to _____

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 001-36349

MEDIWOUND LTD.

(Exact name of Registrant as specified in its charter)

Not applicable
(Translation of Registrant's name into English)

ISRAEL
(Jurisdiction of incorporation or organization)

42 Hayarkon Street
Yavne, 8122745 Israel
(Address of principal executive offices)

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MediWound Ltd.
42 Hayarkon Street
Yavne, 8122745 Israel

(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 each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary shares, par value NIS 0.01 per share	**MDWD**	**Nasdaq Global Market**

Securities registered or to be registered pursuant to Section 12(g) of the Act: **None.**

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act: **None.**

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: **As of December 31, 2021, the registrant had 27,272,818 ordinary shares, par value NIS 0.01 per share, outstanding.**

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 of 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 file, a non-accelerated filer, or an emerging growth company. See the definitions of "large accelerated filer," and "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 for accounting the registrant has used to prepare the financing statements included in this filing:

U.S. GAAP ☐ International Financial 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 ☒

MEDIWOUND LTD.

FORM 20-F
ANNUAL REPORT FOR THE FISCAL YEAR ENDED DECEMBER 31, 2021

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INTRODUCTION

In this annual report, the terms “MediWound,” “we,” “us,” “our” and “the company” refer to MediWound Ltd. and its subsidiaries.

This annual report includes other statistical, market and industry data and forecasts which we obtained from publicly available information and independent industry publications and reports that we believe to be reliable sources. These publicly available industry publications and reports generally state that they obtain their information from sources that they believe to be reliable, but they do not guarantee the accuracy or completeness of the information. Although we believe that these sources are reliable, we have not independently verified the information contained in such publications. Certain estimates and forecasts involve uncertainties and risks and are subject to change based on various factors, including those discussed under the headings “Special Note Regarding Forward-Looking Statements” and “ITEM 3.D. Risk Factors” in this annual report.

Throughout this annual report, we refer to various trademarks, service marks and trade names that we use in our business. The “MediWound” design logo, “MediWound,” “NexoBrid,” “EscharEx” and other trademarks or service marks of MediWound Ltd. appearing in this annual report are the property of MediWound Ltd. We have several other trademarks, service marks and pending applications relating to our solutions. Other trademarks and service marks appearing in this annual report are the property of their respective holders.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

In addition to historical facts, this annual report on Form 20-F contains forward-looking statements within the meaning of Section 27A of the U.S. Securities Act of 1933, as amended (the “Securities Act”), Section 21E of the U.S. Securities Exchange Act of 1934, as amended (the “Exchange Act”) and the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. We make forward-looking statements in this annual report that are subject to risks and uncertainties. These forward-looking statements include information about possible or assumed future results of our business, financial condition, results of operations, liquidity, plans and objectives. In some cases, you can identify forward-looking statements by terminology such as “believe,” “may,” “estimate,” “continue,” “anticipate,” “intend,” “should,” “plan,” “expect,” “predict,” “potential,” or the negative of these terms or other similar expressions. The statements we make regarding the following matters are forward-looking by their nature:

- the timing and conduct of our trials of NexoBrid, EscharEx and our pipeline product candidates, including statements regarding the timing, progress and results of current and future preclinical studies and clinical trials, and our research and development programs;
- the clinical utility, potential advantages and timing or likelihood of regulatory filings and approvals of NexoBrid, EscharEx and our pipeline product candidates;
- our plans to develop and commercialize NexoBrid, EscharEx and our pipeline product candidates;
- our estimates regarding expenses, future revenues, capital requirements and the need for additional financing;
- anticipated funding under our contracts with the U.S. Biomedical Advanced Research and Development Authority;
- our expectations regarding future growth, including our ability to develop new products;
- our commercialization, marketing and manufacturing capabilities and strategy and the ability of our marketing team to cover regional burn centers and units;
- our ability to maintain adequate protection of our intellectual property;
- our estimates regarding the market opportunity for NexoBrid, EscharEx and our pipeline product candidates;
- our expectation regarding the duration of our inventory of intermediate drug substance and products;
- the impact of our research and development expenses as we continue developing product candidates; and
- the impact of government laws and regulations.

The preceding list is not intended to be an exhaustive list of all of our forward-looking statements. The forward-looking statements are based on our beliefs, assumptions and expectations of future performance, taking into account the information currently available to us. These statements are only predictions based upon our current expectations and projections about future events. These statements may be found in the sections of this annual report on Form 20-F entitled "ITEM 3.D. Risk Factors," "ITEM 4. Information on the Company," "ITEM 5. Operating and Financial Review and Prospects," "ITEM 10.E. Taxation—United States Federal Income Taxation—Passive Foreign Investment Company Considerations" and elsewhere in this annual report, including the section entitled "ITEM 4.B. Business Overview" and "ITEM 4.B. Business Overview—Our Focus," which contain information obtained from independent industry sources. Actual results could differ materially from those anticipated in these forward-looking statements due to various important factors, including all the risks discussed in "ITEM 3.D. Risk Factors" and information contained in other documents filed with or furnished to the Securities and Exchange Commission.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that future results, levels of activity, performance and events and circumstances reflected in the forward-looking statements will be achieved or will occur. Except as required by law, we undertake no obligation to publicly update any forward-looking statements for any reason after the date of this annual report to conform these statements to actual results or to changes in our expectations.

PART I

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

Our business faces significant risks. You should carefully consider all of the information set forth in this annual report and in our other filings with the United States Securities and Exchange Commission (the "SEC"), including the following risk factors which we face and which are faced by our industry. Our business, financial condition and results of operations could be materially and adversely affected by any of these risks. In that event, the trading price of our ordinary shares would likely decline and you might lose all or part of your investment. This report also contains forward-looking statements that involve risks and uncertainties. Our results could materially differ from those anticipated in these forward-looking statements, as a result of certain important factors including the risks described below and elsewhere in this report and our other SEC filings. See "Special Note Regarding Forward-Looking Statements" on page i.

Risks Related to Development, Clinical Testing and Regulatory Approval

Product development is a lengthy and expensive process, with an uncertain outcome.

We intend to develop and commercialize pipeline product candidates based on our patented enzymatic technology platform for marketing authorization of NexoBrid and EscharEx in the U.S. and other indications. However, before obtaining regulatory approval for the sale of our pipeline product candidates in any jurisdiction, we must conduct, at our own expense, clinical studies to demonstrate that the products are safe and effective.

Preclinical and clinical testing is expensive, is difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more of our clinical trials can occur at any stage of testing. We may experience numerous unforeseen events during, or as a result of, preclinical testing and the clinical trial process. Even if preclinical or clinical trials are successful, we still may be unable to commercialize the product, as success in preclinical trials, clinical trials or previous clinical trials does not ensure that later clinical trials will be successful.

A number of events could delay or prevent our ability to complete necessary clinical trials for our pipeline product candidates, including:

- regulators may not authorize us to conduct a clinical trial within a country or at a prospective trial site or may require us to change the design of a study;
- delays may occur in reaching agreement on acceptable clinical trial terms with regulatory authorities or prospective sites, or obtaining institutional review board or ethics committee approval;
- our preclinical tests or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional trials or to abandon strategic projects;

- the number of patients required for our clinical trials may be larger than we anticipate, enrollment in our clinical trials may be slower or more difficult than we expect, or patients may not participate in necessary follow-up visits to obtain required data, any of which would result in significant delays in our clinical testing process;

- our third-party contractors, such as a research institute, may fail to comply with regulatory requirements or meet their contractual obligations to us;

- we may be forced to suspend or terminate our clinical trials if the participants are being exposed, or are thought to be exposed, to unacceptable health risks or if any participant experiences an unexpected serious adverse event;

- regulators or institutional review boards may require that we hold, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements;

- undetected or concealed fraudulent activity by a clinical researcher, if discovered, could preclude the submission of clinical data prepared by that researcher, lead to the suspension or substantive scientific review of one or more of our marketing applications by regulatory agencies, and result in the recall of any approved product distributed pursuant to data determined to be fraudulent;

- the cost of our clinical trials may be greater than we anticipate;

- an audit of preclinical or clinical studies by regulatory authorities may reveal noncompliance with applicable protocols or regulations, which could lead to disqualification of the results and the need to perform additional studies;

- political unrest and wars, such as the developing conflict between Russia and Ukraine, which could delay or disrupt business activity, and if such political unrest escalates or spills over to or otherwise impacts additional regions, it could also heighten many of the other risk factors described in this Annual Report;

- delays may occur in obtaining our clinical materials; and

- epidemics or pandemics, such as the COVID-19 pandemic that can affect the overall healthcare infrastructure, including the ability to recruit patients, the ability to conduct studies at medical sites and the pace with which governmental agencies, such as the FDA and foreign regulatory authorities, will review and approve regulatory submissions. Additional government-imposed quarantines and requirements to “shelter at home” or other incremental mitigation efforts also may impact our ability to source supplies for our operations or our ability or capacity to manufacture, sell and support the use of NexoBrid, EscharEx and other candidate products in the future.

Moreover, we do not know whether preclinical tests or clinical trials will begin or be completed as planned or will need to be restructured. Significant delays could also shorten the patent protection period during which we may have the exclusive right to commercialize our pipeline product candidates or could allow our competitors to bring products to the market before we do, impairing our ability to commercialize our pipeline product candidates.

We may be unable to successfully obtain approval of NexoBrid for treatment of severe burns in the United States and other markets.

In the short term, we have been relying, for a significant portion of our revenues from sales of products, on sales of NexoBrid in Europe and in other international markets for the treatment of severe burns and procurement of NexoBrid by the U.S. Biomedical Advanced Research and Development Authority (BARDA) for emergency stockpile as part of the U.S. Department of Health and Human Services' (HHS) mission to build national preparedness for public health medical emergencies. However, our continued growth depends, in large part, on our ability to develop and obtain marketing authorization for NexoBrid for treatment of severe burns in additional markets, especially in the United States (from the U.S. Food and Drug Administration (FDA)). We expect that marketing approval from the FDA, if granted, would enable us to receive additional payments, including milestone payments, transfer price payments and royalties, from Vericel Corporation ("Vericel"), our U.S. commercial partner, who is responsible for commercializing NexoBrid in the North America. In September 2020, the FDA accepted for review our Biologics License Application ("BLA"), which was based on acute data, including primary, secondary and safety endpoints, as well as 12-month safety follow-up data derived from our Phase 3 pivotal study. In June 2021, we received a Complete Response letter from the FDA stating that our BLA was not approved. We had a Type A meeting with the FDA in October 2021 to discuss a path forward for resubmission, in which we gained clarity on a path forward for resubmission of the BLA, and we plan to resubmit our BLA for NexoBrid in mid-2022. We cannot predict how long the FDA may take to review and approve NexoBrid following our planned BLA resubmission, or whether any such approval in the United States will ultimately be granted. For example, if the FDA requests additional information as a part of its review of the BLA for NexoBrid, there is no guarantee that FDA will consider our responses to be sufficient or timely to enable FDA approval by any subsequent PDUFA goal date, particularly in light of delays in the FDA's review caused or exacerbated by the COVID-19 pandemic, including delays in conducting required inspections of our manufacturing facilities. Similarly, we cannot predict how long regulatory authorities outside of the United States and Europe may take to provide NexoBrid with marketing authorization in their jurisdictions or whether such authorizations will be granted at all. A number of companies in the pharmaceutical and biotechnology industry have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials. See "—Product development is a lengthy and expensive process, with an uncertain outcome" and "—Development and commercialization of NexoBrid and EscharEx in the United States and our pipeline product candidates worldwide requires successful completion of the regulatory approval process, and may suffer delays or fail." The failure to receive such marketing authorization, especially in the United States, would have a material adverse impact on our business prospects.

Development and commercialization of NexoBrid and EscharEx in the United States and our pipeline product candidates worldwide requires successful completion of the regulatory approval process, and may suffer delays or fail.

In the United States, as well as other jurisdictions, we are required to apply for and receive marketing authorization before we can market our products, as we have already received for NexoBrid in the European Union and other international markets. This process can be time-consuming and complicated and may result in unanticipated delays. To secure marketing authorization, an applicant generally is required to submit an application that includes the data supporting preclinical and clinical safety and efficacy as well as detailed information on the manufacturing and control of the product, proposed labeling and other information. Before marketing authorization is granted, regulatory authorities generally require the inspection of the manufacturing facility or facilities and quality systems (including those of third parties) at which the product candidate is manufactured and tested, to assess compliance with strictly enforced current good manufacturing practices ("cGMP") and similar foreign requirements such as Good Manufacturing Practices ("GMP") in the European Union, as well as potential audits of the non-clinical and clinical trial sites that generated the data cited in the marketing authorization application to assess compliance with requisite good clinical practices ("GCP").

We cannot predict how long the applicable regulatory authority or agency will take to grant marketing authorization or whether any such authorizations will ultimately be granted. Regulatory agencies, including the FDA and the European Medicines Agency (the "EMA"), have substantial discretion in the approval process, and the approval process and the requirements governing clinical trials vary from country to country. The policies of the FDA, the EMA or other regulatory authorities may change or may not be explicit, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of NexoBrid, EscharEx or our pipeline product candidates. For instance, the regulatory landscape related to clinical trials in the European Union ("EU") recently evolved. The EU Clinical Trials Regulation ("CTR") which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application ("CTA") to be submitted in each member state, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR. Additionally, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. A proposal for revision of several legislative instruments related to medicinal products (potentially revising the duration of regulatory exclusivity, eligibility for expedited pathways, etc.) is expected to be adopted by the European Commission by the end of 2022. The proposed revisions, once they are agreed and adopted by the European Parliament and European Council (not expected before the end of 2024) may have a significant impact on the biopharmaceutical industry in the long term. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. If such actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, or if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are unable to maintain regulatory compliance, we may be subject to enforcement action and our business may be negatively impacted.

In addition, any regulatory approval that we will receive may also contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. For example, as part of the EMA regulatory approval process, we agreed to provide further data from a post-marketing Phase 3 clinical trial of NexoBrid. We believe that our U.S. Phase 3 study will also serve to address this post-marketing commitment to EMA. If EMA is not satisfied with the study results, we will need to perform another costly study to provide such data. Once a product is approved, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submission of safety and other post-marketing information and reports, registration and continued compliance with cGMP and similar foreign requirements and GCP for any clinical trials that we conduct post-approval. Although our manufacturing facility is cGMP-certified, we may face difficulties in obtaining regulatory approval for the manufacturing and quality control process of our pipeline product candidates.

Any delays or failures in obtaining regulatory and marketing approval for NexoBrid in the United States, or for our pipeline product candidates worldwide, would adversely affect our business, prospects, financial condition and results of operations.

Changes in funding or disruptions at FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of FDA and foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, FDA's and foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect FDA's and foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at FDA and other agencies such as the EMA, following its relocation to Amsterdam and resulting staff changes, may also slow the time necessary for new drugs and biologics to be reviewed and/or approved by necessary regulatory authorities, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, on March 10, 2020 FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, on July 10, 2020 FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA utilized this risk-based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, on April 15, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites, among other facilities. According to the guidance, the FDA may request such remote interactive evaluations where the FDA determines that remote evaluation would be appropriate based on mission needs and travel limitations. In May 2021, the FDA outlined a detailed plan to move toward a more consistent state of inspectional operations, and in July 2021, the FDA resumed standard inspectional operations of domestic facilities and was continuing to maintain this level of operation as of September 2021. More recently, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID-19 pandemic. Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

NexoBrid, EscharEx, our current pipeline product candidates or future product candidates may cause unanticipated and undesirable side effects or have other properties, which are currently unknown to us.

NexoBrid, EscharEx and all of our current pipeline product candidates rely on our patented enzymatic platform technology, although their specific formulations or mode of applications may vary. Like most pharmaceutical products, our approval labels for NexoBrid in Europe and other international markets list certain side effects. If we or others identify previously unknown problems with NexoBrid, EscharEx or their underlying proteolytic enzymes, including adverse events of unanticipated severity or frequency, problems with our manufacturers or manufacturing processes, or failure to comply with regulatory requirements, the following consequences, among others, may result, including, without limitation:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- harm to our reputation, reduced demand for our products and loss of market acceptance;
- refusal by the applicable regulatory authority to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

Any of these events could prevent us from achieving or maintaining market acceptance of NexoBrid, our pipeline product candidates or future product candidates, which would adversely affect our business, prospects, financial condition and results of operations.

Regulatory approval for NexoBrid, EscharEx and other pipeline product candidates is and may be limited to specific indications and conditions for which clinical safety and efficacy have been demonstrated, and the prescription off-label uses could adversely affect our business.

The marketing approval for NexoBrid in the European Union and other international markets is limited to the treatment of deep partial- and full-thickness burns in adults. In addition, any additional regulatory approval of NexoBrid for severe burns and any regulatory approval we may receive for any of our pipeline product candidates in the future, would be limited to those specific indications for which such pipeline product candidate had been deemed safe and effective by the EMA, the FDA or another regulatory authority and, like the European Commission marketing approval for NexoBrid, would be subject to a renewal examination five years after the extended marketing approval, which will take place during 2022. Additionally, labeling restrictions in EU limit the manner in which a product may be used. For example, NexoBrid's label provides that it may only be used in specialized burns centers or by burn specialists and that it is not to be applied to more than 15% of the patient's total body surface area. If physicians prescribe the medication for unapproved, or "off-label," uses or in a manner that is inconsistent with the manufacturer's labeling, it could produce results such as reduced efficacy or other adverse effects, and the reputation of our products in the marketplace may suffer. In addition, should any of our future products have a significant price difference and if they are used interchangeably, off-label uses may cause a decline in our revenues or potential revenues. Furthermore, while physicians may choose to prescribe treatments for uses that are not described in the product's labeling and for uses that differ from those approved by regulatory authorities, we cannot promote the products for any indications other than those that are specifically approved by the European Commission, the FDA or other regulatory authorities. Regulatory authorities restrict communications by companies on the subject of off-label use. If our promotional activities fail to comply with these regulations or guidelines, we may be subject to enforcement actions by those authorities. In the United States, "off-label promotion" by pharmaceutical companies has resulted in significant litigation under the Federal False Claims Act, violations of which may result in substantial civil penalties and fines as well as exclusion from government health care programs. More generally, failure to follow the rules and guidelines of regulatory agencies relating to promotion and advertising, such as that promotional materials not be false or misleading, can result in refusal to approve a product, the suspension or withdrawal of an approved product from the market, product recalls, fines, disgorgement of money, operating restrictions, injunctions or criminal prosecution**.**

Although we have received orphan drug designation for NexoBrid in the United States and the European Union and other countries, we may be unable to maintain the benefits associated with such designations, including the potential for market exclusivity.

In the U.S., the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Orphan drug designation in the U.S. entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax credits for certain clinical trial costs and user-fee waivers.

Similarly, in the EU, the European Commission grants orphan designation after receiving the opinion of the EMA Committee for Orphan Medicinal Products on an application for orphan designation. A medicinal product may be designated as orphan if its sponsor can establish that (i) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (ii) either (a) such condition affects no more than 5 in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (iii) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the medicinal product will be of significant benefit to those affected by the condition. Orphan designation in the EU entitles a party to a number of incentives, such as protocol assistance and scientific advice specifically for designated orphan medicines, and potential fee reductions depending on the status of the sponsor.

Although NexoBrid has been designated an orphan drug in the United States, EU and South Korea, Mexico, Japan, UK and Switzerland, there is no guarantee that we will obtain approval or orphan drug exclusivity in the United States or other jurisdictions, or maintain such exclusivity in Europe. Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the disease or condition for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA and foreign regulatory authorities from approving another marketing application, granting a marketing authorization, or accepting an application to extend a marketing authorization for the same drug and disease or condition for that time period, except in limited circumstances. The applicable period is seven years in the United States and ten years in the EU. In the EU, the ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for which it received orphan designation, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity, or where the prevalence of the condition has increased above the threshold. Additionally granting of an authorization for another similar orphan medicinal product where another product has market exclusivity can happen at any time: (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant cannot supply enough orphan medicinal product or (iii) where the applicant consents to a second orphan medicinal product application.

While the marketing exclusivity of an orphan drug prevents other sponsors from obtaining approval of a similar drug for the same disease or condition (unless the sponsor demonstrates clinical superiority or a market shortage occurs), it would not prevent other sponsors from obtaining approval of the same compound for other diseases or conditions, or obtaining approval of a different compound for the same indications as the orphan product. In addition, the FDA or the EMA may revisit any orphan drug designation and retains the ability to withdraw the designation at any time.

Orphan designation neither shortens the development time or regulatory review time of a product nor gives the product any advantage in the regulatory review or approval process. While we may seek additional orphan designations for applicable indications for our current and any future product candidates, we may never receive such designations. Even if we do receive such designations, there is no guarantee that we will enjoy the benefits of those designations.

We may rely on the Animal Rule in conducting trials, which could be time consuming and expensive.

To obtain FDA approval for our product candidates, we may obtain clinical data from trials in healthy human subjects that demonstrate adequate safety, and efficacy data from adequate and well-controlled animal studies under regulations issued by the FDA in 2002, often referred to as the "Animal Rule." Among other requirements, the animal studies must establish that the drug or biological product is reasonably likely to produce clinical benefits in humans. If we use this approach we may not be able to sufficiently demonstrate this correlation to the satisfaction of the FDA, as these corollaries are difficult to establish and are often unclear. Because the FDA must agree that data derived from animal studies may be extrapolated to establish safety and effectiveness in humans, seeking approval under the Animal Rule may add significant time, complexity and uncertainty to the testing and approval process. The FDA may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies, refuse to approve our product candidates, or place restrictions on our ability to commercialize the products. In addition, products approved under the Animal Rule are subject to additional requirements, including post-marketing study requirements, restrictions imposed on marketing or distribution, or requirements to provide information to patients. Further, regulatory authorities in other countries may not have established an "Animal Rule" equivalent, and, consequently, there can be no assurance that we will be able to make a submission for marketing approval in foreign countries based on such animal data

Risks Related to the COVID-19 Pandemic

The COVID-19 pandemic could adversely impact our business, financial condition and results of operations.

The ongoing COVID-19 pandemic has spread throughout Israel where our headquarters and plant are located and in other areas where we have business operations. The spread of COVID-19 could have a negative impact on the value of the Company and on the ability of the Company to raise capital (privately or publicly), conduct strategic deals, and continue to conduct clinical trials in medical centers, and could cause us to suspend the recruitment of patients in studies that remain open. In addition, it could negatively affect our manufacturing operations and global supply chain. In response to the outbreak, we have taken various measures to date, including cost containment plan, executing a global remote work policy, reduction of work related travel, including for our field-based employees, reduction of all in-person meetings and interactions with the healthcare community until further notice, leveraging virtual tools and digital communication technologies to continue important interactions with our employees, healthcare professionals, patients and other stakeholders, conducting remote site monitoring, transportation reimbursement and arranging additional shipments of investigational product to sites and we have instituted additional practices, including alternating shifts, to help ensure the health and safety of our employees who work on critical tasks in our labs and manufacturing facility, as we continue to deliver medicines for patients. In addition, COVID-19 and its variants have had an adverse impact on and may continue to adversely impact the expected timelines of our clinical studies and contribute to delays in obtaining regulatory approvals and in receiving governmental funding. For example, from March 2020 through May 2020, we temporarily suspended the initiation of additional clinical sites and new patient enrollment in our U.S. EscharEx phase 2 study for the treatment of venous leg ulcers ("VLUs"), which resulted in slower recruitment rate than planned. In January 2021, due to COVID-19 related enrollment delays and potentially future pandemic related implications on the conduct of our clinical studies, we decided to accelerate this study by adjusting its enrollment target to 120 patients, down from the 174 originally planned. In addition, in many instances across the industry the FDA's facility inspection schedule has been affected by COVID-19-related travel restrictions, and the FDA stated that it was unable to conduct inspections of NexoBrid's manufacturing facilities in Israel and Taiwan during the 2021 review cycle due to such restrictions, which are required before the FDA can approve the NexoBrid BLA. Additional government-imposed quarantines and requirements to "shelter at home" or other incremental mitigation efforts also may impact our ability to source our products and products candidates in the future. These existing measures have disrupted, and any future actions may result in further disruption, to our business, and may negatively impact our results of operations and financial position.

Our customers may also be adversely impacted by the prolonged impacts of the COVID-19 pandemic. As a result of the deterioration in economic conditions, our customers and potential customers may elect to decrease their spending or reconsider orders, which would adversely affect our business, operating results and financial condition. For example, in light of the significant impact of the COVID-19 pandemic in the U.S. and related expenditures by the U.S. federal government, we may experience delays in deliveries of the procurement orders under our September 2015 agreement with BARDA and such agreement, as well as our other agreements with BARDA, may be suspended or terminated by BARDA. BARDA may terminate the agreements at any time, at its convenience and without any further funding obligations. In addition, there may be limitations of product transportation that can impact our sales to customers.

Our suppliers, including Challenge Bioproducts Corporation Ltd. ("CBC"), may be adversely impacted by the COVID-19 pandemic. As a result, we may face delays or difficulty sourcing components and drug substances for our products and product candidates, which could negatively affect our business and financial results. Even if we are able to find alternate sources for such components and drug substances, they may cost more, which could adversely impact our profitability and financial condition.

The COVID-19 pandemic has significantly impacted global supply chain and shipments costs along with increasing head count costs. Suppliers have been experiencing and may continue to experience shortages, delayed shipments, surcharges and other supply chain issues caused by or related to the COVID-19 pandemic. COVID-19 restrictions have also led to a shortage of personnel to manufacture, package and ship supplies and consumables, further limiting the available supply. If our suppliers are not able to supply the raw materials needed for our preclinical studies and clinical trials, there may be a material adverse impact on our business and financial condition.

As the magnitude of the impact on global markets from COVID-19 and its variants is difficult to predict, the extent to which the pandemic may negatively affect our clinical and operational activities, operating results and financial condition is uncertain.

Risks Related to Manufacturing

If our manufacturing facility in Yavne, Israel were to suffer a serious accident, or if a force majeure event were to materially affect our ability to operate and produce NexoBrid, EscharEx and our pipeline product candidates, all of our manufacturing capacity could be shut down for an extended period.

We currently rely on a single manufacturing facility in Yavne, Israel, and we expect that all of our revenues in the near future will be derived from products manufactured at this facility. If this facility were to suffer an accident or a force majeure event such as war, missile or terrorist attack, earthquake, major fire or explosion, major equipment failure or power failure lasting beyond the capabilities of our backup generators or similar event, our revenues would be materially adversely affected and any of our clinical trials could be materially delayed. In this situation, our manufacturing capacity could be shut down for an extended period, we could experience a loss of raw materials, work in process or finished goods inventory and our ability to operate our business would be harmed. In addition, in any such event, the reconstruction of our manufacturing facility and storage facilities, and obtaining regulatory approval for the new facilities could be time-consuming. During this period, we would be unable to manufacture NexoBrid or our pipeline product candidates. In addition, we currently have limited inventory of NexoBrid that we can supply to our customers in the event that we are unable to further manufacture NexoBrid.

Moreover, our business 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 currently covers the reinstatement value of direct damages that are caused by terrorist attacks or acts of war, we cannot assure you 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.

We are subject to a number of other manufacturing risks, any of which could substantially increase our costs and limit supply of NexoBrid, EscharEx and our pipeline product candidates.

The process of manufacturing NexoBrid, EscharEx and our pipeline product candidates is complex, highly regulated and subject to the risk of product loss due to contamination, equipment failure or improper installation or operation of equipment, or vendor or operator error. Even minor deviations from normal manufacturing processes or quality requirements for our products could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in NexoBrid or our pipeline product candidates or in the manufacturing facilities in which NexoBrid or our pipeline product candidates are or will be made, such manufacturing facilities may need to be closed to investigate and remedy the contamination.

Aside from the significant COVID-19 impact, we may experience any contaminations, major equipment failures, or other similar manufacturing problems of such magnitude, any adverse developments affecting manufacturing operations for NexoBrid or our pipeline product candidates which may result in additional shipment delays, inventory shortages, lot failures, withdrawals or recalls, or other interruptions in the supply of NexoBrid or our pipeline product candidates. We may also have to take inventory write-offs and incur other charges and expenses for our products that fail to meet specifications, undertake costly remediation efforts, or seek costlier manufacturing alternatives.

Our ability to continue manufacturing and distributing our products depends on our continued adherence to cGMP regulations.

The manufacturing processes for our products are governed by detailed cGMP and similar foreign regulations, both for our marketed products in the EU and product candidates in clinical testing in the U.S., EU and Israel. Failure by our manufacturing and quality operations unit to adhere to established regulations or to meet a specification or procedure set forth in cGMP and similar foreign requirements could require that a product or material be rejected and destroyed. Our adherence to cGMP and similar foreign regulations and the effectiveness of our quality control systems are periodically assessed through inspections of our manufacturing facility by regulatory authorities. Such inspections could result in deficiency citations, which would require us to take action to correct those deficiencies to the satisfaction of the applicable regulatory authorities. If critical deficiencies are noted or if we are unable to prevent recurrences, we may have to recall products or suspend operations until appropriate measures can be implemented. Since cGMP and similar foreign regulations reflect ever-evolving standards, we need to regularly update our manufacturing processes and procedures to comply with cGMP and similar foreign regulations. These changes may cause us to incur additional costs and may adversely impact our profitability. For example, more sensitive testing assays (if and when they become available, or due to the discontinuation of the availability of the disposables currently used in production) may be required, or existing procedures or processes may require revalidation, all of which may be costly and time-consuming and could delay or prevent the manufacturing of NexoBrid or launch of a new product.

We may not be able to expand our production or processing capabilities or satisfy future demand.

We are currently seeking to expand our manufacturing capabilities in order to increase our capacity to manufacture NexoBrid and future product candidates and satisfy near term demand. We cannot guarantee that we will be able to obtain the requisite approvals, including meeting regulatory and quality requirements, or the necessary capital resources for procuring this facility, or if we do, that the facility will satisfy additional growing demand. Conversely, there can be no assurance that even if we obtain a new facility, demand for our products will increase proportionately to the increased production capability. Furthermore, we cannot assure that this or similar projects will be implemented in a timely and cost efficient manner, and that our current production will not be adversely affected by the operational challenges of implementing the expansion project.

We depend on a sole supplier to obtain our intermediate drug substance, bromelain SP, which is necessary for the production of our products.

We currently procure bromelain SP, substance key starting material in the manufacturing of NexoBrid, EscharEx and our pipeline product candidates, from a single supplier, Challenge Bioproducts Corporation Ltd. ("CBC"). CBC's manufacturing facilities are located in the Republic of China and it uses proprietary methods to manufacture bromelain SP. Our supply agreement with CBC has no fixed expiration date and can be voluntarily terminated by us, with at least six months' advance written notice, or by CBC, with at least 24 months' advance written notice. Although we have a contractual right to procure this material from other suppliers, subject to payment of a one-time, non-material licensing fee to CBC, procuring this material from any other source would require time and effort which may interrupt our supply of bromelain SP and may cause an interruption of the supply of NexoBrid, EscharEx and our pipeline product candidates to the marketplace and for future clinical trials or other development purposes. Regulatory authorities could require that we conduct additional studies in support of a new supplier, which could result in significant additional costs or delays. Furthermore, there can be no assurance that we would be able to procure alternative supplies of bromelain SP at all or at comparable quality or competitive prices or upon fair and reasonable contractual terms and conditions. Although we believe that we currently store sufficient inventory of bromelain SP in our warehouse and CBC warehouse to continue full capacity operations for approximately two years, this inventory may prove insufficient, and any interruption or failure to source additional bromelain SP from CBC or other third parties in a timely manner, or at all, would adversely affect our business, prospects, financial condition and results of operations. In addition, if CBC experiences any closures and labor shortages as a result of the COVID-19 pandemic, we may face difficulty sourcing bromelain SP, which could negatively affect our revenues**.**

Risks Related to Commercialization

Our revenue growth is depending initially on our ability to commercialize NexoBrid.

We currently have a marketing approval for a single product, NexoBrid, a concentrate of proteolytic enzymes enriched in bromelain, based on our patented enzymatic platform technology, which has been approved for marketing in the EU as well as the European Economic Area ("EEA") (which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland), U.K., Israel, Argentina, Russia, Ukraine, South Korea, Peru, Chile, Taiwan, United Arab Emirates and Eurasian countries for the treatment of adults with deep partial- and full-thickness burns, which we refer to as severe burns. We are currently relying, for a significant portion of our revenues from sales of products, on sales of NexoBrid in Europe and in other international markets for the treatment of severe burns and procurement of NexoBrid by BARDA. In November 2017, the European Commission re-granted a five-year renewal of our NexoBrid marketing authorization and we plan to file for renewal during 2022. We anticipate that, for at least the next several years, our ability to generate revenues and become profitable will depend on the commercial success of NexoBrid in these markets, BARDA's procurement as well as successful launch in new markets such as U.S. following obtaining marketing approval.

The commercial success of NexoBrid, EscharEx and our pipeline product candidates will depend upon their degree of market acceptance.

NexoBrid, EscharEx and our pipeline product candidates may not gain market acceptance by physicians and their teams, healthcare payors, patients and others in the medical community. Although many physicians in burn centers throughout Europe, the United States and other international markets have used NexoBrid for severe burns as part of our clinical trials or since NexoBrid's commercial launch in Europe, Israel, Argentina, South Korea and Russia, we cannot guarantee that use of NexoBrid will be accepted in the market. We need to successfully integrate NexoBrid into the overall treatment of burns in burn centers. If NexoBrid, EscharEx and our pipeline product candidates do not achieve an adequate level of acceptance, we may not generate revenue and we may not achieve or sustain profitability. The degree of market acceptance of NexoBrid in Europe and in other international countries where we receive marketing approval, and of EscharEx and our pipeline product candidates, will depend on a number of factors, some of which are beyond our control, including:

- the willingness of physicians, burn care teams and hospital administrators to administer our products and the acceptance of our products as part of the medical department routine;
- the consent of hospitals to fund/purchase NexoBrid or obtain third-party coverage or reimbursement for our products;
- the ability to offer NexoBrid, EscharEx and our pipeline product candidates for sale at an attractive value;
- the efficacy and potential advantages of NexoBrid, EscharEx and our pipeline product candidates relative to current standard of care;
- the prevalence and severity of any side effects; and
- the efficacy, potential advantages and timing of introduction to the market of alternative treatments.

Failure to achieve market acceptance for NexoBrid, EscharEx or any of our pipeline product candidates, if and when they are approved for commercial sale, will have a material adverse effect on our business, financial condition and results of operations.

We may be unsuccessful in commercializing our products due to unfavorable pricing regulations or third-party coverage and reimbursement policies.

While we are executing a country-specific market access strategy, which includes pricing and/or reimbursement targets for NexoBrid in most of Europe, we cannot guarantee that we will receive favorable hospital, regional or national funding or pricing and reimbursement. Additionally, we cannot predict the pricing and reimbursement of NexoBrid, EscharEx or our pipeline product candidates. The regulations that govern marketing approvals, pricing and reimbursement for new products vary widely from country to country, among regions within some countries and among some hospitals. In some foreign jurisdictions, including the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In other countries, coverage negotiations must occur at the regional or hospital level in order to be included in the hospital formulary. Pricing negotiations with governmental authorities at the regional or hospital level can take considerable time after the receipt of marketing approval for a product candidate.

As a result, even after obtaining regulatory approval for a product in a particular country, we may be subject to price regulations or denied or limited by reimbursement or formulary inclusion, which may delay or limit our commercial launch of the product and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in NexoBrid, EscharEx or our pipeline product candidates, even after obtaining regulatory approval.

Additionally, we cannot be sure that coverage and reimbursement will be available for NexoBrid, EscharEx or any pipeline product candidate that we commercialize in the future, and, if reimbursement is available, whether the level of reimbursement will be adequate. Coverage and reimbursement may affect the demand for, the price of, or the budget allocated for reimbursement for any product for which we obtain marketing approval. Obtaining coverage and adequate reimbursement for our products may be particularly difficult because of the higher prices often associated with products administered under the supervision of a physician. If coverage and reimbursement are not available or are available only at limited levels, we may not be able to successfully commercialize NexoBrid, EscharEx or any pipeline product candidate that we successfully develop. Eligibility for reimbursement does not guarantee that any product will be paid for in all cases or at a rate that covers our costs. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower cost products that are already reimbursed and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in certain other countries, such as the United States. In the United States, third-party payors often rely on the coverage policies and payment limitations imposed by Medicare and other government payors, in setting their own coverage policies and reimbursement rates. Our inability to promptly obtain coverage and profitable payment rates from hospital budget, government-funded and private payors for NexoBrid, EscharEx or any pipeline product candidate could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval for and, if approved, commercialize our product candidates in the United States and affect the prices at which our products may be sold.

The United States and several other jurisdictions are considering, or have already enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that may affect our ability to sell NexoBrid, EscharEx or any of our pipeline product candidates profitably, if approved. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of hospitals, governments, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the market acceptance or demand for NexoBrid, EscharEx or any of our pipeline product candidates, if approved;

- the ability to set a price that we believe is fair for NexoBrid, EscharEx or any of our pipeline product candidates, if approved;
- our ability to generate revenues and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, or ACA, was signed into law and intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the ACA of importance to our potential product candidates are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers’ Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers’ Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research.

Since its enactment, there have been judicial, executive and congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace from February 15, 2021 through August 15, 2021. The executive order 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.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, will stay in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could negatively impact the market for NexoBrid and our other product candidates, if approved, and, accordingly, our financial operations.

There has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which have resulted in several Congressional inquiries and proposed bills 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. The likelihood of implementation of any of these reform initiatives is uncertain, particularly in light of the new incoming Presidential administration. 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.

We expect that other possible healthcare reform measures may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for drugs. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA or comparable regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We face competition from the existing standard of care, and we are furthermore subject to the risk that potential changes in medical practice and technology, or the development by our competitors of products, treatments or procedures that are similar, more advanced, safer or more effective than ours, will render our product candidates obsolete.

The medical, biotechnology and pharmaceutical industries are intensely competitive and subject to significant technological and practice changes. We may face competition from many different sources with respect to NexoBrid, our pipeline product candidates or any product candidates that we may seek to develop or commercialize in the future. Possible competitors may be medical practitioners, pharmaceutical and wound care companies, academic and medical institutions, governmental agencies and public and private research institutions, among others. Should any competitor's product candidates receive regulatory or marketing approval prior to ours, they may establish a strong market position and be difficult to displace, or may diminish the need for our products.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products, treatments or procedures that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any product that we may develop. In addition, we face competition from the current standard of care for eschar removal in severe burns, which includes surgery, where eschar removal can occur by tangential excision, dermabrasion or hydro jet, and non-surgical alternatives, such as topical medications applied to the eschar to facilitate the natural healing process. In chronic and other hard-to-heal wounds, we expect to face competition from current standard of care for debridement via sharp debridement or from the current non-surgical standard of care, either enzymatic debridement, primarily Smith & Nephew Plc's Santyl, a collagenase-based product indicated for debriding chronic dermal ulcers and severely burned areas, or autolytic debridement.

Many of our current or future competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we may have. Mergers and acquisitions in the pharmaceutical and biotechnology industries or wound care markets may result in even more resources being concentrated among a smaller number of our competitors. For example, Healthpoint Biotherapeutics, which marketed Santyl, was acquired by Smith & Nephew Plc in 2012. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs

Risks Related to Our Financial Position and Need for Additional Capital

We are dependent on our contract with BARDA to fund our development activities for NexoBrid in the United States and to procure from us NexoBrid (and to thereby provide us with revenues). If we do not continue to receive funding under this contract, we may need to obtain alternative sources of funding. In addition, if BARDA will suspend or terminate its procurement obligation of NexoBrid it will adversely impact our future revenues.

We have a contract with BARDA, valued at up to $168 million, for the advancement of the development and manufacturing, as well as the procurement, of NexoBrid in the United States (the “First BARDA Contract”). Under the First BARDA Contract, BARDA has agreed to fund $91 million of the development costs of NexoBrid required to obtain marketing approval in the United States and the emergency readiness for NexoBrid deployment. Under the First BARDA Contract, BARDA is procuring from us emergency stockpile of NexoBrid valued at $16.5 million as part of the HHS mission to build national preparedness for public health medical emergencies. The First BARDA Contract also includes options for BARDA (i) to further fund $10 million in development activities for other potential NexoBrid indications, and (ii) to further fund $50 million for additional procurement of NexoBrid. As of December 31, 2021, the Company has received from BARDA approximately $70 million in the aggregate, under the two contracts, and an additional $14.6 million for procurement of NexoBrid for U.S. emergency preparedness.

However, BARDA may terminate the contract at any time, at its convenience, without any further funding obligations. There can be no assurances that BARDA will not terminate the contract. Changes in government budgets and agendas may result in a decreased and de-prioritized emphasis on supporting the development of products for the treatment of severe burns such as NexoBrid and the cessation of the procurement. Any reduction or delay in BARDA funding may force us to suspend the program or seek alternative funding, which may not be available on non-dilutive terms, terms favorable to us or at all. Further, we cannot provide any assurances as to when or whether BARDA’s commitment for procurement of NexoBrid will continue or whether BARDA's options to fund additional development activities for NexoBrid and further fund $50 million for additional procurement of NexoBrid will be exercised.

We have a history of net losses. We expect to continue to incur substantial and increasing net losses for the foreseeable future, and we may never achieve or maintain profitability.

We have incurred significant net losses, including a net loss of $9.2 million for the year ended December 31, 2020 and $13.6 million for the year ended December 31, 2021. As of December 31, 2021, we had an accumulated deficit of $148.5 million. We expect to incur substantial net losses for the foreseeable future. These losses and negative cash flows have had, and will continue to have, an adverse effect on our shareholder's equity and working capital.

We expect to incur significant expenses and increasing operating losses for the foreseeable future.

We anticipate that our expenses and future capital requirements may increase if and as we:

- accelerate our clinical development activities, particularly with respect to our clinical development of EscharEx for the debridement of chronic and other hard-to-heal wounds and our clinical trials for our other pipeline product candidates;

- further scale-up the manufacturing process for NexoBrid;
- seek regulatory and marketing approvals for NexoBrid and any pipeline product candidate that successfully completes clinical trials;
- initiate additional preclinical, clinical or other studies for NexoBrid, EscharEx and our pipeline product candidates, and seek to identify and validate new products;
- commercialize NexoBrid and any pipeline product candidates for which we obtain marketing approval;
- acquire rights to other product candidates and technologies;
- change or add suppliers;
- maintain, expand and protect our intellectual property portfolio;
- attract and retain skilled personnel; and
- experience any delays or encounter issues with any of the above.

We may need substantial additional capital in the future, which may cause dilution to our existing shareholders, restrict our operations or require us to relinquish rights to our pipeline product candidates or intellectual property. If additional capital is not available, we may have to delay, reduce or cease operations.

We may seek additional funding in the future, which may consist of equity offerings, collaborations, licensing arrangements or any other means to develop our pipeline product candidates, increase our commercial manufacturing capabilities, operate our sales and marketing capabilities or other general corporate purposes. Under our shelf registration statement on Form F-3, we may offer from time to time up to $125 million in the aggregate of our ordinary shares, warrants and/or debt securities in one or more series or issuances. In February 2020, we entered into an Open Market Sales Agreement with Jefferies LLC to issue and sell our ordinary shares with gross sales proceeds of up to $15 million, from time to time, through an at the market offering under which Jefferies LLC will act as our sales agent. As of the date hereof, we have not issued or sold any ordinary shares pursuant to the Open Market Sales Agreement. Our prior registered equity offerings diluted then-existing shareholders, and to the extent that we raise additional capital through, for example, the sale of equity or convertible debt securities under our shelf registration statement, our existing shareholders' ownership interest will be further diluted, and the terms may include liquidation or other preferences that adversely affect our shareholders' rights. The incurrence of indebtedness or the issuance of certain equity securities could result in increased fixed payment obligations and could also result in certain restrictive covenants, such as limitations on our ability to incur additional debt or to issue additional equity, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. In addition, the issuance of additional equity securities by us, or the possibility of such issuance, may cause the market price of our ordinary shares to decline. Securing additional financing may also divert our management's attention from our day-to-day activities, which may adversely affect our ability to develop and commercialize NexoBrid, EscharEx and our pipeline product candidates.

Additional funding may not be available to us on acceptable terms, or at all. In the event that we enter into collaborations or licensing arrangements in order to raise capital, we may be required to accept unfavorable terms, including relinquishing or licensing to a third party on unfavorable terms our rights to product candidates or intellectual property that we otherwise would seek to develop or commercialize ourselves or reserve for future potential arrangements when we might be able to achieve more favorable terms.

If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

- delay, scale back or discontinue the development, manufacturing scale-up or commercialization of NexoBrid, EscharEx or our pipeline product candidates;

- seek additional corporate partners for NexoBrid, EscharEx or one or more of our pipeline product candidates on terms that are less favorable than might otherwise be available; or

- relinquish or license to additional parties, on unfavorable terms, our rights to NexoBrid, EscharEx or our pipeline product candidates that we otherwise would seek to develop or commercialize ourselves.

- any such consequence will have a material adverse effect on our business, operating results and prospects and on our ability to develop our pipeline product candidates.

If we fail to manage our growth effectively, our business could be disrupted.

Our future financial performance and ability to successfully commercialize our products and to compete effectively will depend, in part, on our ability to manage any future growth effectively. We have made and expect to continue to make significant investments to enable our future growth through, among other things, new product development, clinical trials for new indications, expansion of our marketing and sales infrastructure and continues exploring for potential business development opportunities. While we believe that our current manufacturing capacity is sufficient to meet the expected near-term commercial demand for NexoBrid, we are planning to scale-up the current capacity, subject to BLA approval, in 2023. We expect the cost will be approximately $8-10 million. We must also be prepared to expand our work force and train, motivate and manage additional employees as the need for additional personnel arises. Even following expansion, our facilities, personnel, systems, procedures and controls may not be adequate to support our future operations, or we may expand, but then fail to grow our sales of NexoBrid or our pipeline product candidates sufficiently to support such operational growth. Any failure to manage future growth effectively could have a material adverse effect on our business and results of operations.

We make business decisions based on forecasts of future sales of our products and pipeline product candidates that may be inaccurate.

Our market estimates are based on many assumptions, including, but not limited to, reliance on external market research, our own internal research, population estimates, estimates of disease diagnostic rates, treatment trends, and market estimates by third parties. Any of these assumptions can materially impact our forecasts and we cannot be assured that the assumptions are accurate. If the market for any of our products or product candidates is less than this data would suggest, the potential sales for the product or pipeline product candidates in question could be adversely affected, and our inventories and net losses could increase.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development and commercialization, we are unable to accurately predict the timing or amount of future expenses or when, or if, we will be able to achieve or maintain profitability. We have financed our operations primarily through the sale of equity securities, licensing agreements and government grants. The size of our future net losses will depend, in part, on the rate of growth or contraction of our expenses and the level and rate of growth, if any, of our revenues. If we are unable to successfully commercialize NexoBrid, EscharEx or one or more of our pipeline product candidates or if revenue from NexoBrid, EscharEx or any pipeline product candidate that receives marketing approval is insufficient, we will not achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability.

Exchange rate fluctuations between the U.S. dollar and the Israeli shekel, the Euro and other non-U.S. currencies may negatively affect our earnings.

The dollar is our functional and reporting currency. However, a significant portion of our operating expenses are incurred in Israeli shekels and Euros. As a result, we are exposed to the risks that the shekel may appreciate relative to the dollar, or, if the shekel instead devalues relative to the dollar, that the inflation rate in Israel may exceed such rate of devaluation of the shekel, or that the timing of such devaluation may lag behind inflation in Israel. In any such event, the dollar cost of our operations in Israel would increase and our dollar-denominated results of operations would be adversely affected. We cannot predict any future trends in the rate of inflation in Israel or the rate of devaluation (if any) of the shekel against the dollar. For example, the shekel appreciated relative to the dollar by 3.3%, 7.0% and 7.8% in 2021, 2020 and 2019, respectively. If the dollar or Euro cost of our operations in Israel increases, our dollar- and Euro-measured results of operations will be adversely affected. Our operations also could be adversely affected if we are unable to effectively hedge against currency fluctuations in the future.

To the extent that we may receive revenues from sales in certain countries, such as certain countries in the Asia Pacific region, where our sales are expected to be denominated in dollars, a strengthening of the dollar in relation to other currencies could make our products less competitive in those foreign markets and collection of receivables more difficult. For further information, see “ITEM 11. Quantitative and Qualitative Disclosures About Market Risk” elsewhere in this annual report.

Risks Related to Healthcare Laws and Other Legal Compliance Matters

Certain of our business practices could become subject to scrutiny by regulatory authorities, as well as to lawsuits brought by private citizens. Failure to comply with applicable law or an adverse decision in lawsuits may result in adverse consequences to us.

The laws governing our conduct in the United States and in foreign jurisdictions are enforceable by criminal, civil and administrative penalties. In the United States, violations of laws such as the Federal Food, Drug and Cosmetic Act (the "FDCA"), the Public Health Service Act, the Federal False Claims Act, provisions of the U.S. Social Security Act, including the "Anti-Kickback Statute," or any regulations promulgated under their authority, may result in significant administrative, civil and criminal sanctions, jail sentences, fines or exclusion from federal and state programs, as may be determined by the U.S. Department of Justice, the Office of Inspector General of the U.S. Department of Health and Human Services (the "OIG"), the Centers for Medicare & Medicaid Services, ("CMS") other regulatory authorities and the courts. There can be no assurance that our activities will not come under the scrutiny of regulators and other government authorities or that our practices will not be found to violate applicable laws, rules and regulations or prompt lawsuits by private citizen "relators" under federal or state false claims laws.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor.

For example, even common business arrangements, such as discounted terms and volume incentives for customers in a position to recommend or choose drugs and devices for patients, such as physicians and hospitals, can result in substantial legal penalties, including, among other things, exclusion from Medicare and Medicaid programs if not carefully structured to comply with applicable requirements. Also, certain business practices, such as payment of consulting fees to healthcare providers, sponsorship of educational or research grants, charitable donations, interactions with healthcare providers and financial support for continuing medical education programs, must be conducted within narrowly prescribed and controlled limits to avoid any possibility of unlawfully inducing healthcare providers to prescribe or purchase particular products or rewarding past prescribing. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the Anti-Kickback Statute has been violated. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations of the federal Anti-Kickback Statute may result in significant civil monetary penalties for each violation, plus up to three times the remuneration involved. Moreover, 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 federal civil False Claims Act. Accordingly, civil penalties for such conduct can further be assessed under the federal False Claims Act. Violations can also result in criminal penalties, including criminal fines and imprisonment. Similarly, violations can result in exclusion from participation in government healthcare programs, including Medicare and Medicaid.

Significant enforcement activity has also taken place under federal and state false claims act statutes. Violations of the federal False Claims Act can result in treble damages, and a penalty for each false claim submitted for payment. Pharmaceutical, device and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-covered, uses. The government may further prosecute conduct constituting a false claim under the criminal False Claims Act. The criminal False Claims Act prohibits the making or presenting of a claim to the government knowing such claim to be false, fictitious, or fraudulent and, unlike the civil False Claims Act, requires proof of intent to submit a false claim.

The federal False Claims Act, as well as certain state false claims acts, also permits relators to file complaints in the name of the United States (and if applicable, particular states). These relators may be entitled to receive up to 30% of total recoveries and have been active in pursuing cases against pharmaceutical companies. Where practices have been found to involve improper incentives to use products, the submission of false claims, or other improper conduct, government investigations and assessments of penalties against manufacturers have resulted in substantial damages and fines. In addition, to avoid exclusion from participation in federal healthcare programs, many manufacturers have been required to enter into Corporate Integrity Agreements that prescribe allowable corporate conduct and impose reporting and disclosure obligations by the manufacturer to the government. Failure to satisfy requirements under the FDCA can also result in a variety of administrative, civil and criminal penalties, including injunctions or consent decrees that prescribe allowable corporate conduct.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Additionally, there has been a recent trend of increased federal and state regulation of payments and transfers of value provided to healthcare professionals and/or entities. The Affordable Care Act, among other things, imposed annual reporting requirements on certain manufacturers of drugs, devices, biologicals and medical supplies for payments and other transfers of value provided by them, directly or indirectly, to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, anesthesiologist assistants, and certified nurse midwives), and teaching hospitals, as well as ownership and investment interests held by physicians and their family members. A manufacturer's failure to submit timely, accurately and completely the required information for all payments, transfers of value or ownership or investment interests may result in significant civil monetary penalties.

In addition, we are subject to analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the governments or otherwise restrict payments that may be made to healthcare providers. For instance, payments made to physicians in certain EU member states must be publicly disclosed. Moreover, agreements with physicians must often be subject of prior notification and/or approval by the physician's employer, their competent professional organization, and/or the competent authorities of the individual EU member states.; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state and foreign laws requiring the registration of pharmaceutical sales representatives, and state and foreign laws governing the privacy and security of health information in certain circumstances. Many of these laws differ from each other in significant ways and often are not preempted by HIPAA thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, which could have a material adverse effect on our business. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, it may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also materially affect our business.

As a public company with securities registered under the U.S. Securities Exchange Act of 1934, as amended (the "Exchange Act"), we are subject to the U.S. Foreign Corrupt Practices Act (the "FCPA"). The FCPA and similar worldwide anti-bribery laws generally prohibit companies and their intermediaries from making improper payments to officials for the purpose of obtaining or retaining business. While we continue to maintain and enhance internal policies mandating compliance with these anti-bribery laws, we may operate in parts of the world that have experienced governmental corruption to some degree and in certain circumstances, strict compliance with anti-bribery laws may conflict with local customs and practices or may require us to interact with doctors and hospitals, some of which may be state controlled, in a manner that is different than in the United States. Our internal control policies and procedures may not be sufficient to effectively protect us against reckless or criminal acts committed by our employees or agents. Violations of these laws, or allegations of such violations, could disrupt our business and result in a material adverse effect on our financial condition, results of operations and cash flows.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information, such as information that we may collect in connection with clinical trials. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulations, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business.

In the United States., HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and its implementing regulations, or collectively HIPAA, imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our customers and strategic partners. For example, the California Consumer Privacy Act ("CCPA"), which went into effect on January 1, 2020, among other things, creates new data privacy obligations for covered companies and provides individual privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Although the law includes limited exceptions, including for "protected health information" maintained by a covered entity or business associate, it may regulate or impact our processing of personal information depending on the context. Further, the California Privacy Rights Act ("CPRA") recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have passed in Virginia and Colorado, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

We are subject to data privacy and security laws in the EU as well as the European Economic Area ("EEA"), including Regulation 2016/679, or the General Data Protection Regulation ("GDPR") with respect to our collection, control, processing, sharing, disclosure and other use of personal data located in the EEA. The GDPR went into effect in May 2018, and companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States; in July 2020, the Court of Justice of the EU ("CJEU") limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses ("SCCs"). The European Commission issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs must be used for relevant new data transfers from September 27, 2021; existing standard contractual clauses arrangements must be migrated to the revised clauses by December 27, 2022. The new SCCs apply only to the transfer of personal data outside of the EEA and not the United Kingdom; the United Kingdom's Information Commissioner's Office launched a public consultation on its draft revised data transfers mechanisms in August 2021. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non-EEA entities subject to the GDPR. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Further, since January 2021, we may also be subject to the UK GDPR, which, together with the UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, meaning the potential of parallel fines of up to the greater of £17.5 million or 4% of global turnover. The European Commission has adopted an adequacy decision in favor of the UK, enabling data transfers from EU member states to the UK without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the European Commission re-assesses and renews/extends that decision and remains under review by the Commission during this period. In September 2021, the UK government launched a consultation on its proposals for wide-ranging reform of UK data protection laws following Brexit. There is a risk that any material changes which are made to the UK data protection regime could result in the European Commission reviewing the UK adequacy decision, and the UK losing its adequacy decision if the European Commission deems the UK to no longer provide adequate protection for personal data. The relationship between the UK and the EU in relation to certain aspects of data protection law remains uncertain, and it is unclear how UK data protection laws and regulations will develop in the medium to longer term.

Laws and regulations affecting government contracts make it more costly and difficult for us to successfully conduct our business.

We must comply with numerous laws and regulations relating to the formation, administration and performance of government contracts, which can make it more difficult for us to retain our rights under our BARDA contracts. These laws and regulations affect how we conduct business with government agencies. Among the most significant government contracting regulations that affect our business are:

- the Federal Acquisition Regulations ("FAR") and agency-specific regulations supplemental to the FAR, which comprehensively regulate the procurement, formation, administration and performance of government contracts;

- business ethics and public integrity obligations, which govern conflicts of interest and the hiring of former government employees, restrict the granting of gratuities and funding of lobbying activities and include other requirements such as the Anti-Kickback Statute and Foreign Corrupt Practices Act;

- export and import control laws and regulations; and

- laws, regulations and executive orders restricting the use and dissemination of information classified for national security purposes and the exportation of certain products and technical data.

Any material changes in applicable laws and regulations could restrict our ability to maintain our BARDA contracts or obtain new contracts with the U.S. federal government.

We could be subject to product liability lawsuits, which could result in costly and time-consuming litigation and significant liabilities.

The development of biopharmaceutical products involves an inherent risk of product liability claims and associated adverse publicity. Our products may be found to be harmful or to contain harmful substances. This exposes us to substantial risk of litigation and liability or may force us to discontinue production of certain products. Although we have product liability insurance covering up to $10 million for claims in countries where NexoBrid is sold through our sales force or through our distributors, the coverage may not insure us against all claims that may be asserted against us. Product liability insurance is costly and often limited in scope. There can be no assurance that we will be able to obtain or maintain insurance on reasonable terms or to otherwise protect ourselves against potential product liability claims that could impede or prevent commercialization of NexoBrid, EscharEx or our pipeline product candidates. Furthermore, a product liability claim could damage our reputation, whether or not such claims are covered by insurance or are with or without merit. A product liability claim against us or the withdrawal of a product from the market could have a material adverse effect on our business or financial condition. Furthermore, product liability lawsuits, regardless of their success, would likely be time-consuming and expensive to resolve and would divert management's time and attention, which could seriously harm our business.

We are subject to extensive environmental, health and safety, and other laws and regulations.

Our business involves the controlled use of chemicals. The risk of accidental contamination or injury from these materials cannot be eliminated. If an accident, spill or release of any such chemicals or substances occurs, we could be held liable for resulting damages, including for investigation, remediation and monitoring of the contamination, including natural resource damages, the costs of which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures. Although we maintain workers' compensation insurance to cover the costs and expenses that may be incurred because of injuries to our employees resulting from the use of these materials, this insurance may not provide adequate coverage against potential liabilities. Additional or more stringent laws and regulations affecting our operations may be adopted in the future. We may incur substantial capital costs and operating expenses and may be required to obtain consents to comply with any of these or certain other laws or regulations and the terms and conditions of any permits required pursuant to such laws and regulations, including costs to install new or updated pollution control equipment, modify our operations or perform other corrective actions at our respective facilities. In addition, fines and penalties may be imposed for noncompliance with environmental, health and safety and other laws and regulations or for the failure to have, or comply with the terms and conditions of, required environmental or other permits or consents.

The United Kingdom's departure from the European Union could adversely affect our business.

Following a national referendum and enactment of legislation by the government of the United Kingdom, the United Kingdom formally withdrew from the EU and ratified a trade and cooperation agreement governing its future relationship, commonly known as Brexit. The agreement, which was applied provisionally from January 1, 2021 and entered into force on May 1, 2021, addresses trade, economic arrangements, law enforcement, judicial cooperation and a governance framework including procedures for dispute resolution, among other things. Because the agreement merely sets forth a framework in many respects and will require complex additional bilateral negotiations between the United Kingdom and the EU as both parties continue to work on the rules for implementation, significant political and economic uncertainty remains about how the precise terms of the relationship between the paries will differ from the terms before withdrawal. Since January 1, 2021, however, the United Kingdom has operated under a separate regulatory regime to the EU. EU laws regarding medicinal products only apply in respect of the United Kingdom to Northern Ireland (as set out in the Protocol on Ireland/Northern Ireland). The EU laws that have been transposed into United Kingdom law through secondary legislation remain applicable. While the United Kingdom has indicated a general intention that new laws regarding the development, manufacture and commercialization of medicinal products in the United Kingdom will align closely with EU law, there are limited detailed proposals for future regulation of medicinal products. The trade and cooperation agreement includes specific provisions concerning medicinal products, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued (such mutual recognition can be rejected by either party in certain circumstances), but does not foresee wholesale mutual recognition of United Kingdom and EU pharmaceutical regulations. For example, it is not clear to what extent the United Kingdom will adopt legislation aligned with, or similar to, the EU Clinical Trial Regulation ("CTR") that will become applicable on January 31, 2022 and which will significantly reform the assessment and supervision processes for clinical trials throughout the EU. Therefore, there remains political and economic uncertainty regarding to what extent the regulation of medicinal products will differ between the United Kingdom and the EU in the future. Any divergences will increase the cost and complexity of running our business, including with respect to the conduct of clinical trials. Brexit also materially impacted the regulatory regime with respect to the approval of our product candidates. Great Britain is no longer covered by the EU's procedures for the grant of marketing authorizations (Northern Ireland is covered by the centralized authorization procedure and can be covered under the decentralized or mutual recognition procedures). As of 1 January 2021, all existing centralized marketing authorizations, such as the authorizations we have for NexoBrid, were automatically converted into United Kingdom marketing authorizations effective in Great Britain and issued with a United Kingdom marketing authorization number on January 1, 2021 (unless marketing authorization holders opted out of this scheme). A separate marketing authorization is now required to market drugs in Great Britain. It is currently unclear whether the regulator in the United Kingdom, the Medicines and Healthcare products Regulatory Agency is sufficiently prepared to handle the increased volume of marketing authorization applications that it is likely to receive. Any delay in obtaining, or an inability to obtain, any regulatory approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in Great Britain and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in Great Britain for our product candidates, which could significantly and materially harm our business. Brexit could adversely affect European and worldwide economic and market conditions and could contribute to instability in global financial and foreign exchange markets, including volatility in the value of the sterling and euro. Any of these effects of Brexit, and others we cannot anticipate, could adversely affect our business, results of operations, financial condition and cash flows.

Risks Related to Our Intellectual Property Rights

Our success depends in part on our ability to obtain and maintain protection for the intellectual property relating to, or incorporated into, our technology and products.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our intellectual property and proprietary technologies, our products and their uses, as well as our ability to operate without infringing upon the proprietary rights of others. We rely on a combination of patents, trademark and trade secret laws, non-disclosure and confidentiality agreements, licenses, assignments of invention agreements and other restrictions on disclosure and use to protect our intellectual property rights.

As of December 31, 2021, we had been granted a total of 64 patents and have 27 pending patent applications. The family of patents that covers NexoBrid specifically includes 35 granted patents worldwide. EscharEx is covered in 7 patents and 24 national phase applications. However, there can be no assurance that patent applications relating to our products, processes or technologies will result in patents being issued, that any patents that have been issued will be adequate to protect our intellectual property or that we will enjoy patent protection for any significant period of time. Additionally, any issued patents may be challenged by third parties, and patents that we hold may be found by a judicial authority to be invalid or unenforceable. Other parties may independently develop similar or competing technology or design around any patents that may be issued to or held by us. Our current patents will expire or they may otherwise cease to provide meaningful competitive advantage, and we may be unable to adequately develop new technologies and obtain future patent protection to preserve our competitive advantage or avoid adverse effects on our business.

Our patent protection may be limited, subjecting us to challenges by competitors.

At present, we consider our patents relating to our enzymatic platform technology, which underlies NexoBrid, EscharEx and our current pipeline product candidates, to be material to the operation of our business as a whole. Our patents which cover NexoBrid claim specific mixtures of proteolytic enzymes, methods of producing such mixtures and methods of treatment using such mixtures. Although the protection achieved is significant for NexoBrid, EscharEx and our pipeline product candidates, when looking at our patents' ability to block competition, the protection offered by our patents may be, to some extent, more limited than the protection provided by patents which claim chemical structures that were previously unknown. If our patents covering NexoBrid in various jurisdictions were subject to a successful challenge or if a competitor were able to successfully design around them, our business and competitive advantage could be significantly affected.

In addition, the patent landscape in the biotechnology field is highly uncertain and involves complex legal, factual and scientific questions, and changes in either patent laws or in the interpretation of patent laws in the United States and other countries may diminish the value and strength of our intellectual property or narrow the scope of our patent protection. In addition, we may fail to apply for or be unable to obtain patents necessary to protect our technology or products or enforce our patents due to lack of information about the exact use of our process by third parties. Even if patents are issued to us, they may be challenged, narrowed, invalidated, held to be unenforceable or circumvented, which could limit our ability to prevent competitors from using similar technology or marketing similar products, or limit the length of time our technologies and products have patent protection. In addition, we are a party to license agreement with Mark Klein, that imposes various obligations upon us as a licensee, including the obligation to make milestone and royalty payments contingent on the sales of NexoBrid. If we fail to comply with these obligations, the licensor may terminate the license, in which event we might not be able to market any product that is covered by the licensed intellectual property, including NexoBrid.

In order to preserve and enforce our patents and other intellectual property rights, we may need to assert claims or file lawsuits against third parties. Such lawsuits could entail significant costs to us and divert our management's attention from developing and commercializing our products. Lawsuits may ultimately be unsuccessful and may also subject us to counterclaims and cause our intellectual property rights to be challenged, narrowed, invalidated or held to be unenforceable.

The timing of a patent application, grant, and expiration may put us at a disadvantage compared to our competitors.

Our material patents also may not afford us protection against competitors with similar technology. Because patent applications in the United States and many other jurisdictions are typically not published until 18 months after their filing, if at all, and because publications of discoveries in scientific literature often lag behind actual discoveries, neither we nor our licensors can be certain that we or they were the first to make the inventions claimed in our or their issued patents or pending patent applications, or that we or they were the first to file for protection of the inventions set forth in such patent applications. As a result, the patents we own and license may be invalidated in the future, and the patent applications we own and license may not be granted. For example, if a third party has also filed a patent application covering an invention similar to one covered in one of our patent applications, we may be required to participate in an adversarial proceeding known as an "interference proceeding," declared by the U.S. Patent and Trademark Office or its foreign counterparts, to determine priority of invention. The costs of these proceedings could be substantial and our efforts in them could be unsuccessful, resulting in a loss of our anticipated patent position. In addition, if a third party prevails in such a proceeding and obtains an issued patent, we may be prevented from practicing technology or marketing products covered by that patent. Additionally, patents and patent applications owned by third parties may prevent us from pursuing certain opportunities such as entering into specific markets or developing certain products. Finally, we may choose to enter into markets where certain competitors have patents or patent protection over technology that may impede our ability to compete effectively.

We may not be able to protect our intellectual property rights in all jurisdictions.

Effective protection of our intellectual property rights may be unavailable or limited in some countries, and even if available, we may fail to pursue or obtain necessary intellectual property protection in such countries, including because filing, prosecuting, maintaining and defending patents on product candidates in all countries throughout the world would be prohibitively expensive. In addition, the legal systems of certain countries do not favor the aggressive enforcement of patents and other intellectual property rights, and the laws of certain foreign countries do not protect our rights to the same extent as the laws of the United States. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products, and we may be unable to prevent such competitors from importing such infringing products into territories where we have patent protection but where enforcement is not as strong as in the United States or into jurisdictions in which we do not have patent protection. These products may compete with our product candidates and our patents and other intellectual property rights may not be effective or sufficient to prevent them from competing in those jurisdictions.

Our currently issued NexoBrid Family patents are nominally due to expire at various dates between 2025 and 2029. However, because of the extensive time required for development, testing and regulatory review of a potential product, and although such delays may entitle us to patent term extensions, it is possible that, before NexoBrid can be commercialized in additional international jurisdictions and/or before any of our future products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantages of the patent. The international PCT patent applications relating to EscharEx were filed on January 30, 2017. National phase applications corresponding to these PCT applications were filed in several jurisdictions and the expiration date of the seven patents that issued and those that will be issued is January 30, 2037, absent patent-term adjustment and/or extensions. Our pending and future patent applications may not lead to the issuance of patents or, if issued, the patents may not provide us with any competitive advantage. We also cannot guarantee that:

- any of our present or future patents or patent claims or other intellectual property rights will not lapse or be invalidated, circumvented, challenged or abandoned;
- our intellectual property rights will provide competitive advantages or prevent competitors from making or selling competing products;
- our ability to assert our intellectual property rights against potential competitors or to settle current or future disputes will not be limited by our agreements with third parties;
- any of our pending or future patent applications will be issued or have the coverage originally sought;
- our intellectual property rights will be enforced in jurisdictions where competition may be intense or where legal protection may be weak; or
- we will not lose the ability to assert our intellectual property rights against, or to license our technology to, others and collect royalties or other payments.

We may be unable to identify all past or future unauthorized uses of our intellectual property.

Additionally, unauthorized use of our intellectual property may have occurred or may occur in the future. Any failure to identify unauthorized use of, and otherwise adequately protect, our intellectual property could adversely affect our business, including by reducing the demand for our products. Any reported adverse events involving counterfeit products that purport to be our products could harm our reputation and the sale of our products. Moreover, if we are required to commence litigation related to unauthorized use, whether as a plaintiff or defendant, such litigation would be time-consuming, force us to incur significant costs and divert our attention and the efforts of our management and other employees, which could, in turn, result in lower revenue and higher expenses.

In addition to patented technology, we rely on our unpatented proprietary technology, trade secrets, processes and know-how.

We rely on proprietary information, such as trade secrets, know-how and confidential information, to protect intellectual property that may not be patentable or that we believe is best protected by means that do not require public disclosure. We generally seek to protect this proprietary information by entering into confidentiality agreements, or consulting, services or employment agreements that contain non-disclosure and non-use provisions with our employees, consultants, contractors, scientific advisors and third parties. However, we may fail to enter into the necessary agreements, and even if entered into, these agreements may be breached or otherwise fail to prevent disclosure, third-party infringement or misappropriation of our proprietary information, may be limited as to their term and may not provide an adequate remedy in the event of unauthorized disclosure or use of proprietary information. We have limited control over the protection of trade secrets used by our suppliers and service providers and could lose future trade secret protection if any unauthorized disclosure of such information occurs. In addition, our proprietary information may otherwise become known or be independently developed by our competitors or other third parties. To the extent that our employees, consultants, contractors, scientific advisors and other third parties use intellectual property owned by others in their work for us, disputes may arise as to the related rights or resulting know-how and inventions. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our and relevant third parties' proprietary rights and failure to obtain or maintain protection for our proprietary information could adversely affect our competitive business position. In addition, if a third party is able to establish that we are using their proprietary information without their permission, we may be required to obtain a license to such information or, if such a license is not available, re-design our products to avoid any such unauthorized use or temporarily delay or permanently stop manufacturing or sales of the affected products. Furthermore, laws regarding trade secret rights in certain markets where we operate may afford little or no protection to our trade secrets.

We also rely on physical and electronic security measures to protect our proprietary information, but we cannot provide assurance that these security measures will not be breached or will provide adequate protection for our property. There is a risk that third parties may obtain and improperly utilize our proprietary information to our competitive disadvantage. We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our confidential information. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. We may not be able to detect or prevent the unauthorized use of such information or take appropriate and timely steps to enforce our intellectual property rights.

Some of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including potential competitors. While we take steps to prevent our employees from using the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have inadvertently or otherwise used or disclosed intellectual property, trade secrets or other proprietary information of any such employee's former employer. Litigation may be necessary to defend against these claims and, even if we are successful in defending ourselves, could result in substantial costs to us or be distracting to our management. If we fail to defend any such claims successfully, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel.

If we are unable to protect our trademarks from infringement, our business prospects may be harmed.

We own trademarks that identify "MediWound," "NexoBrid" and "EscharEx," among others, and have registered these trademarks in certain key markets. Although we take steps to monitor the possible infringement or misuse of our trademarks, it is possible that third parties may infringe, dilute or otherwise violate our trademark rights. Any unauthorized use of our trademarks could harm our reputation or commercial interests. In addition, our enforcement against third-party infringers or violators may be unduly expensive and time-consuming, and the outcome may be an inadequate remedy.

We may be subject to claims that we infringe, misappropriate or otherwise violate the intellectual property rights of third parties.

Our development, marketing or sale of NexoBrid, EscharEx or our pipeline product candidates may infringe or be accused of infringing one or more claims of an issued patent to which we do not hold a license or other rights. We may also be subject to claims that we are infringing, misappropriating or otherwise violating other intellectual property rights, such as trademarks, copyrights or trade secrets. Third parties could therefore bring claims against us or our strategic partners that would cause us to incur substantial expenses, including litigation costs or costs associated with settlement, and, if successful against us, could cause us to pay substantial damages. Further, if such a claim were brought against us, we could be forced to temporarily delay or permanently stop manufacturing or sales of NexoBrid, EscharEx or our pipeline product candidates that are the subject of the suit.

If we are found to be infringing, misappropriating or otherwise violating the patent or other intellectual property rights of a third party, or in order to avoid or settle claims, we may choose or be required to seek a license from a third party and be required to pay license fees or royalties or both, which could be substantial. 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 nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened claims, we or our strategic partners are unable to enter into licenses on acceptable terms.

There have been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical and biotechnology industries. In addition, to the extent that we gain greater visibility and market exposure as a public company in the United States, we face a greater risk of being involved in such litigation. In addition to infringement claims against us, we may become a party to other patent litigation and other proceedings, including interference, opposition, re-examination and similar proceedings before the U.S. Patent and Trademark Office and its foreign counterparts, regarding intellectual property rights with respect to NexoBrid, EscharEx or our pipeline product candidates. The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. A negative outcome could result in liability for monetary damages, including treble damages and attorneys' fees if, for example, we are found to have willfully infringed a patent. A finding of infringement could prevent us from developing, marketing or selling a product or force us to cease some or all of our business operations. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace, and patent litigation and other proceedings may also absorb significant management time.

Under applicable employment laws, we may not be able to enforce covenants not to compete.

We generally enter into non-competition agreements with our employees. These agreements prohibit our employees, if they cease working for us, from competing directly with us or working for our competitors or clients for a limited period. We may be unable to enforce these agreements under the laws of the jurisdictions in which our employees work and it may be difficult for us to restrict our competitors from benefitting from the expertise our former employees or consultants developed while working for us. For example, Israeli labor courts have required employers seeking to enforce non-compete undertakings of a former employee to demonstrate that the competitive activities of the former employee will harm one of a limited number of material interests of the employer which have been recognized by the courts, such as the protection of a company's trade secrets or other intellectual property.

We may become subject to claims for remuneration or royalties for assigned service invention rights by our employees, which could result in litigation and adversely affect our business.

A significant portion of our intellectual property has been developed for us by our employees in the course of their employment. Under the Israeli Patent Law, 5727-1967, or the Patent Law, inventions conceived by an employee in the course and as a result of or arising from his or her employment with a company are regarded as "service inventions," which belong to the employer, absent a specific agreement between the employee and employer giving the employee proprietary rights. The Patent Law also provides under Section 134 that if there is no agreement between an employer and an employee as to whether the employee is entitled to consideration for service inventions, and to what extent and under which conditions, the Israeli Compensation and Royalties Committee, or the Committee, a body constituted under the Patent Law, shall determine these issues. Section 135 of the Patent law provides criteria for assisting the Committee in making its decisions. According to case law handed down by the Committee, an employee's right to receive consideration for service inventions is a personal right and is entirely separate from the proprietary rights in such invention. Therefore, this right must be explicitly waived by the employee. A decision handed down in May 2014 by the Committee clarifies that the right to receive consideration under Section 134 can be waived and that such waiver can be made orally, in writing or by behavior like any other contract. The Committee will examine, on a case by case basis, the general contractual framework between the parties, using interpretation rules of the general Israeli contract laws. Further, the Committee has not yet determined one specific formula for calculating this remuneration, nor the criteria or circumstances under which an employee's waiver of his right to remuneration will be disregarded. Similarly, it remains unclear whether waivers by employees in their employment agreements of the alleged right to receive consideration for service inventions should be declared as void being a depriving provision in a standard contract. We generally enter into assignment-of-invention agreements with our employees pursuant to which such individuals assign to us all rights to any inventions created in the scope of their employment or engagement with us. Although our employees have agreed to assign to us service invention rights and have specifically waived their right to receive any special remuneration for such service inventions beyond their regular salary and benefits, we may face claims demanding remuneration in consideration for assigned inventions. As a consequence of such claims, we could be required to pay additional remuneration or royalties to our current or former employees or be forced to litigate such claims, which could negatively affect our business.

Risks Related to an Investment in Our Ordinary Shares

The market price of our ordinary shares may be subject to fluctuation and you could lose all or part of your investment.

Our ordinary shares were first offered publicly in our IPO in March 2014 at a price of $14.00 per share, and our ordinary shares have subsequently traded as high as $18.16 per share and as low as $1.47 per share through March 15, 2022. The market price of our ordinary shares on the Nasdaq Global Market may fluctuate as a result of a number of factors, some of which are beyond our control, including, but not limited to:

- actual or anticipated variations in our and our competitors' results of operations and financial condition;
- market acceptance of our products;
- general economic and market conditions and other factors, including factors unrelated to our operating performance;
- the mix of products that we sell and related services that we provide;
- changes in earnings estimates or recommendations by securities analysts, if our ordinary shares continue to be covered by analysts;
- publication of the results of preclinical or clinical trials for NexoBrid, EscharEx or any of our pipeline product candidates;
- failure by us to achieve a publicly announced milestone;
- delays between our expenditures to develop and market new or enhanced products and the generation of sales from those products;
- development of technological innovations or new competitive products by others;
- announcements of technological innovations or new products by us;
- regulatory developments and the decisions of regulatory authorities as to the marketing of our current products or the approval or rejection of new or modified products;
- developments concerning intellectual property rights, including our involvement in litigation;
- changes in our expenditures to develop, acquire or license new products, technologies or businesses;
- changes in our expenditures to promote our products;
- changes in the structure of healthcare payment systems;
- our sale or proposed sale, or the sale by our significant shareholders, of our ordinary shares or other securities in the future;
- changes in key personnel;
- success or failure of our research and development projects or those of our competitors; and
- the trading volume of our ordinary shares.

These factors and any corresponding price fluctuations may materially and adversely affect the market price of our ordinary shares and result in substantial losses being incurred by our investors. In the past, following periods of market volatility, public company shareholders have often instituted securities class action litigation. If we were involved in securities litigation, it could impose a substantial cost upon us and divert the resources and attention of our management from our business.

Future sales of our ordinary shares could reduce the market price of our ordinary shares.

If we or our existing shareholders, our directors or their affiliates or certain of our executive officers, sell a substantial number of our ordinary shares in the public market, the market price of our ordinary shares could decrease significantly. The perception in the public market that we or our shareholders might sell our ordinary shares could also depress the market price of our ordinary shares and could impair our future ability to obtain capital, especially through an offering of equity securities.

We have made significant offerings of our ordinary shares in the past and may do so again in the future. For example, on April 23, 2019, the SEC declared effective our shelf registration statement on Form F-3, which registered the resale of 11,240,127 shares that are subject to registration rights. All shares sold pursuant to an offering covered by that registration statement (or a subsequent shelf registration that we may file to replace it after it expires) will be freely transferable. See "ITEM 7.B. Related Party Transactions—Registration Rights Agreement." In February 2020, we entered into an Open Market Sales Agreement with Jefferies LLC to issue and sell our ordinary shares with gross sales proceeds of up to $15 million, from time to time, through an at the market offering under which Jefferies LLC will act as our sales agent. As of the date hereof, we have not issued or sold any ordinary shares pursuant to the Open Market Sales Agreement. Sales by us or our shareholders of a substantial number of ordinary shares in the public market could cause the market price of our ordinary shares to decline or could impair our ability to raise capital through a future sale of, or pay for acquisitions using, our equity securities.

In addition, as of March 15, 2022, 3,834,697 ordinary shares were subject to outstanding option and RSU awards granted to employees and office holders under our share incentive plans, including 2,534,103 ordinary shares issuable under currently exercisable share options and RSUs. On April 28, 2014, we filed a registration statement on Form S-8 registering the issuance of up to 3,032,742 ordinary shares issuable under our share incentive plans, which amount included 960,932 ordinary shares issuable upon the exercise of option awards previously granted under our 2003 Israeli Share Option Plan and 1,482,044 ordinary shares issuable under our 2014 Equity Incentive Plan. On January 1, 2016, 2018, 2019, 2020 and 2021, the shares available for issuance under our 2014 Equity Incentive Plan automatically increased by 431,006, 540,955, 543,577, 544,055 and 544,738 shares, respectively. As of March 15, 2022, 4,325,624 shares remained available for issuance under our share incentive plans, which amount includes 490,927 ordinary shares subject to outstanding awards. Shares included in such registration statement may be freely sold in the public market upon issuance, except for shares held by affiliates who have certain restrictions on their ability to sell.

The significant share ownership position of Clal Biotechnology Industries Ltd. may limit your ability to influence corporate matters.

As of March 15, 2022, Clal Biotechnology Industries Ltd. ("CBI"), beneficially owns or controls, directly and indirectly, 33.8% of our issued and outstanding ordinary shares. Accordingly, CBI is able to significantly influence the outcome of matters required to be submitted to our shareholders for approval, including decisions relating to the election of our board of directors and the outcome of any proposed merger or consolidation of the company. CBI's interests may not be consistent with those of our other shareholders. In addition, CBI's significant interest in us may discourage third parties from seeking to acquire control of us, which may adversely affect the market price of our ordinary shares.

We have never paid cash dividends on our share capital, and we do not anticipate paying any cash dividends in the foreseeable future.

We have never declared or paid cash dividends on our share capital, nor do we anticipate paying any cash dividends on our share capital in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. As a result, capital appreciation, if any, of our ordinary shares will be an investor's sole source of gain for the foreseeable future. In addition, Israeli law limits our ability to declare and pay dividends, and may subject our dividends to Israeli withholding taxes. See "ITEM 8.A. Consolidated Statements and Other Financial Information—Dividend Policy," "ITEM 10.B. Articles of Association—Dividend and liquidation rights" and "ITEM 10.E. Taxation—Israeli Tax Considerations and Government Programs."

As a foreign private issuer, we are permitted, and intend, to follow certain home country corporate governance practices instead of otherwise applicable SEC and Nasdaq requirements.

As a foreign private issuer, we are permitted to, and do, follow certain home country corporate governance practices instead of those otherwise required under the Nasdaq Stock Market listing rules for domestic U.S. issuers. For instance, we follow home country practice in Israel with regard to the (i) quorum requirement for shareholder meetings, (ii) independent director oversight of director nominations requirement, (iii) independence requirement for the board of directors and (iv) shareholder approval for certain transactions other than a public offering involving issuances of a 20% or more interest in the company. See "ITEM 16G. Corporate Governance." We may in the future elect to follow home country practices in Israel with regard to other matters as well, such as the formation and composition of the nominating and corporate governance committee, separate executive sessions of independent directors and the requirement to obtain shareholder approval for certain dilutive events (such as for the establishment or amendment of certain equity-based compensation plans, issuances that will result in a change of control of the company, 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. company listed on the Nasdaq Global Market may provide less protection to you than what is accorded to investors under the Nasdaq Stock Market listing rules applicable to domestic U.S. issuers. See "ITEM 16G. Corporate Governance."

As a foreign private issuer, we are not subject to the provisions of Regulation FD or U.S. proxy rules and are exempt from filing certain Exchange Act reports.

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 and current reports and financial statements with the SEC as frequently or as promptly as U.S. domestic companies whose securities are registered under the Exchange Act, and we are generally exempt from filing quarterly reports with the SEC under the Exchange Act. Moreover, we are not required to comply with Regulation FD, which prohibits the selective disclosure of material nonpublic information to, among others, broker-dealers and holders of a company's securities under circumstances in which it is reasonably foreseeable that the holder will trade in the company's securities on the basis of the information. Even though we intend to comply voluntarily with Regulation FD, these exemptions and leniencies will reduce the frequency and scope of information and protections to which you are entitled as an investor.

For so long as we qualify as a foreign private issuer, we are not required to comply with the proxy rules applicable to U.S. domestic companies, including the requirement applicable to emerging growth companies to disclose the compensation of our Chief Executive Officer and other two most highly compensated executive officers on an individual, rather than an aggregate, basis. Nevertheless, the regulations promulgated under the Israeli Companies Law, 5759-1999 (the "Israeli Companies Law") require us to disclose the annual compensation of our five most highly compensated officers on an individual, rather than on an aggregate, basis. See "ITEM 6.B. Compensation." Under the Companies Law regulations, this disclosure is required to be included in the proxy statement for our annual meeting of shareholders each year, which we furnish to the SEC under cover of a Report of Foreign Private Issuer on Form 6-K. Because of that disclosure requirement under Israeli law, we are also including such information in this annual report, pursuant to the disclosure requirements of Form 20-F.

We would lose our foreign private issuer status if a majority of our outstanding ordinary shares are held of record by U.S. shareholders and we fail to meet additional requirements necessary to avoid loss of foreign private issuer status. Although we have elected to comply with certain U.S. regulatory provisions, our loss of foreign private issuer status would make such provisions mandatory. The regulatory and compliance costs to us under U.S. securities laws as a U.S. domestic issuer may be significantly higher. If we lose our foreign private issuer status, we will be required to file periodic reports and registration statements on U.S. domestic issuer forms with the SEC, which are more detailed and extensive than the forms available to a foreign private issuer. We would also be required to follow U.S. proxy disclosure requirements, including the requirement to disclose more detailed information about the compensation of our senior executive officers on an individual basis. We may also be required to modify certain of our policies to comply with accepted governance practices associated with U.S. domestic issuers. Such conversion and modifications will involve additional costs. In addition, we would lose our ability to rely upon exemptions from certain corporate governance requirements on U.S. stock exchanges that are available to foreign private issuers.

If we are unable to satisfy the requirements of Section 404 of the Sarbanes-Oxley Act, or if our internal control over financial reporting or our disclosure controls and procedures are not effective, investors may lose confidence in the accuracy and the completeness of the reports we furnish or file with the SEC, the reliability of our financial statements may be questioned and our share price may suffer.

We are required to comply with the internal control, evaluation and certification requirements of Section 404 of the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act"). Pursuant to Section 404(a) of the Sarbanes-Oxley Act, we are required to furnish a report by management on the effectiveness of our internal control over financial reporting. If we become an accelerated filer or a large accelerated filer, we will be required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes Oxley Act.

To maintain the effectiveness of our disclosure controls and procedures and our internal control over financial reporting, we expect that we will need to continue to enhance existing, and implement new, financial reporting and management systems, procedures and controls to manage our business effectively and support our growth in the future. The process of evaluating our internal control over financial reporting requires an investment of substantial time and resources, including by our Chief Financial Officer and other members of our senior management. The determination and any remedial actions required could divert internal resources and take a significant amount of time and effort to complete and could result in us incurring additional costs that we did not anticipate, including the hiring of outside consultants.

Irrespective of compliance with Section 404, any failure of our internal controls could have a material adverse effect on our stated results of operations and harm our reputation. As a result, we may experience higher than anticipated operating expenses, as well as higher independent auditor fees during and after the implementation of these changes. If we are unable to implement any of the required changes to our internal control over financial reporting effectively or efficiently, it could adversely affect our operations, financial reporting or results of operations. Further, if our internal controls over financial reporting are not effective, the reliability of our financial statements may be questioned and our share price may suffer.

Our U.S. shareholders may suffer adverse tax consequences if we are characterized as a passive foreign investment company.

Generally, if for any taxable year 75% or more of our gross income is passive income, or at least 50% of the average quarterly value of our assets (which may be determined in part by the market value of our ordinary shares, which is subject to change) are held for the production of, or produce, passive income, we would be characterized as a passive foreign investment company ("PFIC") for U.S. federal income tax purposes. Based on our current estimates of our gross income and gross assets and the nature of our business, we do not believe we were classified as a PFIC for the taxable year ended December 31, 2021. There can be no assurance that we will not be considered a PFIC for the current or any future taxable year. PFIC status is determined as of the end of the taxable year and depends on a number of factors, including the value of a corporation's assets and the amount and type of its gross income. Furthermore, the value of our gross assets is likely to be determined in large part by reference to our market capitalization. As such, a decline in the value of our ordinary shares or an increase in the value of our passive assets (including cash and short term investments), for example, may result in our becoming a PFIC. If we are characterized as a PFIC, our U.S. shareholders may suffer adverse tax consequences, including having gains realized on the sale of our ordinary shares treated as ordinary income, rather than as capital gain, the loss of the preferential rate that may be applicable to dividends received on our ordinary shares by individuals who are U.S. Holders (as defined in "ITEM 10.E. Taxation—United States Federal Income Taxation"), and having interest charges apply to distributions by us and the proceeds of share sales. Certain elections exist that may alleviate some of the adverse consequences of PFIC status and would result in an alternative treatment (such as mark-to-market treatment) of our ordinary shares. However, we do not intend to provide the information necessary for U.S. holders to make qualified electing fund elections if we are classified as a PFIC. See "ITEM 10.E. Taxation—United States Federal Income Taxation—Passive Foreign Investment Company Considerations."

If a U.S. person is treated as owning at least 10% of our ordinary shares, such holder may be subject to adverse U.S. federal income tax consequences.

If a U.S. person is treated as owning (directly, indirectly, or constructively) at least 10% of the value or voting power of our ordinary shares, such person may be treated as a "U.S. shareholder" with respect to each "controlled foreign corporation" in our group (if any). Since our group includes one or more U.S. subsidiaries, certain of our non-U.S. subsidiaries will be treated as controlled foreign corporations (regardless of whether or not we are treated as a controlled foreign corporation). A U.S. shareholder of a controlled foreign corporation may be required to report annually and include in its U.S. taxable income its pro rata share of "Subpart F income," "global intangible low-taxed income," and investments in U.S. property by controlled foreign corporations, regardless of whether the Company makes any distributions. An individual that is a U.S. shareholder with respect to a controlled foreign corporation generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a U.S. shareholder that is a U.S. corporation. Failure to comply with these reporting obligations may subject a U.S. shareholder to significant monetary penalties and may prevent the statute of limitations with respect to such U.S. shareholder's U.S. federal income tax return for the year for which reporting was due from starting. We cannot provide any assurances that we will assist holders of ordinary shares in determining whether any of our non-U.S. subsidiaries is treated as a controlled foreign corporation or whether any holder of ordinary shares is treated as a U.S. shareholder with respect to any such controlled foreign corporation or furnish to any U.S. shareholders information that may be necessary to comply with the aforementioned reporting and tax paying obligations. The United States Internal Revenue Service has provided limited guidance on situations in which investors may rely on publicly available information to comply with their reporting and taxpaying obligations with respect to foreign-controlled controlled foreign corporations. A U.S. holder should consult its tax advisors regarding the potential application of these rules to an investment in the ordinary shares.

Risks Primarily Related to our Operations in Israel

Our headquarters, manufacturing and other significant operations are located in Israel and, therefore, our results may be adversely affected by political, economic or military instability in Israel and by conflicts between Israel and neighboring terrorist groups or countries.

Our headquarters, manufacturing and research and development facilities are located in Yavne, Israel. In addition, the majority of our key employees, officers and directors are residents of Israel. In recent years, there has been political, instability in Israel, including four national elections within the last two-plus years. Over the past decade, there have been multiple hostilities between Israel and Hamas (an Islamist militia and political group in the Gaza strip) and in the summer of 2006, there was an armed conflict between Israel and Hezbollah (an Islamist militia and political group in Lebanon). Even during times without formal conflict, Hamas and other terrorist groups in the Gaza strip have shot rockets into southern Israel, which have sometimes damaged civilian and commercial property.

In recent years, Iran, which has threatened to attack Israel and is widely believed to be developing nuclear weapons, has been expanding its influence in Syria and in Lebanon through Hezbollah and other proxy terrorist groups. Although Iran's activities have not directly affected the political and economic conditions in Israel, Iran's purpose is widely believed to take control of the Middle East, including Israel. Israel has responded with attacks on Iranian military operations in Syria. These events and any future political, economic and military instability have the potential to interrupt our operations by damaging our facilities (to the extent rocket attacks against Israel reach the region of our headquarters) or preventing our employees, officers and directors from working. Such interruptions or stoppages may result in a material adverse effect on our business, operations and results of operations.

Our commercial insurance may leave us subject to a risk of a loss if a terrorist attack or act of war occurs.

Our commercial insurance does not cover losses that may occur as a result of an event associated with the security situation in the Middle East. The reinstatement value of direct damages that are caused by terrorist attacks or acts of war that the Israeli government is currently committed to covering might not be maintained or, if maintained, might not 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. Any armed conflict involving Israel could adversely affect our operations and results of operations.

Our operations may be disrupted by the obligation of our employees to perform military service.

As of December 31, 2021, we had 67 employees based in Israel, certain of whom may be called upon to perform up to 54 days (and in the case of non-officer commanders or officers, up to 70 or 84 days, respectively) of military reserve duty in each three-year period until they reach the age of 40 (and in some cases, depending on their specific military profession, up to 45 or even 49 years of age). In certain emergency circumstances, these employees may be called to immediate and unlimited active duty. Our operations could be disrupted by the absence of a significant number of employees related to military service, which could materially adversely affect our business and results of operations.

Boycotts and various Middle Eastern business restrictions in the region may adversely impact our ability to operate sell our products.

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 whether as a result of hostilities in the region or otherwise. In addition, there have been increased efforts by activists to cause companies and consumers to boycott Israeli goods based on Israeli government policies. Recently, Israel has signed bilateral peace agreements with several Middle Eastern (including Arab) countries, forging new economic ties with them. Nevertheless, if the actions by boycott activists become more widespread and successful, that may adversely impact our ability to sell our products.

Provisions of Israeli law and our articles of association may delay, prevent or otherwise impede a merger with, or an acquisition of, us, even when the terms of such a transaction are favorable to us and our shareholders.

Israeli corporate law regulates mergers, requires tender offers for acquisitions of shares above specified thresholds, requires special approvals for transactions involving directors, officers or significant shareholders and regulates other matters that may be relevant to such types of transactions. For example, a tender offer for all of a company's issued and outstanding shares can only be completed if the acquirer receives positive responses from the holders of at least 95% of the issued share capital. Completion of the tender offer also requires approval of a majority of the offerees that do not have a personal interest in the tender offer, unless, following consummation of the tender offer, the acquirer would hold at least 98% of the company's outstanding shares. Furthermore, the shareholders, including those who indicated their acceptance of the tender offer, may, at any time within six months following the completion of the tender offer, petition an Israeli court to alter the consideration for the acquisition, unless the acquirer stipulated in its tender offer that a shareholder that accepts the offer may not seek such appraisal rights. See "ITEM 10.B. Articles of Association—Acquisitions Under Israeli law" for additional information.

Furthermore, Israeli tax considerations may make potential transactions unappealing to us or to our shareholders whose country of residence does not have a tax treaty with Israel exempting such shareholders from Israeli tax. 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 a number of conditions, including, in some cases, a holding period of two years from the date of the transaction during which sales and dispositions of shares of the participating companies are subject to certain restrictions. 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 disposition of the shares has occurred.

We have received Israeli government grants for certain research and development activities. The terms of those grants require us to satisfy specified conditions and to pay penalties in addition to repayment of the grants upon certain events.

Our research and development efforts have been financed in part through grants from the Israeli Innovation Authority ("IIA"), formerly operating as the Israeli Office of the Chief Scientist (the "OCS"). The total gross amount of grants actually received by us from the IIA, including accrued LIBOR interest (or such other interest rate that the IIA may set in the future) and net of royalties actually paid as of December 31, 2021, totaled approximately 13.7 million and the amortized cost (using the interest method) of the liability as of that date totaled approximately 8.1 million. As of December 31, 2021, we had accrued and paid net royalties to the IIA in an amount of 0.36 million. As of December 31, 2018 we determined that we will no longer be supported by the IIA. As a result, we did not submit applications for IIA grants in 2020 and 2021 and we do not plan to submit in 2022.

The IIA grants that we have received are repayable by payment of royalties from the sale of products developed as part of the programs for which grants were received. Our obligation to pay these royalties is contingent on our actual sale of such products and services. In the absence of such sales, no payment of such royalties is required.

Even following full repayment of any IIA grants, we must nevertheless continue to comply with the requirements of the Encouragement of Research, Development and Technological Innovation in the Industry Law, 5744-1984 (formerly known as the Law for the Encouragement of Industrial Research and Development, 5744-1984), and related regulations (collectively, the "Innovation Law"). When a company develops know-how, technology or products using IIA grants, the terms of these grants and the Innovation Law restrict the transfer outside of Israel of such know-how, and the manufacturing or manufacturing rights of such products, technologies or know-how, without the prior approval of the IIA. Therefore, if aspects of our technologies are deemed to have been developed with IIA funding, the discretionary approval of an IIA committee would be required for any transfer to third parties outside of Israel of know-how or manufacturing or manufacturing rights related to those aspects of such technologies. We may not receive those approvals. Furthermore, the IIA may impose certain conditions on any arrangement under which it permits us to transfer technology or development out of Israel.

The transfer of IIA-supported technology or know-how or manufacturing or manufacturing rights related to aspects of such technologies outside of Israel may involve the payment of significant penalties and other amounts, depending upon the value of the transferred technology or know-how, the amount of IIA support, the time of completion of the IIA-supported research project and other factors. If our products are manufactured outside of Israel, assuming we receive prior approval from the IIA for the foreign manufacturing, we may be required to pay increased royalties. The increase in royalties depends on the manufacturing volume that is performed outside of Israel. These restrictions and requirements for payment may impair our ability to sell our technology assets outside of Israel or to outsource or transfer development or manufacturing activities with respect to any product or technology outside of Israel. Furthermore, the consideration available to our shareholders in a transaction involving the transfer outside of Israel of technology or know-how developed with IIA funding (such as a merger or similar transaction) may be reduced by any amounts that we are required to pay to the IIA.

It may be difficult to enforce a judgment of a U.S. court against us, our officers and directors or the Israeli experts named in this annual report in Israel or the United States, to assert U.S. securities laws claims in Israel or to serve process on our officers and directors and these experts.

We are incorporated in Israel. All of our executive officers and three of our directors listed in this annual report reside outside of the United States, and most of our assets and most of the assets of these persons are located outside of the United States. Therefore, a judgment obtained against us, or any of these persons, including a judgment based on the civil liability provisions of the U.S. federal securities laws, may not be collectible in the United States and may not be enforced by an Israeli court. It also may be difficult for you to effect service of process on these persons in the United States or to assert U.S. securities law claims in original actions instituted in Israel. Israeli courts may refuse to hear a claim based on an alleged violation of U.S. securities laws reasoning that Israel is not the most appropriate forum in which to bring such a claim. In addition, even if an Israeli court agrees to hear a claim, it may determine that Israeli law and not U.S. law is applicable to the claim. If U.S. law is found to be applicable, the content of applicable U.S. law must be proven as a fact by expert witnesses, which can be a time-consuming and costly process. Certain matters of procedure will also be governed by Israeli law. There is little binding case law in Israel that addresses the matters described above. As a result of the difficulty associated with enforcing a judgment against us in Israel, you may not be able to collect any damages awarded by either a U.S. or foreign court.

Your rights and responsibilities as a shareholder will be governed by Israeli law, which differs in some material respects from the rights and responsibilities of shareholders of U.S. companies.

Since we are incorporated under Israeli law, the rights and responsibilities of our shareholders are governed by our articles of association and Israeli law. These rights and responsibilities differ in some respects from the rights and responsibilities of shareholders in U.S.-based corporations. In particular, a shareholder of an Israeli company has a duty to act in good faith and in a customary manner in exercising its rights and performing its obligations towards 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 certain matters, such as an amendment to the company's articles of association, an increase of the company's authorized share capital, a merger of the company and approval of related party transactions that require shareholder approval. A shareholder also has a general duty to refrain from discriminating against other shareholders. In addition, a controlling shareholder or a shareholder who knows that it possesses the power to determine the outcome of a shareholders' vote or to appoint or prevent the appointment of an office holder in the company or has another power with respect to the company, has a duty to act in fairness towards the company. However, Israeli law does not define the substance of this duty of fairness. See "ITEM 6.C. Board Practices." Some of the parameters and implications of the provisions that govern shareholder behavior have not been clearly determined. These provisions may be interpreted to impose additional obligations and liabilities on our shareholders that are not typically imposed on shareholders of U.S. corporations.

Additionally, the quorum requirements for meetings of our shareholders are lower than is customary for domestic issuers. As permitted under the Companies Law, pursuant to our articles of association, the quorum required for an ordinary meeting of shareholders will consist of at least two shareholders present in person, by proxy or by other voting instrument in accordance with the Companies Law, who hold at least 25% of our outstanding ordinary shares. For an adjourned meeting at which a quorum is not present, the meeting may generally proceed irrespective of the number of shareholders present at the end of half an hour following the time fixed for the meeting.

General Risk Factors

If equity research analysts do not continue to publish research or reports about our business or if they issue unfavorable commentary or downgrade our ordinary shares, the price of our ordinary shares could decline.

The trading market for our ordinary shares relies in part on the research and reports that equity research analysts publish about us and our business. We do not have control over these analysts and we do not have commitments from them to write research reports about us. The price of our ordinary shares could decline if no research reports are published about us or our business, or if one or more equity research analysts downgrades our ordinary shares or if those analysts issue other unfavorable commentary or cease publishing reports about us or our business.

Item 4. INFORMATION ON THE COMPANY

A. History and Development of the Company

Our History

MediWound Ltd. ("MediWound") is a company limited by shares organized under the laws of the State of Israel in January 2000. We are registered with the Israeli Registrar of Companies. Our registration number is 51-289494-0. Our principal executive offices are located at 42 Hayarkon Street, Yavne 8122745, Israel, and our telephone number is +972 (77)-971-4100. Our website address is www.MediWound.com. Information contained on, or that can be accessed through, our website does not constitute a part of this annual report and is not incorporated by reference herein. We have included our website address in this annual report solely for informational purposes. Our agent for service of process in the United States is Puglisi & Associates, located at 850 Library Avenue, Suite 204, Newark, Delaware 19711, and its telephone number is +1 (302) 738-6680. The 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.

Principal Capital Expenditures

See “ITEM 5.B. Liquidity and Capital Resources.”

B. Business Overview

We are a biopharmaceutical company that develops, manufactures and commercializes novel, cost effective, bio-therapeutic solutions for tissue repair and regeneration. Our strategy leverages our breakthrough enzymatic technology platform into a diversified portfolio of biotherapeutics across multiple indications to pioneer solutions for unmet medical needs. Our current portfolio is focused on next-generation protein-based therapies for burn and wound care and tissue repair.

Our first innovative biopharmaceutical product, NexoBrid, has received marketing authorization in Europe and other international markets for removal of dead or damaged tissue, known as eschar, in adults with deep partial- and full-thickness thermal burns, also referred to as severe burns. NexoBrid, a concentrate of proteolytic enzymes enriched in bromelain, represents a new paradigm in burn care management, and our clinical trials have demonstrated, with statistical significance, its ability to non-surgically and rapidly remove the eschar earlier relative to existing standard of care upon patient admission, without harming viable tissues. In September 2020, the FDA accepted for review our Biologics License Application (“BLA”), which was based on acute data, including primary, secondary and safety endpoints, as well as 12-month safety follow-up data derived from our Phase 3 pivotal study. In June 2021, we received a Complete Response Letter (“CRL”) from the FDA stating that our BLA was not approved. We had a Type A meeting with the FDA in October 2021 to discuss a path forward for resubmission, in which we gained clarity on a path forward for resubmission of the BLA, and we plan to resubmit our BLA for NexoBrid in mid-2022.

We commercialize NexoBrid globally through multiple sales channels. We sell NexoBrid to burn centers in the European Union, United Kingdom, Norway, Switzerland and Israel, primarily through our direct sales force, focusing on key burn centers and Key Opinion Leaders ("KOL") management, while establishing additional local distribution channels to extend our outreach in the European Union. In the United States, we entered into exclusive license and supply agreements with Vericel Corporation to commercialize NexoBrid in North America upon FDA's approval. We have signed distribution agreements with local distributors in multiple international markets, focusing in Asia Pacific, EMEA, CEE and LATAM, which are responsible for obtaining local marketing authorization within the relevant territory.

EscharEx, our next-generation enzymatic therapy under development, is a topical biological drug candidate for the debridement of chronic and other hard-to-heal wounds. EscharEx active pharmaceutical ingredient (API) is a concentrate of proteolytic enzymes enriched in bromelain. In two completed phase 2 trials, EscharEx was well tolerated and has demonstrated safety and efficacy in the debridement of various chronic and other hard-to-heal wounds, within a few daily applications. EscharEx is an investigational product, currently under a U.S. phase 2 study.

Our third innovative product candidate, MW005, is a topically applied biological drug candidate for the treatment of non-melanoma skin cancers, based on the same API of NexoBrid and EscharEx products, a concentrate of proteolytic enzymes enriched in bromelain. We launched a new clinical development program to evaluate our drug product candidate MW005 in patients with non-melanoma skin cancer. The Clinical development program of MW005 is supported by the results from several toxicological and other preclinical studies, a clinical case series, as well as vast clinical experience from NexoBrid and EscharEx, which share the same active substance.

We manufacture NexoBrid, EscharEx and our product candidates in our state-of-the-art, cGMP-compliant, sterile pharmaceutical products manufacturing facility at our headquarters in Yavne, Israel.

Key Recent Developments

NexoBrid

In June 2021, we received a CRL from the FDA stating that our BLA seeking the approval of NexoBrid for eschar removal in adults with deep partial-thickness and/or full-thickness thermal burns was not approved. The FDA identified issues related to the Chemistry, Manufacturing and Controls ("CMC") section of the BLA and requested additional CMC information; The FDA also stated that inspections of NexoBrid's manufacturing facilities in Israel and Taiwan are required before the FDA can approve the BLA, but it was unable to conduct the required inspections during the current review cycle due to COVID-19 related travel restrictions. In addition, the CRL cited certain observations identified during good clinical practice (GCP) inspections related to the U.S. Phase 3 study (DETECT), and requested that we provide its perspective on the potential impact, if any, of these observations on the efficacy findings in the study. Following a productive Type A meeting conducted with the FDA in October 2021, we gained clarity on a path forward for resubmission of our NexoBrid BLA, which is anticipated in mid-2022.

In July 2021, we announced positive results from our pivotal NexoBrid phase 3 pediatric clinical study (CIDS) for eschar removal of severe thermal burns, including the 12-month safety follow-up. The study met all three primary endpoints with a high degree of statistical significance, as well as certain secondary endpoints. NexoBrid demonstrated a significant reduction in time to achieve complete eschar removal and significant reduction in wound area requiring surgical excision while demonstrating non-inferiority to standard-of-care in quality of scars. In addition, the study showed that NexoBrid was safe and well-tolerated. The long-term follow-up for cosmesis and function, quality of life and safety measurements is ongoing, and data is expected in the first half of 2023.

In February 2022 we announced that the Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response within the U.S. Department of Health and Human Services, has expanded its awarded contract with us by providing supplemental funding of $9 million to support the NexoBrid BLA resubmission with the FDA and the ongoing expanded access treatment protocol (NEXT).

In February 2022, we announced that the U.S. Department of Defense (DoD), through the Medical Technology Enterprise Consortium (MTEC), has awarded MediWound a $1.7 million research project for the development of NexoBrid as a non-surgical solution for field-care burn treatment for the U.S. Army.

In March 2022, we entered into an underwriting agreement with Oppenheimer & Co., Inc., a representative of the several underwriters (the "Underwriters"), relating to the issuance and sale of an aggregate of 5,208,333 of our ordinary shares at a price per share equal to $1.92. Total gross proceeds of the offering was approximately $10.0 million. The offering closed on March 7, 2022 and we received approximately $8.7 million in net proceeds, after deducting underwriting discounts and commissions and estimated offering expenses. Certain entities affiliated with CBI purchased approximately $2.8 million of ordinary shares in the offering at the public offering price. The Underwriters received the same underwriting discount on the shares purchased by these entities as they will on any other shares sold to the public in this offering. The securities purchased by these entities are subject to lock-up agreements with the Underwriters. We also granted the Underwriters a 30-day option to purchase up to an additional 781,249 ordinary shares at the public offering price, less underwriting discounts and commissions.

EscharEx

In January 2022, we announced positive topline results from the U.S.phase 2 study of EscharEx for the debridement of venous leg ulcers (VLUs). These topline results demonstrated that the study met its primary endpoint, demonstrating that patients treated with EscharEx had a statistically significant higher incidence of complete debridement compared to the gel vehicle, with a p-value of 0.004 and no safety issues were observed. Patient follow-up is ongoing and additional data, including secondary and exploratory endpoints as well as additional safety measurements, which will allow further evaluation of clinical benefits, is expected in the second quarter of 2022.

In addition, in December 2021, we announced positive initial data from our ongoing open-label, phase 2 pharmacology study of EscharEx in the debridement of VLUs and diabetic foot ulcers (DFUs). Based on this initial data, EscharEx demonstrated safe and effective debridement of lower leg ulcers within a few daily applications. We expect to share the full data set from this study in the first half of 2022.

MW005

In July 2021, we initiated a U.S. phase I/II study of MW005 for the treatment of low-risk basal cell carcinoma (BCC). We expect data from the study to be available in the first half of 2022.

Our Focus:

Burn Care

NexoBrid, a concentrate of proteolytic enzymes enriched in bromelain, is an easy to use, topically-applied product that removes eschar in four hours without harming the surrounding healthy tissues. Eschar removal is a critical first step in the successful healing of severe burns and chronic and other hard-to-heal wounds. Under existing SOC, burn eschar may be removed either by employing certain existing topical agents that have been found to be minimally effective or that take a significantly longer period of time to work, or by resorting to non-selective surgery, which is traumatic and may result in loss of blood and viable tissue. NexoBrid's rapid and selective debridement alleviates the known risks associated with eschar, such as infection, eventual sepsis, wound deterioration and consequential scarring, and it allows physicians to reach an informed decision on further treatment at an earlier stage by direct visual assessment of the actual burn depth. Furthermore, NexoBrid minimizes the burden associated with invasive surgical procedures, reduces the need for skin grafting and sacrifice of healthy tissue from donor sites on a patient's body and generally results in a more favorable overall long-term patient outcome. NexoBrid has been investigated in hundreds of patients across more than 22 countries and four continents in nine completed Phase 2, Phase 3 and post-marketing clinical studies. Over 9,000 burn patients have been treated with NexoBrid in the market since 2013 and the safety and efficacy data reported from post marketing data sources are consistent with the data available from clinical trials and no new safety signals were observed.

There have been hundreds of presentations and several award winning abstracts of NexoBrid in international and national scientific conferences, and NexoBrid has been presented in about 90 peer-reviewed papers, resulting in support of burn specialists and key opinion leaders. Awareness of NexoBrid continues to grow through our marketing efforts in countries where NexoBrid is approved and our and multinational clinical development.

Burn Wounds

Burns are life threatening and debilitating traumatic injuries causing considerable morbidity and mortality. A burn may result from thermal, electrical or chemical means that destroy the skin to varying depths. According to Critical Care, an international clinical medical journal, burns are also among the most expensive traumatic injuries because of long and costly hospitalization, rehabilitation and wound and scar treatment.

Most burn injuries involve part of or the entire thickness of the skin and in some cases, the deeper subcutaneous fat tissue or underlying structures. The severity of the burn depends on three main factors:

- The extent of the surface that the burn occupies is usually referred to as percent of total body surface area ("TBSA"). A burn on an adult's entire palm would generally amount to 1% TBSA, and the average hospitalized patient has a burn covering approximately 9% TBSA. Burns covering more than 15-20% TBSA usually require hospitalization and may result in dehydration, shock and increased risk of mortality.

- The depth of the burn, referred to in terms of "degree" is generally classified into four categories:

    - *Superficial or first degree burns.* Such burns do not penetrate the basal membrane and usually heal naturally.

    - *Dermal/partial thickness or second degree burns.* Such burns are characterized by varying amounts of damaged dermis and can be further subdivided into superficial and deep partial-thickness burns. Superficial partial-thickness burns may heal spontaneously after removal of the covering thin eschar. Conversely, deep partial-thickness burns are often difficult for physicians to accurately diagnose before eschar removal and may progress and transform into full-thickness burns if not debrided in a timely manner, depending on the magnitude of latent tissue death of the surrounding skin.

    - *Full thickness or third degree burns.* Such burns are characterized by death of the entire dermal tissue down to the subcutaneous fat and must be debrided and treated by autografting, which is the process of harvesting skin from healthy donor sites on a patient's body and transplanting it on the post-debridement, clean wound bed.

    - *Fourth degree burns.* Such burns, which are rare, extend beyond the subcutaneous fat tissue into the underlying structures, such as muscle or bone, and also require debridement and further substantial treatment.

- Other factors include the age of the victim, the body part where the burn occurred and any co-morbidities of the patient. For example, some patients may require hospitalization regardless of the TBSA or degree of the burn, such as children, the elderly or victims with burns to the extremities, joints or head/neck area or with co-morbidities such as smoke inhalation, diabetes or obesity.

When patients are hospitalized for a severe burn, the first step in the treatment after patient stabilization and resuscitation is usually eschar removal. The eschar is the burned tissue in the wound, which is deprived of blood and isolated from all natural systemic defense mechanisms. Debridement is an essential first step in the treatment of patients with severe burns, allowing for:

- the prevention of local infection, sepsis (a systemic inflammatory response caused by severe infection) and additional damage to surrounding viable tissue; and

- the initiation of the body's healing process and scar prevention.

In addition to minimizing the possibility of additional complications, once the eschar is removed, a physician may properly diagnose the true extent of the trauma by a direct visual assessment of the clean wound bed. An informed treatment strategy can be decided upon only if the depth of the burn and extent of the tissue damage is known. Diagnosis of burn depth is difficult, especially because the burn commonly changes its appearance during the first days after injury due to burn progression. Burns that are initially difficult to classify due to the presence of eschar are referred to as "indeterminate" burns. This ambiguity can delay the assessment of the burn depth and formulation of proper treatment. Unless the burns are life-threatening, definitive treatment is postponed for several days post-injury until diagnosis is clearer, when burn progression by death of the surrounding and underlying tissue has already occurred and ended. During this delay, local and systemic effects of post-burn inflammation and bacterial contamination can occur. Therefore, earlier, selective eschar removal is essential to prevent eschar-related complications and to allow the physician to reach an informed decision on further treatment.

Currently, there are two main treatment modalities for debridement:

- Surgical debridement
    - Surgical debridement predominantly includes tangential excision, a procedure in which a surgeon amputates the entire dead tissue mass, layer after layer, down to healthy, viable tissue. The excision is extended into healthy intact tissue to make sure that no trace of the eschar remains, resulting in up to an estimated 30-50% of healthy tissue being excised during this procedure. Other methods include dermabrasion, in which a mechanically powered, hand-held rotating abrading cylinder is used to slowly scrape off tissue, and hydro surgery, in which a high-pressure flow of water abrades the tissue. These alternative methods have attempted to limit the trauma associated with tangential excision, but entail spray of contaminated eschar or take a significantly longer time to complete than tangential excision.
    - The benefits of surgical eschar removal are that it is usually fast and effective. Disadvantages include the significant trauma of the procedure, associated blood loss, risk of surgery in delicate areas of the body such as hands, added costs, and, most importantly, the loss of viable tissue that necessitates additional surgical procedures for harvesting skin from healthy donor sites and autografting.
    - Due to the disadvantages of surgery in extensive burns some surgeons limit their debriding surgery to only a part of the affected area in a single session (15-30% TBSA in most centers), thus delaying full debridement by days. After several days, complications related to eschar contamination may begin and some of the benefits of the earlier debridement may not be realized. On the other hand, when excising burns immediately, all suspected necrotic tissue will be excised, inevitably resulting in over-excision, especially in “indeterminate” burns, as after surgical excision, the remaining skin often no longer has any spontaneous healing potential and will heal only by autografting.
- Non-surgical debridement
    - Non-surgical debridement includes many different treatment options that do not require direct surgical removal of the skin to remove eschar. With non-surgical debridement, the eschar is naturally, but slowly, removed by contaminant microorganisms, tissue autolysis, or self-decomposition, and the inflammatory process that may lead to serious local and systemic complications. In seeking to facilitate such natural processes, topical medication, anti-microbial agents, enzymes and biological/chemical applications are often applied onto the eschar.
    - The benefits of this approach are that it is non-surgical, reduces trauma to the patient and is easier to apply. Disadvantages include numerous dressing changes and mechanical scraping with limited debridement efficacy. This prolongs the eschar removal process, which may lead to death of the tissue surrounding the initial burn wound, causing partial-thickness wounds to transform into full-thickness wounds and forming granulation tissue that may develop into heavy scars.

As demonstrated in our clinical trials, NexoBrid combines the advantages of surgical and non-surgical debridement modalities by providing rapid and effective eschar removal while not harming viable tissues. This allows for earlier direct visual assessment of the burn wound in order to formulate proper treatment.

Market Opportunity

Severe burns require specialized care in hospitals or burn centers. Approximately 100,000 patients with severe burns are hospitalized every year in the United States and Europe. The prevalence of patients with severe burns is even higher in emerging economies. For example, approximately 400,000 patients are hospitalized every year with burns in India according to a study conducted by IMS Health. The severe burn patients are predominantly treated by specialists in approximately 250 burn centers in Europe and the United States, as well as at burn units of large hospitals in Europe. We believe these patients can benefit from NexoBrid’s effective and selective, non-surgical eschar removal.

In addition to our current marketing of NexoBrid in Europe, we have signed local distribution agreements for distribution of NexoBrid in Europe, Latin America, certain Asia-Pacific countries, members of the Commonwealth of Independent States (“CIS”), and the Middle East and we plan to target additional markets in these territories by leveraging our approved registration file for additional regional marketing authorizations.

In addition to the market opportunities for NexoBrid discussed above, we believe that NexoBrid has the potential to play a critical role in the event of a mass casualty incident ("MCI"), which is generally defined as any incident in which emergency medical services resources, such as personnel and equipment, are overwhelmed by the number and severity of casualties. A variety of public emergencies may give rise to an MCI, such as terrorist attacks, natural disasters, fires and explosions. One example of an MCI is a mass burn casualty disaster, which is defined by the American Burn Association as a catastrophic event in which the number of burn victims exceeds the capacity of the local burn center to provide optimal care. If a significant number of burn victims arrive at a burn center following an event, some victims may go untreated until the bottleneck is resolved. The use of non-surgical means that are capable of providing rapid eschar removal without harming healthy tissues, particularly during public health emergencies, could potentially reduce the time, labor and resource burdens associated with the current standard-of-care, thereby enabling the treatment of more patients. In the event of a mass burn casualty disaster, healthcare professionals can use NexoBrid to begin treatment at the patient's bedside without the need for a surgical team and facilities. NexoBrid has demonstrated in clinical studies, with statistical significance, its ability to non-surgically and rapidly remove eschar in a single four-hour application. Once the acute treatment has been completed, the wound can be covered with available means and further managed once the MCI is under control and the bottlenecks resolved. NexoBrid has been recognized by BARDA as a medical countermeasure for treatment of burns in the event of a MCI.

BARDA Contracts

In September 2015, we were awarded the First BARDA Contract for treatment of thermal burn injuries, which was valued at up to $112 million. In July 2017 and in May 2019, BARDA expanded its commitment by an aggregate supplemental amount of $41 million. In March 2020, BARDA further expanded its commitment by additional $5.5 million to support emergency readiness for NexoBrid deployment upon request of use of NexoBrid in mass casualty situations and in February 2022 BARDA expanded its awarded contract by providing supplemental funding of $9 million to support the NexoBrid BLA resubmission to the FDA and the continuous expanded access program (collectively the "First BARDA Contract").

The First BARDA Contract is our primary contract with BARDA and relates to the advancement of the development and manufacturing, as well as the procurement of NexoBrid as a medical countermeasure as part of U.S. preparedness for mass casualty events.

Under the First BARDA Contract, BARDA provided technical assistance and a total of up to $91 million in funding for NexoBrid development activities required to achieve U.S. marketing approval from the FDA. These activities include the NexoBrid Phase 3 (DETECT) study and subsequent requirements for BLA submission, the ongoing Phase 3 pediatric (CIDS) study and the NexoBrid expanded access treatment protocol (NEXT). In January 2020, BARDA committed an additional $16.5 million to procure NexoBrid as part of the HHS mission to build national preparedness for public health medical emergencies. The contract further includes a $10 million option to fund development of other potential NexoBrid indications and an option to procure additional NexoBrid valued at up to $50 million.

In September 2018, we were awarded the second BARDA contract (the "Second BARDA Contract"), which is an additional, separate contract to develop NexoBrid for the treatment of Sulfur Mustard injuries as part of BARDA's preparedness for mass casualty events. The Second BARDA Contract provides approximately $12 million of funding to support research and development activities up to pivotal studies in animals under the U.S. FDA Animal Rule and contains options for BARDA to provide additional funding of up to $31 million for additional development activities, animal pivotal studies, and the BLA submission for licensure of NexoBrid for the treatment of Sulfur Mustard injuries.

As of December 31, 2021, the Company has received approximately $70 million in funding in the aggregate, from BARDA under the two contracts, and an additional $14.6 million for procurement of NexoBrid for U.S. emergency preparedness.

Each BARDA contract may be terminated by BARDA at any time at BARDA's discretion.

NexoBrid Clinical History

NexoBrid, our innovative biopharmaceutical product, has received marketing authorization from the EMA and the Israeli, Argentinean, South Korean, Russian, Peruvian, Chilean, Taiwanese, Ukrainian, Eurasian states and United Arab Emirates Ministries of Health for the removal of eschar in adults with deep partial- and full-thickness thermal burns. The active ingredient of NexoBrid is a concentrate of proteolytic enzymes enriched in bromelain extracted from the pineapple stems. Proteolysis is a breakdown of proteins into smaller building blocks, polypeptides or amino acids. Our research and development strategy is centered around our validated proteolytic enzyme platform technology, focused on next-generation bio-active therapies for burn and wound care and biological medicinal products for tissue repair. Our research and development team further developed and optimized our enzymatic platform technology, which is the basis for NexoBrid, EscharEx and all other pipeline product candidates. One vial of NexoBrid containing 2 grams of concentrate of proteolytic enzymes enriched in bromelain is sufficient for treating a burn wound area of 1% total body surface area (TBSA).

We developed NexoBrid to fulfill the previously unmet need for a non-surgical effective and selective debriding agent that combines the efficacy and speed of surgery with the non-invasiveness of non-surgical methods. NexoBrid enhances the ability of physicians to conduct an earlier direct visual assessment of the burn depth to reach an informed decision on further treatment as well as to reduce the surgical burden and achieve a favorable long-term patient outcome.

NexoBrid has been investigated in hundreds of patients across 22 countries and four continents in nine completed Phase 2 and Phase 3 and post-marketing clinical studies. While we are marketing our product for the removal of eschar in burn wounds under the name “NexoBrid,” in clinical trials the product has been referred to as “Debridase” and “Debrase.”

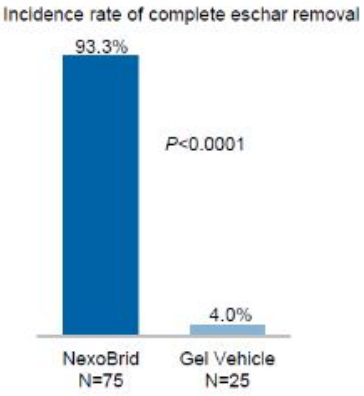
The following table sets forth information regarding the completed clinical trials of NexoBrid:

	Trial 1	**Trial 2**	**Trial 3**	**Trial 4**	**Trial 5**	**Trial 6**	**Trial 7**	**Trial 8**	**Trial 9**
Study Type	Retrospective Phase 2 Investigator initiated	Dose range Phase 2	Prospective Phase 2 IND/FDA	Phase 2 IND/FDA	Phase 3 EMA	Phase 3b EMA	Phase 2 EMA	Post approval safety study EMA	Phase 3 IND/FDA
Design	Data collected from files of patients treated with NexoBrid	Parallel, controlled, observer-blind, randomized, single-center	Parallel, controlled, observer-blind, three-arm, randomized, multi-center	Parallel, controlled, open label, three-arm, randomized, single-center	Parallel, controlled, open label, two-arm, randomized, multi-center	Parallel, controlled, blinded, two-arm, multi-center	Open label, single-arm, multi-center	Observational retrospective data collection	Parallel, controlled, open label, three-arm, randomized, multi-center
Main Objectives	Safety and efficacy	Comparison of efficacy and safety	Safety and efficacy	Safety	Safety Efficacy	Long-term scar assessment Quality of life	Safety and pharmacokinetics Efficacy	Effectiveness of the risk minimization activities	Safety Efficacy
Wound Types	Deep partial/full thickness thermal burns	Deep partial /full thickness thermal burns	Deep partial /full thickness thermal burns	Deep partial /full thickness thermal burns	Deep partial/ full thickness thermal burns	Scar formation	Deep partial/full thickness thermal burns	Burns which were treated with NexoBrid in the market	Deep partial/ full thickness thermal burns
Number of Patients	154	20	140	30	182	89	36	160	175
Study Length	1985-2000	2002-2005	2003-2004	2006-2007	2006-2009	2011	2009-2015	2017-2019	2015-2020
Location	Israel	Israel	International	United States	International	International	International	Europe	International

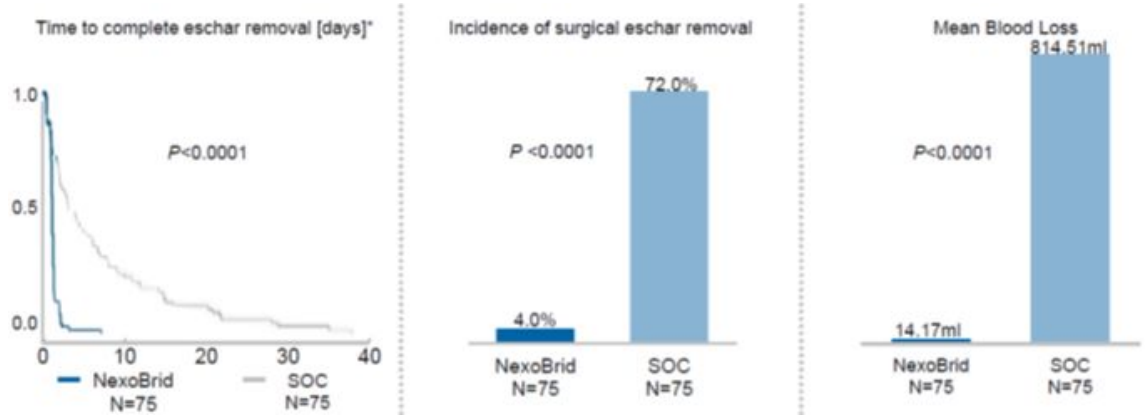
Recent completed clinical trials

U.S. Phase 3 Study – DETECT study (Trial 9)

The DETECT study is a prospective, multicenter, multinational, randomized, controlled, assessor blinded Phase 3 study, performed in subjects with thermal burns, to evaluate the efficacy and safety of NexoBrid compared to Gel Vehicle and compared to SOC in 175 hospitalized patients with severe burns of up to 30% TBSA randomized in a 3:1:3 ratio, with 12-month and 24-month follow-ups. The study involved 44 burn centers. The study objectives were to evaluate the efficacy and safety of NexoBrid by removing burn eschar earlier and reducing surgical burden and related blood loss in hospitalized patients with severe burns. Complete eschar removal was the primary endpoint of the study and was tested against the Gel Vehicle control arm. The primary analysis was based on whether complete eschar removal was achieved in all target wounds of a patient. The analysis compared all randomized patients to the NexoBrid arm to all randomized patients to the Gel Vehicle control arm. Secondary endpoints included reduction in the need for surgical eschar removal (surgical burden), earlier eschar removal, and blood loss, which were tested against the SOC control arm. All secondary endpoints were analyzed and compared all patients randomized to the NexoBrid arm to all patients randomized to the SOC control arm. The study met its primary endpoint with statistical significance. Patients treated with NexoBrid demonstrated a significantly higher incidence of complete eschar removal compared with patients treated with the Gel Vehicle (NexoBrid: 93.3% (70/75) vs. Gel Vehicle: 4.0% (1/25), p<0.0001[1]).



The study included secondary endpoints that were all met with statistical significance and provided further insight on several efficacy parameters: (i) Patients treated with NexoBrid demonstrated shorter time to achieve complete eschar removal compared with patients treated with SOC (median time - NexoBrid: 1 day vs. SOC: 3.8 days, p<0.0001[2]); (ii) Patients treated with NexoBrid demonstrated a significantly lower incidence of surgical eschar removal compared with patients treated with SOC (NexoBrid: 4.0% (3/75) vs. SOC: 72.0% (54/75), p<0.0001[3]); (iii) and Patients treated with NexoBrid incurred significantly lower blood loss during the eschar removal procedure compared with patients treated with SOC (mean volume – NexoBrid: 14.2 ml vs. SOC: 814.5 ml, p<0.00014). In addition, Patients treated with NexoBrid had a non-inferior time to complete wound closure compared with patients treated with SOC (p=0.0003[5]). The study Data Safety Monitoring Board ("DSMB") concluded after all patients had been treated that the overall safety profile of NexoBrid in the study is consistent with the safety data known from previous studies.



[1] Fisher's exact test
[2] Generalized Wilcoxon-Gehan test
[3] Logistic regression model - Wald test
[4] Wilcoxon test pooled using Rubin's rules
[5] Accelerated failure time model
* Kaplan-Meier analysis

The twelve- and twenty four-month patients' follow-up safety data of cosmesis, function and quality of life were found to be comparable across all study arms, and no new safety signals were observed.

The study also serves to address our post approval commitment to EMA. This study is funded by BARDA. See "—BARDA Contracts" above.

Ongoing clinical trials

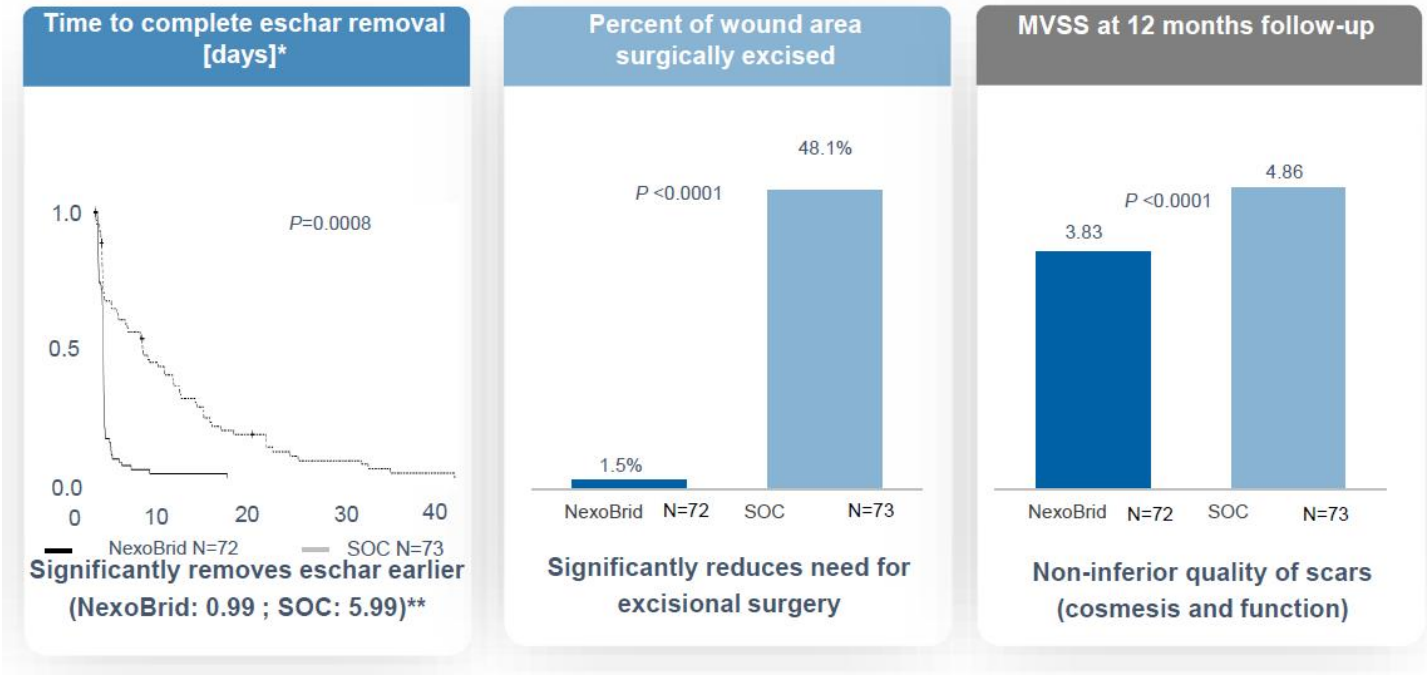
Pediatric investigational plan – CIDS study

The CIDS study is a Phase 3, multicenter, multinational, randomized, controlled, open-label study in children with thermal burns. The study objectives are to evaluate the efficacy and safety of treatment with NexoBrid compared with SOC in hospitalized children with severe thermal burns of 1% to 30% total body surface area (TBSA). We expanded this study also to United States burn centers, following approval of the study protocol by the FDA. The study is underway in accordance with a study design endorsed by the FDA and the EMA as part of the agreed Pediatric Investigational Plan ("PIP") to support extension of the indication to pediatric patients. The CIDS study includes pediatric patients of all ages, from newborn to eighteen years of age, offering NexoBrid to this important and sensitive group of patients. The primary endpoints evaluate early eschar removal, surgical burden and cosmesis and function with a 12-month follow-up.

The European Medicines Agency ("EMA") endorsed the study design as part of the agreed-upon Pediatric Investigational Plan ("PIP") to support the indication label expansion to include pediatric patients. The primary endpoints included early eschar removal, reduction of wound area surgically excised (surgical need) and non-inferiority cosmesis and function at twelve months follow-up from wound closure. Secondary endpoints included reduction in the need for surgical excision for eschar removal (surgical need), blood loss, reduction of the need for autograft in DPT wounds and non-inferiority in cosmesis and function at twenty-four months follow-up from wound closure. Additional extended long term cosmesis and function assessment at more than 30 months from wound closure was added to the protocol. Non-inferiority of the time to complete wound closure and other standard safety measurements were also compared with the SOC control arm.

The study was expanded to include burn centers in the United States following agreement with the FDA, under the same protocol with alignment to the U.S. phase 3 study (DETECT) protocol for adult population. The non-inferiority of cosmesis and function at twelve months and twenty-four months from wound closure were defined as safety measurements. In addition, reduction in surgical need was measured only by reduction in incidence of surgical excision for eschar removal.

In July 2021, we announced positive top-line results, which include acute phase and 12-month follow-up data analysis. The study enrolled 145 pediatric patients, from newborn to eighteen years of age, randomized to either NexoBrid or SOC at a ratio of 1:1, across 36 burn centers worldwide. The study met all three primary endpoints with a high degree of statistical significance, as well as certain secondary endpoints. NexoBrid demonstrated a significant reduction in time to achieve complete eschar removal and significant reduction in wound area requiring surgical excision while demonstrating non-inferiority to standard-of-care in quality of scars. In addition, the study showed that NexoBrid was safe and well-tolerated. The long-term follow-up for cosmesis and function, quality of life and safety measurements is ongoing, and data is expected in the first half of 2023. This study is funded by BARDA. See "—BARDA Contracts" above.



Expanded access treatment protocol (NEXT)

The NEXT protocol, which we initiated in October 2019, is an open-label, single-arm treatment protocol which allows for the treatment of up to 200 burn patients with deep partial- and full-thickness thermal burns up to 30 percent of total body surface area. In September 2020, the FDA agreed to allow the NEXT protocol to be expanded to include pediatric as well as adult burn patients. NEXT protocol is being funded by BARDA. See "—BARDA Contracts" above. NEXT has been designed to be consistent with current real-life burn treatment practices in the U.S. and up to 30 U.S. burn centers are anticipated to participate. We received FDA concurrence that patients can be treated under the NEXT protocol in a burn MCI that is not a declared national emergency. We have provided documents for consideration by the FDA supporting the use of NexoBrid in a declared national medical emergency contingent upon the FDA issuance of an Emergency Use Authorization (EUA). The EUA is a mechanism by which the FDA can allow an unapproved medical product that qualifies as a mass casualty medical countermeasure to be used in a public health emergency.

Wound Care

Our second innovative product candidate, EscharEx, is a bio-active therapeutic product under development for debridement of chronic and other hard-to-heal wounds. EscharEx is complementary to the large number of existing advanced wound healing therapies, which require a clean wound bed in order to heal the wound. EscharEx active substance (API) is a concentrate of proteolytic enzymes enriched in bromelain and as such, benefits from the wealth of existing development data on NexoBrid. The mechanism of action of EscharEx is mediated by the proteolytic enzymes that cleaves and removes the necrotic tissue and prepare the wound bed for healing. In two Phase 2 studies that we conducted, EscharEx well-tolerated and demonstrated safety and efficacy in the debridement of chronic and other hard-to-heal wounds, in a few daily applications. In the U.S, we are conducting a Phase 2 clinical study with the second generation EscharEx, for the treatment of venous leg ulcers (VLUs). The study is built on the positive data from the completed Phase 2 study of the first-generation EscharEx. The study is designed to assess the safety and efficacy of EscharEx compared to gel vehicle (placebo control) and non-surgical standard-of-care (either enzymatic or autolytic debridement). Topline results announced in January 2022 demonstrated that the study met its primary endpoint, demonstrating that patients treated with EscharEx had a statistically significant higher incidence of complete debridement compared to the gel vehicle, with a p-value of 0.004.

Chronic and Other Hard-to-Heal Wounds

The chronic and other hard-to-heal wound market consists of a broader addressable population of more than 14 million patients in Europe and the United States alone suffering from chronic wounds such as VLUs, Diabetic Foot Ulcers (DFUs), pressure ulcers and additional patients suffering from surgical/traumatic hard-to-heal wounds. Chronic and other hard-to-heal wounds represent a $25 billion burden to the U.S. healthcare system. Chronic and hard-to-heal wounds are caused by impairment in the biochemical and cellular healing processes due to local or systemic conditions and generally can take several weeks to heal, if not longer. Such wounds can lead to significant morbidity, including pain, infection, impaired mobility, hospitalization, reduced productivity, amputation and mortality. In each of the various wound types, the presence of the eschar is a frequent cause for "chronification" of wounds and the removal of eschar is the key step to commence healing. Eschar needs to be removed to prevent further deterioration of the wound that may result in additional adverse patient outcomes. If not effectively treated, these wounds can lead to potentially severe complications including further infection, osteomyelitis, fasciitis, amputation and mortality. Most advanced wound care therapies, including negative pressure wound therapy, such as V.A.C. Therapy, and skin substitutes such as Apligraf and Dermagraft and human amniotic tissue products, are complementary to our lead product candidate, EscharEx, as these products require a clean wound bed to effectively heal a wound. Four common chronic and other hard-to-heal wounds are:

- *Venous leg ulcers*. VLUs develop as a result of vascular insufficiency, or the inability for the vasculature of the leg to return blood back toward the heart properly. Based on our comprehensive market research study on EscharEx that involved more than 200 healthcare professionals in the U.S. and Europe, which was updated in 2019, the VLU overall prevalence is approximately 3.3 million (1% of total U.S. population). Furthermore, the annual incidence of VLUs in the U.S. alone, is approximately 960,000 (accounting for 45% recurrence), of which approximately 690,000 undergo debridement in a given year. These ulcers usually form on the sides of the lower leg, above the ankle and below the calf, and are slow to heal and often recur if preventative steps are not taken. The risk of VLUs can increase as a result of a blood clot forming in the deep veins of the legs, obesity, smoking, lack of physical activity or work that requires many hours of standing.

- *Diabetic foot ulcers*. Diabetes can lead to a reduction in blood flow, which can cause patients to lose sensation in their feet and may prevent them from noticing injuries, sometimes leading to the development of DFUs, which are open sores or ulcers on the feet that may take several weeks to heal, if ever. Based on our comprehensive market research study conducted in 2015 on EscharEx that involved more than 200 healthcare professionals in the U.S. and Europe and, which was updated in 2019, there are estimated 31 million diabetics in 2019 (9.4% of the U.S. population). The annual incidence of DFUs in the United States alone, is approximately 990,000 (accounting for 45% recurrence), of which approximately 820,000 undergo debridement in a given year.

- *Pressure ulcers.* Pressure ulcers form as a result of pressure sores, or bed sores, which are injuries to the skin or the tissue beneath the skin. Constant pressure on an area of skin reduces blood supply to the area and over time can cause the skin to break down and form an open ulcer. These often occur in patients who are hospitalized or confined to a chair or bed, and usually form over bony areas, where there is little cushion between the bone and the skin, such as lower parts of the body. Annually, 2.5 million pressure ulcers are treated in the United States in acute care facilities alone.

- *Surgical/traumatic wounds.* Surgical wounds form as a result of various types of surgical procedures such as investigative or corrective, minor or major, open (traditional) or minimal access surgery, elective or emergency, and incisions (simple cuts) or excision (removal of tissue), among others. Traumatic wounds form as a result of cuts, lacerations or puncture wounds, which have caused damage to the skin and underlying tissue. Severe traumatic wounds may require surgical intervention to close the wound and stabilize the patient. Surgical/traumatic hard-to-heal wounds develop for various reasons, such as local surgical complications, suboptimal closure techniques, presence of foreign materials, exposed bones or tendons and infection. In the United States, millions receive post-surgical wound care annually.

Market Opportunity

Currently, surgery (sharp debridement) is generally considered a first-line option. Sharp debridement is an effective method to debride a wound, however, requires surgically skilled physicians performing surgery with patients under, anesthesia, which in elderly patients with various co-morbidities is accompanied with a higher risk of local and systemic complications. Surgery may also involve hemorrhage which could be more difficult to control due to a high incidence of use of anticoagulants in this population. Surgery on wounds may very easily become infected with the infection propagating to surrounding soft and boney tissues ending in life threatening major complication or amputation. Very often even minor, limited sharp debridement exposes other sensitive tissue, such as tendons, deep vessels/nerves and bones that may become infected or may be severely damaged, necessitating additional, more extensive debridement or even amputation. Due to these limitations, chronic wounds are treated by conservative methods while autolytic and enzymatic debridement are most commonly-used non-sharp methods. This includes collagenase-based enzymatic debriding ointment, hydrogels and other topical dressings, which require numerous application sessions and a long time (6-8 weeks) to achieve a clean wound bed, if they achieve this at all. Thus, there is an unmet medical need for a non-surgical rapid and effective debridement agent for the outpatient setting, nursery care facilities and patients home. Given high demand for an effective non-surgical debridement technique outside of wound care clinic settings and clinical data generated to date, EscharEx has the potential to expand the current use of enzymatic debridement across all sites of care and achieve substantial market share. As documented in the Phase 2 study described below, EscharEx significantly improved the rate of complete debridement after few once-daily applications, thus potentially facilitating wound debridement without the need for surgery.

EscharEx Clinical History

EscharEx is a topical agent being developed for debridement of chronic and other hard-to-heal wounds, in order to fulfill an unmet need for a non-surgical rapid and effective debridement mean. EscharEx is based on the same active substance as NexoBrid but differs in other aspects, such as in formulation and presentation. Based on our current pre-clinical studies, the second generation EscharEx demonstrated even higher potency in lower doses, which could further contribute to EscharEx's efficacy and tolerability. This advanced generation of EscharEx has been designed in accordance with the current treatment workflow and reimbursement programs, providing a non-surgical easy-to-use, potent product for daily application, which we believe will enhance patient compliance and improve quality of care. Based on the feedback received from different stakeholders, we believe that our second generation EscharEx can better address the unmet medical need for a non-surgical rapid and effective product, particularly in the outpatient setting, where the majority of patients are treated, and has a greater potential to achieve substantial market share.

Second generation EscharEx is more differentiated from NexoBrid, which further limits the chances for competition between the two products.

Non-clinical safety studies performed with NexoBrid support EscharEx development, and we have already completed successfully bridging toxicology studies. In a pre-IND meeting the FDA stated that existing toxicology data for EscharEx, including cross-referenced NexoBrid data, could be sufficient to support initiation of clinical studies in the product. The FDA also stated that the second generation EscharEx formulation, manufacturing process and controls were sufficient to initiate dosing in Humans.

Completed clinical trials

We completed a first Phase 2 feasibility study in Israel for chronic and other hard-to-heal wound technology. In January 2017 we completed and announced the final results of a second Phase 2 prospective study in Israel and Europe. In November 2017, we announced the final results of a second cohort of the second Phase 2 study. Based on the completed studies, we believe that our product candidate may be effective for debridement of chronic and other hard-to-heal wounds.

First Phase 2 feasibility study—Israel

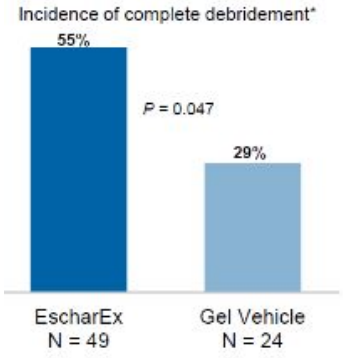
This first Phase 2 feasibility study was conducted in Israel to study the efficacy of our technology on chronic and other hard-to-heal wounds. The study assessed 24 patients at two sites. The results showed that our technology was effective in debriding various chronic and other hard-to-heal wound etiologies, such as DFUs, VLUs, pressure sores and trauma on diseased skin.

Second Phase 2 study—Israel/E.U. – First Cohort

This second Phase 2 study was a prospective, controlled, assessor-blinded, randomized, multi-center Phase 2 study in Israel and Europe. The study objectives were to evaluate the efficacy and safety of EscharEx in comparison to the Gel Vehicle[1] at a ratio of 2:1 for the treatment of a variety of chronic and other hard-to-heal wounds, in three etiologies, DFUs, VLUs and post-surgical or traumatic hard-to-heal wounds.

The primary endpoint assessed incidence of complete non-viable tissue removal (debridement) at the end of the debridement period (within up to 10 daily applications) and the secondary endpoints assessed various efficacy and safety endpoints, including wound bed preparation and wound healing.

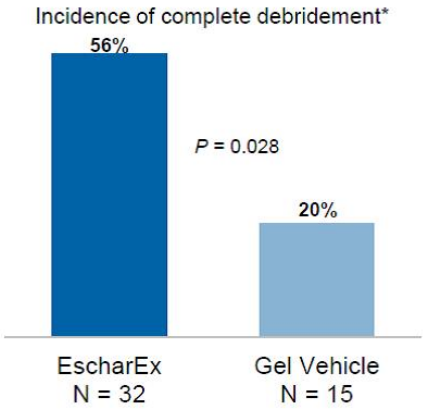
In January 2017 we reported final results of the first cohort of 73 patients. The average wound age in the EscharEx arm was more than double (72.8 weeks) that of the gel vehicle group (30.8 weeks). The average wound size was 33.6 cm^2 in the EscharEx arm vs. 25.8 cm^2 in the gel vehicle group. Despite the larger wounds and that wounds treated with EscharEx were older than wounds treated with gel vehicle (72.8 vs. 30.8 weeks), the study met its primary endpoint. EscharEx demonstrated a statistically significant higher incidence of complete debridement at the end of the debridement period. Patients treated with EscharEx demonstrated a higher incidence of complete debridement (55% or 27/49) compared with patients treated with the hydrogel[6] vehicle (29% or 7/24) with p=0.047.

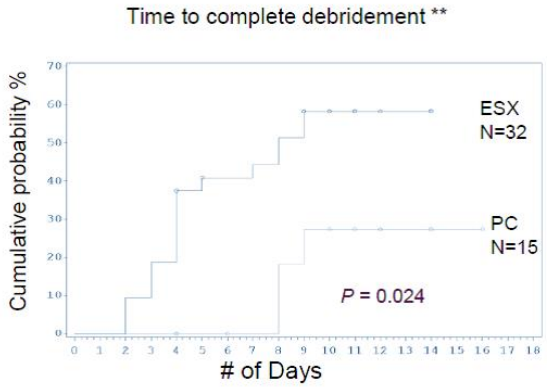


*w/i 10 daily applications

Predefined sub-group analyses showed that 50% of patients with DFUs treated with EscharEx (8/16) achieved complete debridement at the end of the debridement period compared with 14.3% of patients with DFUs treated with hydrogel vehicle (1/7). In addition, 62.5% of patients with VLUs treated with EscharEx (10/16) achieved complete debridement at the end of the debridement period compared with 25% of patients with VLUs treated with hydrogel vehicle (2/8). Post hoc analysis showed that 56.3% of patients with DFU or VLU in the EscharEx group had complete debridement at the end of the debridement period compared with 20.0% in hydrogel vehicle group (p=0.028).

The study included secondary endpoints that provide further insight into number of efficacy and safety parameters. The secondary endpoint of time to complete debridement demonstrated a clear trend (p=0.075) that strongly suggests that not only is there a difference in the incidence of debridement, as confirmed by the primary endpoint, but that debridement occurred earlier in the group treated by EscharEx. The advantage in time to complete debridement was corroborated by the statistically significant post hoc result in the subgroup of patients with DFUs or VLUs that were treated with EscharEx (p=0.024).





Post hoc analysis showed that of patients who achieved complete debridement in the EscharEx group, 93% (25/27) completed the debridement within 7 days (4-5 applications on average).

[6] Hydrogel is not a true sham placebo as it is a common and widely used treatment for the debridement of chronic wounds.

The overall patient demographics were comparable across both arms. No deleterious effect on wound healing was observed and no material differences were found in reported adverse events. The overall safety was comparable between the arms.

Second Phase 2 study—Israel/E.U. – Second Cohort

After successfully completing the first cohort of the study which included 73 patients recruited in 15 clinical sites, we initiated a second cohort of patients to demonstrate safety and tolerability over extended periods of application to further support the product's convenient application. In this second cohort, we recruited 38 patients from two etiologies, either DFUs or VLUs, over extended periods of application (24-72 hours) with up to eight applications, randomizing the patients to two study arms EscharEx or gel vehicle at a ratio of 2:1. The second cohort of the study included 38 patients. The primary objective was to assess safety.

EscharEx met its primary safety endpoint in this cohort, and the overall patient demographics and wound baseline characteristics were comparable across the arms in the second cohort. No related systemic adverse events were reported and adverse events related to local application were mild to moderate, reversible and resolved during the trial. Vital signs, pain scores, infection rates, laboratory parameters and blood loss were comparable between the two arms of the trial. Overall, no material safety concerns were identified.

Ongoing clinical trials

EscharEx U.S. Phase 2 Study in Venous Leg Ulcer (VLU) Patients

In December 2019, we initiated a U.S. Phase 2 adaptive design clinical study of EscharEx for the treatment of venous leg ulcers (VLUs). The study is a multicenter, prospective, randomized, placebo-controlled, adaptive design study, evaluating the safety and efficacy of EscharEx in debridement of VLUs compared to gel vehicle (placebo control) and non-surgical standard-of-care of either enzymatic or autolytic debridement. The study enrolled 120 patients, with 119 treated, at approximately 20 clinical sites, primarily in the United States. Study participants were randomized to either EscharEx, gel vehicle placebo control, or non-surgical standard-of-care, at a ratio of 3:3:2, with a three-month follow-up. The primary endpoint was incidence of complete debridement (non-viable tissue removal), clinically assessed, during the assessment period (up to 8 treatment applications within 14 days), compared to gel vehicle placebo control. Secondary and exploratory endpoints assess time to achieve complete debridement, reduction of pain, reduction of wound area, granulation tissue and quality of life, enabling evaluation of clinical benefits compared to both gel vehicle and non-surgical standard-of-care. Incidence and time to achieve wound closure will be assessed as safety measurements.

In January 2022 we announced positive topline results from this study. These topline results showed that the study met its primary endpoint with high degree of statistical significance, demonstrating that patients treated with EscharEx had a statistically significant higher incidence of complete debridement compared to the gel vehicle. The study randomized 120 patients, of which 119 patients were treated by either EscharEx (n=46), a gel vehicle (n=43), or a non-surgical standard-of-care consisting of either enzymatic or autolytic debridement (n=30). Patients treated with EscharEx demonstrated a statistically significant higher incidence of complete debridement during the 14-day measurement period within up to 8 applications compared to patients treated with gel vehicle (EscharEx: 63% (29/46) vs. gel vehicle: 30% (13/43), p-value=0.004). EscharEx efficacy superiority remained statistically significant compared to gel vehicle also after adjusting for pre-specified covariates ascribed to patient baseline characteristics, wound size and age, regions, and sites. Incidence of complete debridement of the non-surgical standard-of-care arm, during the same 14-day measurement period, was 13% (4/30). In addition, the Independent Data Monitoring Committee reviewed the data of all patients treated and no safety concerns were identified in the study population. EscharEx was well-tolerated and overall safety was comparable between the arms. No differences were found in reported adverse events and no serious adverse event was related to study treatment. Patient baseline characteristics were comparable across all study arms. Patient follow-up is ongoing and additional data, including secondary and exploratory endpoints as well as additional safety measurements, which will allow further evaluation of clinical benefits, is expected in the second quarter of 2022.

EscharEx Pharmacology Study

In December 2021, we announced positive initial data from seven of the maximum fifteen patients in our ongoing open-label, phase 2 pharmacology study of EscharEx in the debridement of lower leg ulcers (VLUs and DFUs). Based on this initial data, EscharEx demonstrated safe and effective debridement of lower leg ulcers within a few daily applications. In addition, evaluation of wounds' tissue samples (biopsies) and fluorescence images indicated reduction of biofilm and bacterial load following the treatment with EscharEx. We expect to share the full data set from this study in the first half of 2022.

The development of EscharEx for the debridement of chronic and other hard-to-heal wound indications is in Phase 2 studies, and there is no certainty that EscharEx will achieve all of the objectives of the trials as required or that the FDA will allow at this stage to initiate further studies or that we will successfully complete the development to obtain a marketing authorization for EscharEx. MediWound currently expects to request an end-of-Phase 2 meeting with the FDA in the second half of 2022, to discuss program results and the potential Phase 3 pivotal plan for EscharEx. See "ITEM 3.D. Risk Factors—Development and commercialization of NexoBrid and EscharEx in the United States and our pipeline product candidates worldwide requires successful completion of the regulatory approval process, and may suffer delays or fail."

Non-Melanoma Skin Cancer

MW005, is a topically applied biological product candidate for the treatment of non-melanoma skin cancers, based on the same active substance of NexoBrid and EscharEx, a concentrate of proteolytic enzymes enriched in bromelain. The clinical development plan of MW005 is supported by the results from several toxicological and other preclinical studies, as well as vast clinical experience from NexoBrid and EscharEx, which share the same active substance. We launched a new clinical program to evaluate our drug product candidate MW005 in patients with non-melanoma skin cancer.

Non-melanoma Skin Cancers

Cancers of the skin are by far the most common of all types of cancer with about approximately 5.4 million basal and squamous cell skin cancers are diagnosed each year in the US. The number of these cancers has been increasing for many years due to combination of better skin cancer detection, people getting more sun exposure, and people living longer.

- Basal cell carcinomas - basal cell carcinoma (BCC) starts in the basal cell layer, which is the lower part of the epidermis. If not removed completely, basal cell carcinoma can come back (recur) in the same place on the skin. People who have had basal cell skin cancers are also more likely to get new ones in other places. BCCs are uncontrolled and abnormal growths that arise in the basal cells of the skin and the tumors primarily affect photoexposed areas, most commonly in the head, and infrequently appear on per genital and genitalia regions. The main cause of BCC is chronic ultraviolet (UV) exposure. BCC is the most common form of skin cancer, accounting for 75-80% of all skin cancers

- Squamous cell carcinomas - Squamous cell carcinomas (SCC) start in the flat cells in the upper (outer) part of the epidermis

- Actinic keratosis - Actinic keratosis (AK), also known as solar keratosis, is a pre-cancerous skin condition caused by too much exposure to the sun. People who have them usually develop more than one. A small percentage of AKs may turn into squamous cell skin cancer.

- Bowen disease - Bowen disease (squamous cell carcinoma in situ), is the earliest form of squamous cell skin cancer

Market opportunity

Basal cell carcinoma is a non-melanoma skin cancer that arises from the basal layer of epidermis and its appendages and is the most diagnosed skin cancer in the US (~4.3 million cases annually).

Under existing standard of care, low-risk patients are treated with tumor resection via either standard surgical excision or Mohs micrographic surgery. Recurrence rates for these sharp methods of tumor removal are low (~5% at 5 years), and procedure is considered straightforward with limited patient downtime or side effects. Topical products (5-FU and Imiquimod) are used primarily in superficial lesions, but have limited use and are reserved for surgery ineligible patients. Drawbacks include longer treatment duration (>6 weeks), low efficacy (~14% at 5 years), and side effects such as scarring, skin-site reactions, and fatigue/flu-like illness. High-risk patients are also primarily treated with surgery; surgery-ineligible patients are treated with oral hedgehog pathway inhibitors, which are effective in the short-term, but have high recurrence rates / safety concerns. There is a need for more effective, safer topical products in low-risk superficial basal cell carcinoma for surgery-ineligible patients (e.g., site of tumor is challenging for excision or may result in cosmetic issues) or for patients for whom surgery is not appropriate (e.g., older / frail patients, or those with challenges in seeking pre and post-surgical appointments) and current topical agents may be avoided due to long treatment durations and because they result in an unpleasant treatment process for patients.

MW005 Clinical History

Ongoing clinical trials

U.S. Phase I/II Study in basal cell carcinoma Patients

In July 2021, we initiated a U.S. phase I/II study of MW005 for the treatment of low-risk basal cell carcinoma (BCC). The phase I/II open-label, randomized clinical study in BCC is designed to evaluate safety and tolerability of MW005 using different schedules of administration, as well as provide a preliminary evaluation of efficacy as measured by the percentage of target lesion with complete histological clearance. The trial will enroll up to 32 patients, comprised of 2 cohorts of 16 patients each, with histologically confirmed superficial or nodular BCC and will be conducted at three leading clinical centers in the U.S. We expect data to be available in the first half of 2022.

Although we have conducted preclinical trials, the development of MW005 for non-melanoma skin cancer indications is still in its preliminary phase and there is no certainty that it will achieve all the aims of the trials as required and/or successfully complete the approval process for such indication. See "ITEM 3.D. Risk Factors—Development and commercialization of NexoBrid and EscharEx in the United States and our pipeline product candidates worldwide requires successful completion of the regulatory approval process, and may suffer delays or fail."

Research and Development

Our research and development strategy is centered around our validated proteolytic enzyme platform technology, focused on next-generation protein-based therapies for burn and wound care, and for tissue repair, which underlies NexoBrid and EscharEx, into additional product candidates for high-value indications. For more information regarding our research and development expenses, see "ITEM 5.C. Research and Development, Patents and Licenses, etc."

Pre-Clinical Clinical Studies

We conduct clinical studies and preclinical studies to support the efficacy and safety of our products and their ingredients and to extend and validate their benefits for human health. Preclinical studies allow us to substantiate the safety of our products and obtain preliminarily indications of their pharmacological and safety profile. As of the date hereof, we had conducted more than 50 non-GLP8 and GLP preclinical studies. All pre-clinical safety and toxicology studies were conducted according to the principles of Good Laboratory Practices ("GLP"), and twelve clinical studies, according to the principles of Good Clinical Practices ("GCP"), for NexoBrid, EscharEx and our pipeline product candidates. As a result, we have developed significant experience in planning, designing, executing, analyzing and publishing clinical studies.

Our research and development team manages our clinical studies and coordinates the project planning, trial design, execution, outcome analyses and clinical study report submission. During the design, execution and analyses of our studies, our research and development team consults with key opinion leaders and top-tier consultants in the relevant field of research to optimize both design and execution, as well as to strengthen the scientific, medical and regulatory compliance level of the investigational plan. Our clinical studies have been conducted in collaboration with leading medical and research centers throughout the world.

Manufacturing, Supply and Production

We operate a manufacturing facility in Yavne, Israel, in a building that we sub-lease from Clal Life Sciences L.P., with 31 employees as of December 31, 2021. This facility allows us to manufacture sterile biopharmaceutical products, such as NexoBrid. The facility meets current cGMP requirements, as certified by each of the EMA, the Israeli Ministry of Health and South Korean ministry of health. Our facility is subject to audits for reassessment of cGMP compliance, which are preformed periodically by regulatory authorities and was re-approved as cGMP-compliant for an additional three years term as of the audit date, until 2023. Additionally, as we seek regulatory approval NexoBrid in the United States the FDA will need to inspect our plant to confirm it meets all regulatory requirements. In addition, other regional applicable authorities may also need to inspect our plant to confirm it meets all regulatory requirements in order to obtain marketing authorization in these jurisdictions. Applicable changes in our production processes for NexoBrid must be approved by the EMA and similar authorities in other jurisdictions.

While we believe that our current manufacturing capacity at the facility is sufficient to meet the expected near-term commercial demand for NexoBrid, we are planning to scale-up the current capacity, subject to BLA approval, in 2023. We expect the cost will be approximately $8-10 million.

The starting material used by us in the manufacturing of NexoBrid and our other product candidates is bromelain SP, which is derived from pineapple plant stems. We have entered into an agreement with CBC, dated January 11, 2001, as amended on February 28, 2010, pursuant to which CBC uses proprietary methods to manufacture bromelain SP and supplies us with this intermediate drug substance in bulk quantities. According to the terms of the agreement, CBC shall not, and shall not permit related companies or a third party to, manufacture, use, supply or sell the raw materials for the use or production of a product directly or indirectly competing with any of our products. Our supply agreement with CBC has no fixed expiration date and can be voluntarily terminated by us, with at least six months' advance written notice, or by CBC, with at least 24 months' advance written notice.

Upon obtaining bromelain SP from CBC, we further process it into the drug substance and then into the drug product to finally create the powder form of NexoBrid. The necessary inactive ingredients contained in NexoBrid, or the excipients, are readily available and generally sold to us by multiple suppliers. In addition to this powder, we manufacture a sterile gel substance by combining water for injections produced by us at our facility and additional excipients.

Marketing, Sales and Distribution

We commercialize globally NexoBrid via multiple sales channels:

Europe

In Europe and Israel, we sell NexoBrid, primarily through our own sales force consisting of a marketing team of specialized and knowledgeable sales representatives in Europe, focusing on leading burn centers and Key Opinion Leaders (KOL) management. We have obtained national reimbursement for NexoBrid in Belgium and Italy and we continue to locally execute our market access strategy for most of Europe to obtain procurement by burn centers and hospitals as part of their budget, or under local, regional or national reimbursement, depending on the specific process required in each country. We believe that additional burn units in large hospitals as well as smaller hospitals will follow the treatment trends once established by the burn centers. See "—Government Legislation and Regulation—Pharmaceutical Coverage, Pricing and Reimbursement." Furthermore, we are establishing additional distribution channels through local partners to extend outreach in EU (Sweden, Finland, the Baltic states, France, Switzerland (Romandie region), Greece, Malta, Bulgaria, Cyprus, Portugal, the Netherlands and Luxemburg), where NexoBrid is already approved for marketing as part of the European marketing authorization. In addition to receiving marketing authorization for NexoBrid in the European Union, key opinion leaders in the burn care field worldwide are already aware of NexoBrid's efficiency in removing eschar due to hundreds of scientific presentations and several award winning abstracts at international and national conferences and about 100 peer-reviewed papers.

North America

Vericel License and Supply Agreements

On May 6, 2019, we entered into exclusive license and supply agreements with Vericel to commercialize NexoBrid in all countries of North America (which we refer to as the "Territory").

NexoBrid is currently under registration stage in the U.S., and pursuant to the terms of the License Agreement described below, we will continue to conduct all clinical and other activities described in the development plan to support the BLA resubmission with the FDA under the supervision of a Central Steering Committee comprised of members of each of our Company and Vericel.

License Agreement.

We entered into a license agreement (the "License Agreement") with Vericel pursuant to which we granted Vericel an exclusive license, with the right to grant sublicenses, to develop and commercialize NexoBrid and any improvements of NexoBrid (the "Licensed Product") in the Territory.

Pursuant to the terms of the License Agreement, Vericel will have exclusive control regarding the commercialization of Licensed Products in the Territory and must use commercially reasonable efforts to commercialize Licensed Products within the Territory. We and Vericel have made customary representations and warranties and have agreed to certain customary covenants, including confidentiality and indemnification.

Within 10 days of signing the License Agreement, Vericel paid us an upfront fee of $17.5 million (the "Upfront Payment"). Vericel is obligated to pay us $7.5 million upon U.S. regulatory approval of the BLA for NexoBrid and up to $125 million upon certain sales milestones. The first sales milestone of $7.5 million is triggered when annual net sales of the Licensed Products in the Territory exceed $75 million. Vericel is also obligated to pay us tiered royalties on net sales of Licensed Products ranging from mid-high single-digit to mid-teen percentages, subject to certain customary reductions, a percentage of gross profits on committed purchases and a royalty on additional purchases by BARDA. The royalties will expire on a product-by-product and country-by-country basis upon the latest to occur of (i) twelve years following the first commercial sale of such Licensed Product in such country, (ii) the earliest date on which there are no valid claims of MediWound patent rights covering such Licensed Product in such country, and (iii) the expiration of the regulatory exclusivity period for such Licensed Product in such country (the "Royalty Term"). Such royalties are subject to reduction in the event that (a) Vericel must license additional third-party intellectual property in order to develop, manufacture or commercialize a Licensed Product, or (b) biosimilar competition occurs with respect to the Licensed Product in any country within the Territory. After the expiration of the applicable royalties for the Licensed Product in any country within the Territory, the license for such Licensed Product in such country would become a fully paid-up, royalty-free, perpetual and irrevocable license.

The License Agreement expires on the date of expiration of all royalty obligations due under the agreement unless earlier terminated in accordance with its terms. Either party may terminate the agreement upon the failure of the other party to comply with its material obligations under the agreement if that failure is not remedied within certain specified cure periods or in the event of a party's insolvency. In addition, Vericel may terminate the agreement upon 150 days written notice to us.

Supply Agreement.

On May 6, 2019, concurrently with our entry into the License Agreement, we entered into a supply agreement (the "Supply Agreement") with Vericel pursuant to which we are obligated to supply Vericel with NexoBrid for sale in the Territory on an exclusive basis for the first five years of the term of the Supply Agreement. The Supply Agreement requires us to take steps to ensure that our manufacturing capacity meets Vericel's demand for NexoBrid. In addition, after the exclusivity period or upon supply failure, Vericel will be permitted to establish an additional or alternate source of supply.

Pursuant to the Supply Agreement, we will supply NexoBrid to Vericel based on Vericel's fixed orders on a unit price basis. After a specified period, the unit price, on an annual basis, may be increased based on the United States Producer Price Index for Chemical Manufacturing published by the Bureau of Labor Statistics.

The Supply Agreement's initial term is five years (the "Initial Term"), with Vericel required to provide us with notice regarding whether it plans to extend the Initial Term for an additional two years by the third anniversary of the Supply Agreement. After the Initial Term and optional two-year extension, Vericel, at its sole discretion, may choose to extend the Supply Agreement's term for additional one-year periods for a potential total term of fifteen years.

The Supply Agreement will automatically terminate upon the expiration or termination of the License Agreement. Either party may terminate the Supply Agreement upon the failure of the other party to comply with its material obligations under the Supply Agreement if such failure is not remedied within certain specified cure periods. After the Initial Term, Vericel may terminate the Supply Agreement upon 12 months' prior written notice to us, and we may terminate the Supply Agreement upon 36 months prior written notice to Vericel.

BARDA

Pursuant to the First BARDA Contract, BARDA has initiated the procurement of NexoBrid valued at $16.5 million, for emergency stockpile as part of the HHS mission to build national preparedness for public health medical emergencies. BARDA purchased inventory is being managed by MediWound under vendor managed inventory. As of December 31, 2021, the Company has received $14.6 million for procurement of NexoBrid for U.S. emergency preparedness.

Under our exclusive license and supply agreements with Vericel, we will equally split the gross profits on the initial procurement and receive a double-digit royalty on any additional future BARDA purchases of NexoBrid. Please see "Vericel License and Supply Agreements" above.

Other International Markets

In other international markets, we sell NexoBrid through local distributors with which we have distribution agreements, focusing on Asia Pacific, EMEA, CEE and LATAM. We have signed local distribution agreements for distribution in Argentina, Russia, South Korea, Colombia, Mexico, Peru, Chile, Ecuador, Panama, India, Bangladesh, Sri Lanka, Turkey, Japan, Australia, New-Zealand, Singapore, Ukraine, Taiwan and United Arab Emirates.

Our distributors in Argentina, South Korea, Russia, Peru, Chile, Taiwan, United Arab Emirates and Eurasian countries have obtained marketing authorization. Our additional distributors have filed or are in the process of filing for market authorization in their respective territories and are expected to launch NexoBrid after receipt of local regulatory approval, which may take a year or more to be granted, and, consequently, may occur in certain markets during 2022. We have launched NexoBrid in Argentina, South Korea, Russia, Taiwan, Chile and United Arab Emirates and expect additional launches following receipt of local marketing authorizations. We plan to enter other international markets through collaboration with local distributors and leverage our approved registration file in Europe to obtain regional marketing authorizations.

For a breakdown of our consolidated revenues by geographic markets and by categories of operations for the years ended December 31, 2020 and 2021, please see "Item 5.A Operating and Financial Review and Prospects—Operating Results."

Intellectual Property

Our intellectual property and proprietary technology are important to the development, manufacture and sale of NexoBrid, EscharEx and our future pipeline product candidates. We seek to protect our intellectual property, core technologies and other know-how through a combination of patents, trademarks, trade secrets, non-disclosure and confidentiality agreements, licenses, assignments of invention and other contractual arrangements with our employees, consultants, partners, suppliers, customers and others. Additionally, we rely on our research and development program, clinical trials, know-how and marketing and distribution programs to advance our products and product candidates. As of December 31, 2021, we had been granted a total of 64 patents and have 27 pending patent applications. The family of patents that covers NexoBrid specifically includes 35 granted patents worldwide. EscharEx is covered by 7 patents and 24 national phase applications.

The main patents for our proteolytic enzyme technology which underlies NexoBrid, EscharEx and our current pipeline product candidates have been issued in Europe, the United States and other international markets. Our patents which cover NexoBrid claim specific mixtures of proteolytic enzymes, methods of producing such mixtures and methods of treatment using such mixtures. Although the protection achieved is significant for NexoBrid, EscharEx and our pipeline product candidates, when looking at our patents' ability to block competition, the protection offered by our patents may be, to some extent, more limited than the protection provided by patents which claim chemical structures which were previously unknown. Absent patent-term extensions, the NexoBrid patents are nominally set to expire in 2025 and in 2029 in the United States. The NexoBrid patents issued in Europe and in other foreign jurisdictions are nominally set to expire in 2025. The patents and the national phase applications relating to EscharEx, if the national phase applications are granted, will expire on January 30, 2037, absent any patent-term adjustment and/or extensions.

While our policy is to obtain patents by application, license or otherwise, to maintain trade secrets and to seek to operate without infringing on the intellectual property rights of third parties, technologies related to our business have been rapidly developing in recent years. Additionally, patent applications that we may file or license from third parties may not result in the issuance of patents, and our issued patents and any issued patents that we may receive in the future may be challenged, invalidated or circumvented. For example, we cannot predict the extent of claims that may be granted or enforceable in our patents nor can we be certain of the priority of inventions covered by pending third-party patent applications filed in the U.S. If third parties prepare and file patent applications that also claim technology or therapeutics to which we have rights, we may have to participate in proceedings to determine priority of invention, which could result in substantial costs to us, even if the eventual outcome is favorable to us. Moreover, because of the extensive time required for clinical development and regulatory review of a product we may develop, it is possible that, before NexoBrid can be commercialized in additional jurisdictions and/or before any of our future products can be commercialized, related patents will expire a short period following commercialization, thereby reducing the advantage of such patent. Loss or invalidation of certain of our patents, or a finding of unenforceability or limited scope of certain of our intellectual property rights, could have a material adverse effect on us. See "ITEM 3.D. Risk Factors — Our success depends in part on our ability to obtain and maintain protection for the intellectual property relating to, or incorporated into, our technology and products."

In addition to patent protection, we also rely on trade secrets, including unpatented know-how, technology innovation, drawings, technical specifications and other proprietary information in attempting to develop and maintain our competitive position. We also rely on protection available under trademark laws, and we currently hold various registered trademarks, including "MediWound," "NexoBrid" and "EscharEx" in various jurisdictions, including the United States, the European Union and Israel.

Klein License Agreement

In September 2000, we signed an exclusive license agreement, as amended in June 2007, with Mark Klein, a third party, for use of certain patents and intellectual property (the "Klein License Agreement"). Under the Klein License Agreement, we received an exclusive license to use the third party's patents and intellectual property to develop, manufacture, market and commercialize NexoBrid and its pipeline product candidates for the treatment of burns and other wounds. The claims of such patents are directed to a process of preparing a mixture of escharase and proteolytic enzymes and cover the underlying proteolytic mixture of escharase and proteolytic enzymes prepared by that specific process. Pursuant to the Klein License Agreement, we are obligated to keep accounting records related to the sales of NexoBrid and its pipeline product candidates and pay royalties as discussed below. The Klein License Agreement may be terminated by Mark Klein, subject to notice and dispute resolution provisions of the Klein License Agreement, in the event of our breach, bankruptcy petition, insolvency or failure to achieve a development milestone within six months of a target date. We have already achieved all development milestones under the Klein License Agreement.

In consideration for the Klein License Agreement, we paid an aggregate amount of $1.0 million following the achievement of certain development milestones. In addition, we undertook to pay royalties of 1.5-2.5% from revenues, 10% of royalties received from sublicensing and 2% of lump-sum payments received from sublicensing up to $1 million and 4% above $1 million, in each case relating to products based on the licensed patents and intellectual property, for a term of 10-15 years, as applicable, from the date of the first commercial delivery in a major country. In addition, under the Klein License Agreement, we agreed to pay a one-time lump-sum amount of $1.5 million upon reaching aggregate revenues of $100 million from the sale of such products.

Competition

NexoBrid received orphan drug status in the European Union on July 31, 2002 and in the United States on August 20, 2003 for debridement of deep partial- and full-thickness burns in hospitalized patients. In the United States and the European Union, a sponsor that develops an orphan drug has marketing exclusivity for seven years post-approval by the FDA and for ten years post-approval by the EMA, respectively. The exclusive marketing rights in both regions are subject to certain exceptions, including the development of a clinically significant benefit over the prevalent SOC. Once the market exclusivity for our orphan indication expires in a given jurisdiction, subject to other protections such as patents, we could face competition from other companies that may attempt to develop other products for the same indication.

The medical, biotechnology and pharmaceutical industries are intensely competitive and subject to significant technological change and changes in practice. While we believe that our innovative technology, knowledge, experience and scientific resources provide us with competitive advantages, we may face competition from many different sources with respect to NexoBrid, EscharEx, MW005 and our existing pipeline product candidates or any product candidates that we may seek to develop or commercialize in the future. Possible competitors may include medical practitioners, pharmaceutical and wound care companies, academic and medical institutions, governmental agencies and public and private research institutions, among others. Any product that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

In addition, we face competition from the current SOC. The current SOC for eschar removal in severe burns is surgery, where eschar removal can be performed by tangential excision, dermabrasion or hydro jet, or non-surgical alternatives, such as applying topical medications to the eschar to facilitate the natural healing process. Consequently, we face competition from traditional surgical procedures and topical agents. However, based on our clinical trials, we believe that NexoBrid has a sustainable competitive advantage over the current non-surgical alternatives and is less invasive than surgery in removing eschar in patients with burn wounds. See "—NexoBrid and Our Clinical History" for the results of our clinical trials.

Although we are in the clinical and preclinical phases for our pipeline product candidates for debridement of chronic and other hard-to-heal wounds and treatment of low risk basal cell carcinoma and connective tissue disorders and other indications, respectively, if one of our pipeline product candidates receives approval in the future, we would compete with traditional surgery and existing non-surgical and other treatments. In chronic and other hard-to-heal wounds, we expect to face competition from current standard of care for debridement by sharp debridement or from the current non-surgical standard of care, either enzymatic debridement, primarily Smith & Nephew Plc's Santyl, a collagenase-based product indicated for debriding chronic dermal ulcers and severely burned areas or autolytic debridement.

The current standard of care for treatment of low risk basal cell carcinoma, is surgical excision. In superficial basal cell carcinoma and inoperable nodular basal cell carcinoma, we expect to face competition from current topical applications such as imiquimod and 5FU.

In addition to the currently available products, other products may be introduced to debride chronic and other hard-to-heal wounds or treat superficial and nodular basal cell carcinoma and connective tissue disorders during the time that we engage in necessary development. Accordingly, if one of our pipeline product candidates is approved, our main challenge in the market would be to educate physicians seeking alternatives to surgery to use our product instead of already existing treatments. While we are still in the development stages, based on our studies, we believe that our pipeline product candidates will be more effective than the current non-surgical alternatives and less invasive than surgery in removing eschar in chronic and other hard-to-heal wounds or tumor resection and may be comparable or perhaps better than currently available treatments for connective tissue disorders.

Government Legislation and Regulation

Our business is subject to extensive government regulation. Regulation by governmental authorities in the United States, the European Union and other jurisdictions is a significant factor in the development, manufacture and marketing of NexoBrid and in ongoing research and development activities.

European Union

The approval process of medicinal products in the European Union generally involves satisfactorily completing each of the following:

- laboratory tests, animal studies and formulation studies all performed in accordance with the applicable E.U. GLP or GMP regulations;
- submission to the relevant authorities of a clinical trial application ("CTA"), which must be approved before human clinical trials may begin;
- performance of adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication;
- submission to the relevant competent authorities of a marketing authorization application ("MAA"), which includes the data supporting preclinical and clinical safety and efficacy as well as detailed information on the manufacture and composition and control of the product development and proposed labeling as well as other information;

- inspection by the relevant national authorities of the manufacturing facility or facilities and quality systems (including those of third parties) at which the product is produced, to assess compliance with strictly enforced GMP;

- potential audits of the non-clinical and clinical trial sites that generated the data in support of the MAA; and

- review and approval by the relevant competent authority of the MAA before any commercial marketing, sale or shipment of the product.

Quality/preclinical studies

In order to assess the potential safety and efficacy of a product, tests include laboratory evaluations of product characterization, analytical tests and controls, as well as studies to evaluate toxicity and pharmacological effects in animal studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with the relevant E.U. regulations and requirements. The results of such tests, together with relevant manufacturing control information and analytical data, are submitted as part of the CTA. Non-clinical studies are performed to demonstrate the health or environmental safety of new biological substances. Non-clinical studies must be conducted in compliance with the principles of good laboratory practice ("GLP") as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trial approval

Clinical drug development is often described as consisting of four temporal phases (Phase 1-4). See, for example, the EMA's note for guidance on general considerations for clinical trials (CPMP/ICH/291/95).

- Phase 1 (Most typical kind of study: Human Pharmacology);

- Phase 2 (Most typical kind of study: Therapeutic Exploratory);

- Phase 3 (Most typical kind of study: Therapeutic Confirmatory); and

- Phase 4 (Variety of Studies: Therapeutic Use).

Studies in Phase 4 are all studies other than routine surveillance performed after drug approval and are related to the approved indication.

The phase of development provides an inadequate basis for classification of clinical trials because one type of trial may occur in several phases. The phase concept is a description, not a set of requirements. The temporal phases do not imply a fixed order of studies since for some drugs in a development plan the typical sequence will not be appropriate or necessary.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization ("ICH") guidelines on good clinical practices ("GCP") as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation ("CTR") which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database.

While the Clinical Trials Directive required a separate CTA to be submitted in each member state, to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed.

The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR.

Pediatric investigation plan ("PIP")

We initiated a PIP study in November 2014.

On January 26, 2007, Regulation (EC) 1901/2006 came into force with its primary purpose being the improvement of the health of children without subjecting children to unnecessary trials, or delaying the authorization of medicinal products for use in adults. The regulation established the Pediatric Committee ("PDCO"), which is responsible for coordinating the EMA's activities regarding pharmaceutical drugs for children. The PDCO's main role is to determine which studies the applicant needs to perform in the pediatric population as part of the PIP.

All applications for marketing authorization for new pharmaceutical products that were not authorized in the EU prior to January 26, 2007 must include the results of studies carried out in children of different ages. The PDCO determines the requirements and procedures of such studies, describing them in a PIP. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The PDCO can grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO can also grant waivers when development of a medicine in children is not needed or is not appropriate, such as for diseases that only affect the elderly population.

Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA confirms that the applicant complied with the studies' requirements and measures listed in the PIP. Since the regulation became effective, several incentives for the development of medicines for children become available in the European Union, including:

- medicines that have been authorized for marketing in the EU with the results of PIP studies included in the product information are eligible for an extension of their supplementary protection certificate extension (if any is in effect at the time of approval) by six months. This is the case even when the studies' results are negative;
- for orphan medicines, such as NexoBrid, the incentive is an additional two years of market exclusivity instead of one;
- scientific advice and protocol assistance at the EMA are free of charge for questions relating to the development of medicines for children; and
- medicines developed specifically for children that are already authorized, but are not protected by a patent or supplementary protection certificate, can apply for a pediatric use marketing authorization ("PUMA"). If a PUMA is granted, the product will benefit from 10 years of market protection as an incentive.

In November 2021, we received positive scientific advice from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) related to the pediatric label extension for NexoBrid. EMA's CHMP agreed to assess a potential pediatric label extension on NexoBrid for the treatment of thermal burns, based on the available safety and efficacy results of the pivotal Phase 3 pediatric clinical study with its 12-month follow-up, and that the long-term follow up data are likely to be supportive data. Based on the feedback, the Company anticipates submitting a pediatric label extension request in the first half of 2022.

Marketing authorization

Authorization to market a product in the EU member states proceeds under one of four procedures: a centralized authorization procedure, a mutual recognition procedure, a decentralized procedure or a national procedure. Marketing authorization may be granted only to an applicant established in the European Union. Through our wholly-owned German subsidiary, we received approval for NexoBrid pursuant to the centralized authorization procedure.

The centralized procedure provides for the grant of a single marketing authorization that is valid throughout the EU and the European Economic Area ("EEA") countries, and including Norway, Iceland and Lichtenstein. The centralized procedure is compulsory for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products ("ATMPs") and products with a new active substance indicated for the treatment of certain diseases, and is optional for products which constitute a significant therapeutic, scientific, or technical innovation or for which a centralized process is in the interest of patients. Products that have received orphan designation in the EU, such as NexoBrid, will qualify for this centralized procedure, under which each product's MAA is submitted to the EMA. Under the centralized procedure in the European Union, the maximum time frame for the evaluation of an MAA by the EMA is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee of Medicinal Products for Human Use).

In general, if the centralized procedure is not followed, there are three alternative procedures where applications are filed with one or more members state medicines regulators, each of which will grant a national marketing authorization:

- *Mutual recognition procedure.* If an authorization has been granted by one-member state, or the Reference Member State, an application may be made for mutual recognition in one or more other member states, or the Concerned Member State(s).

- *Decentralized procedure.* The decentralized procedure may be used to obtain a marketing authorization in several European member states when the applicant does not yet have a marketing authorization in any country.

- *National procedure.* Applicants following the national procedure will be granted a marketing authorization that is valid only in a single member state. Furthermore, this marketing authorization is not based on recognition of another marketing authorization for the same product awarded by an assessment authority of another member state. If marketing authorization in only one-member state is preferred, an application can be filed with the national competent authority of a member state. The national procedure can also serve as the first phase of a mutual recognition procedure.

It is not always possible for applicants to follow the national procedure. In the case of medicinal products in the category for which the centralized authorization procedure is compulsory, that procedure must be followed. In addition, the national procedure is not available in the case of medicinal product dossiers where the same applicant has already obtained marketing authorization in one of the other European Union member state or has already submitted an application for marketing authorization in another member state and the application is under consideration. In the latter case, applicants must follow a mutual recognition procedure.

After a drug has been authorized and launched, it is a condition of maintaining the marketing authorization that all aspects relating to its quality, safety and efficacy must be kept under review. Sanctions may be imposed for failure to adhere to the conditions of the marketing authorization. In extreme cases, the authorization may be revoked, resulting in withdrawal of the product from sale.

Period of authorization and renewals

Marketing authorization is valid for an initial five-year period and may be renewed thereafter on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder shall provide the EMA or other applicable competent authority a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the end of the initial five-year period. Once renewed, the marketing authorization is valid for an unlimited period, unless the EMA or other applicable competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the E.U. market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization shall cease to be valid. On November 2017, the European Commission granted a five-year renewal of our NexoBrid marketing authorization, and we plan to file for renewal during 2022.

Orphan designation

On July 31, 2002, NexoBrid received orphan drug status in the European Union, and on December 20, 2012, the EMA confirmed NexoBrid's designation as an orphan drug for marketing authorization.

In the EU, the Committee for Orphan Medicinal Products assesses orphan drug designation. The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product can be designated as an orphan if its sponsor can establish that (1) the product is intended for the diagnosis, prevention or treatment of a life threatening or chronically debilitating condition; (2) either (a) such condition affects not more than five in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from the orphan status, would not generate sufficient return in the EU to justify the necessary investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized for marketing in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition.

In the EU, orphan drug designation also entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if, at the end of the fifth year, the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity or a safer, more effective or otherwise clinically superior product is available. Granting of an authorization for another similar orphan medicinal product where another product has market exclusivity can happen at any time if: (i) the second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior, (ii) inability of the applicant to supply sufficient quantities of the orphan medicinal product or (iii) where the applicant consents to a second orphan medicinal product application. A company may voluntarily remove a product from the orphan register.

Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Regulatory data protection

Without prejudice to the law on the protection of industrial and commercial property, some marketing authorizations benefit from an "8+2(+1)" year period of regulatory protection. During the first eight years from the grant of the innovator company's marketing authorization, data exclusivity applies. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. After the eight years have expired, a generic company can make use of the preclinical and clinical trial data of the originator in their regulatory applications but still cannot market their product until the end of 10 years. An additional one year of market exclusivity can be obtained if, during the first eight years of those 10 years, the marketing approval holder obtains an approval for one or more new therapeutic indications which, during the scientific evaluation prior to their approval, are determined to bring a significant clinical benefit in comparison with existing therapies. Under the current rules, a third party may reference the preclinical and clinical data of the reference product beginning eight years after first approval, but the third party may market a generic version only after 10 (or 11) years have lapsed.

Additional data protection can be applied for when an applicant has complied with all requirements as set forth in an approved PIP.

Post-Approval Requirements

Similar to the United States, both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the member states. The holder of a marketing authorization must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports ("PSURs").

All new MAA must include a risk management plan ("RMP") describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the marketing authorization. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

Failure to comply with the aforementioned EU and member state laws may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The aforementioned EU rules are generally applicable in the EEA.

The United Kingdom ("UK") left the EU on January 31, 2020, following which existing EU medicinal product legislation continued to apply in the United Kingdom during the transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement ("TCA") and became effective on the January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations.

EU laws which have been transposed into UK law through secondary legislation continue to be applicable as "retained EU law". However, new legislation such as the EU CTR or in relation to orphan medicines will not be applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favour of the Secretary of State or an 'appropriate authority' to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency ("MHRA") is the UK's standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain ("GB"); broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published a guidance on how various aspects of the UK regulatory regime for medicines will operate in GB and in Northern Ireland following the expiry of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, importing, exporting, and pharmacovigilance and is relevant to any business involved in the research, development, or commercialization of medicines in the UK. The new guidance was given effect via the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019 (the "Exit Regulations").

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder chooses to opt-out. After Brexit, companies established in the UK cannot use the centralized procedure and instead must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain an MA to commercialize products in the UK. The MHRA may rely on a decision taken by the an Commission on the approval of a new (centralized procedure) MA when determining an application for a GB authorization; or use the MHRA's decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in GB.

There will be no pre-MA orphan designation. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same, but have been tailored for the market, i.e., the prevalence of the condition in GB, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in GB.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, regulations, and standards govern the collection, use, access to, confidentiality and security of health-related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, certain laws govern the privacy and security of personal data, including health-related data in the EU/EEA and in other foreign jurisdictions. For example, the GDPR imposes strict requirements for processing the personal data of individuals within the EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Further, from January 1, 2021, companies have had to comply with the GDPR and also the UK GDPR, which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. The UK GDPR mirrors the fines under the GDPR, i.e., fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Manufacturing

The manufacturing of authorized drugs, for which a separate manufacturer's license is mandatory, must be conducted in strict compliance with the EMA's cGMP requirements and comparable requirements of other regulatory bodies, which mandate the methods, facilities and controls used in manufacturing, processing and packing of drugs to assure their safety and proper identification. The EMA monitors compliance with its GMP requirements through mandatory registration of facilities and inspections of those facilities. The EMA may have a coordinating role for these inspections while the responsibility for carrying them out rests with the competent authority of the member state under whose responsibility the manufacturer falls. Failure to comply with these requirements could interrupt supply and result in delays, unanticipated costs and lost revenues, and could subject the applicant to potential legal or regulatory action, including but not limited to warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil and criminal penalties. In January 2013, the EU and Israel signed the Protocol on Conformity Assessment and Acceptance of Industrial Products (the "ACAA"), which covers medicinal products. The ACAA provides for mutual recognition of the conclusions of inspections of compliance of manufacturers and importers with the principles and guidelines of EU GMP and equivalent Israeli cGMP. Certification of the conformity of each batch to its specifications by either the importer or the manufacturer established in Israel or in the EU shall be recognized by the other party without re-control at import from one party to the other.

Marketing and promotion

The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union, notably under Directive 2001/83 and subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. The applicable legislation aims to ensure that information provided by holders of marketing authorizations regarding their products is truthful, balanced and accurately reflects the safety and efficacy claims authorized by the EMA or by the applicable national authority of the authorizing member state. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another. Failure to comply with these requirements can result in adverse publicity, warning letters, mandated corrective advertising and potential civil and criminal penalties.

United States

Review and approval of biologics

In addition to E.U. regulations, NexoBrid is an investigational drug in the United States and is therefore subject to various U.S. regulations. In the United States, the FDA regulates biologics under the Federal, Food, Drug and Cosmetic Act ("FDCA"), the Public Health Service Act, and their respective implementation regulations. On March 24, 2011, the FDA classified NexoBrid as a biological product. Biologics require the submission of a BLA and licensure by the FDA prior to being marketed in the United States. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant to a variety of administrative or judicial sanctions as well as enforcement actions brought by the FDA, the U.S. Department of Justice or other governmental entities. Possible sanctions may include the FDA's refusal to approve pending BLAs or supplements, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties.

The process required by the FDA prior to marketing and distributing a biologic in the United States generally involves the following:

- completion of laboratory tests, animal studies and formulation studies in compliance with the FDA's GLP and GMP regulations, as applicable;
- submission to the FDA of an investigational new drug application ("IND"), which must become effective before clinical trials may begin;
- approval by an independent institutional review board ("IRB") at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with GCP to establish the safety and efficacy of the product for each indication;
- preparation and submission to the FDA of a BLA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP requirements, and to assure that the facilities, methods and controls are adequate to preserve the product's safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCP; and
- payment of user fees and FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and efficacy of the product candidate. Preclinical safety tests must be conducted in compliance with FDA regulations regarding good laboratory practices. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND which must become effective before clinical trials may commence. Some preclinical testing may continue even after the IND is submitted.

Clinical trials in support of a BLA

Clinical trials involve the administration of an investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin.

In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their website, ClinicalTrials.gov.

For purposes of BLA approval, clinical trials are typically conducted in three sequential phases, which may overlap or be combined. In the United States, the three phases are generally described as follows:

Phase 1: The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

Phase 2: The investigational product is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

Phase 3: The investigational product is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Submission of a BLA to the FDA

The results of the preclinical studies and clinical trials, together with other detailed information, including information on the manufacture, control and composition of the product, are submitted to the FDA as part of a BLA requesting approval to market the product candidate for a proposed indication. Under the Prescription Drug User Fee Act (PDUFA), as amended, applicants are required to pay user fees to the FDA for reviewing a BLA. These user fees, as well as the annual program fees required for approved products, can be substantial. Each BLA submitted to the FDA for approval is typically reviewed for administrative completeness and reviewability within 60 days following submission of the application. If found complete, the FDA will "file" the BLA, which triggers a full review of the application. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission. The FDA's established goals are to review and act on standard applications within ten months after it accepts the application for filing, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may convene an advisory committee to provide clinical insight on application review questions.

Before approving a BLA, the FDA generally inspects the facilities at which the product is manufactured or facilities that are significantly involved in the product development and distribution process, and will not approve the product unless cGMP compliance is satisfactory. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product will be produced, the FDA may issue an approval letter or a Complete Response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response letter will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the Complete Response letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification.

The FDA may deny approval of a BLA if applicable statutory or regulatory criteria are not satisfied, or may require additional testing or information, which can delay the approval process. FDA approval of any application may include many delays or may never be granted. If a product is approved, the approval will impose limitations on the indicated uses for which the product may be marketed, will require that warning statements be included in the product labeling, may impose additional warnings to be specifically highlighted in the labeling (e.g., a Black Box Warning), which can significantly affect promotion and sales of the product, may require that additional studies be conducted following approval as a condition of the approval and may impose restrictions and conditions on product distribution, prescribing or dispensing. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use. A REMS program may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate healthcare providers of the drug's risks, or other elements to assure safe use, such as limitations on who may prescribe or dispense the drug, dispensing only under certain circumstances, special monitoring and the use of patient registries.

Once a product is approved, marketing the product for other indicated uses or making certain manufacturing or other changes requires FDA review and approval of a supplemental BLA or a new BLA, which may require additional clinical data. In addition, further post-marketing testing and surveillance to monitor the safety or efficacy of a product may be required. Also, product approvals may be withdrawn if compliance with regulatory standards is not maintained or if safety or manufacturing problems occur following initial marketing. In addition, new government requirements may be established that could delay or prevent regulatory approval of our product candidates under development.

Post-approval requirements

Any biologic products for which we receive FDA approvals are subject to pervasive continuing regulation by the FDA. Certain requirements include, among other things, record-keeping requirements, reporting adverse experiences with the product, providing the FDA with updated safety and efficacy information annually or more frequently for specific events, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. These promotion and advertising requirements include, among others, standards for direct-to-consumer advertising, prohibitions against promoting drugs for uses or in patient populations that are not described in the drug's approved labeling, known as "off-label use," and other promotional activities, such as those considered to be false or misleading. Failure to comply with FDA requirements can have negative consequences, including the immediate discontinuation of noncomplying materials, adverse publicity, enforcement letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties. Such enforcement may also lead to scrutiny and enforcement by other government and regulatory bodies. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not encourage, market or promote such off-label uses. As a result, "off-label promotion" has formed the basis for litigation under the Federal False Claims Act, violations of which are subject to significant civil fines and penalties.

The manufacturing of NexoBrid, EscharEx and our pipeline product candidates are and will be required to comply with applicable FDA manufacturing requirements contained in the FDA's cGMP regulations. NexoBrid is manufactured at our production plant in Yavne, Israel, which is cGMP certified. The FDA's cGMP regulations require, among other things, quality control and quality assurance, as well as the corresponding maintenance of comprehensive records and documentation. Biologic manufacturers and other entities involved in the manufacture and distribution of approved drugs and biologics are also required to register their establishments and list any products they make with the FDA and to comply with related requirements in certain states. These entities are further subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. In addition, a BLA holder must comply with post-marketing requirements, such as reporting of certain adverse events. Such reports can present liability exposure, as well as increase regulatory scrutiny that could lead to additional inspections, labeling restrictions or other corrective action to minimize further patient risk. Discovery of problems with a product after approval may result in serious and extensive restrictions on the product, manufacturer or holder of an approved BLA, as well as lead to potential market disruptions. These restrictions may include recalls, fines, warning letters, or untitled letters, clinical holds on clinical studies, refusal of the FDA to approve pending applicants or supplements to approved applications, product seizure or detention, or refusal to permit the import or export of products, suspension or revocation of a product license approval until the FDA is assured that quality standards can be met, and continuing oversight of manufacturing by the FDA under a "consent decree," which frequently includes the imposition of costs and continuing inspections over a period of many years, as well as possible withdrawal of the product from the market. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented. Other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

The FDA also may impose a number of post-approval requirements as a condition of approval of a BLA. For example, the FDA may require post-marketing testing, or Phase 4 testing, as well as REMS and/or surveillance to monitor the effects of an approved product or place other conditions on an approval that could otherwise restrict the distribution or use of NexoBrid.

Orphan designation and exclusivity

On August 20, 2003, NexoBrid received orphan drug designation in the United States. Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan product designation before submitting a BLA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation, the product will be entitled to orphan product exclusivity. Orphan product exclusivity means that FDA may not approve any other applications for the same product for the same disease or condition for seven years, except in certain limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than that designated in its orphan product application, it may not be entitled to exclusivity. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. The fast track program is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, new products are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a fast track product has opportunities for frequent interactions with the review team during product development and, once a BLA is submitted, the product may be eligible for priority review. A fast track product may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

A product intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product, including involvement of senior managers.

Any marketing application for a biologic submitted to the FDA for approval, including a product with a fast track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition compared to marketed products. For products containing new molecular entities, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date, compared with ten months under standard review.

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

In 2017, FDA established a new regenerative medicine advanced therapy, or RMAT, designation as part of its implementation of the 21st Century Cures Act, which was signed into law in December 2016. To qualify for RMAT designation, the product candidate must meet the following criteria: (1) it qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (2) it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition. Like fast track and breakthrough therapy designation, RMAT designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate and eligibility for rolling review and priority review. Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites. Once approved, when appropriate, the FDA can permit fulfillment of post-approval requirements under accelerated approval through the submission of clinical evidence, clinical studies, patient registries, or other sources of real world evidence such as electronic health records; through the collection of larger confirmatory datasets; or through post-approval monitoring of all patients treated with the therapy prior to approval.

Fast track designation, breakthrough therapy designation, priority review, accelerated approval, and RMAT designation do not change the standards for approval but may expedite the development or approval process.

Pediatric studies and exclusivity

Under the Pediatric Research Equity Act of 2003, a BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Separately, in the event the FDA issues a Written Request for pediatric data relating to a product, a BLA sponsor who submits such data may be entitled to pediatric exclusivity. Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States which, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing exclusivity, including other non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to the Written Request from the FDA for such data. The data do not need to show that the product is effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot accept or approve another application.

The Animal Rule

In the case of product candidates that are intended to treat certain rare life-threatening diseases, conducting controlled clinical trials to determine efficacy may be unethical or unfeasible. Under regulations issued by the FDA in 2002, often referred to as the "Animal Rule", the approval of such products can be based on clinical data from trials in healthy human subjects that demonstrate adequate safety and efficacy data from adequate and well-controlled animal studies. Among other requirements, the animal studies must establish that the drug or biological product is reasonably likely to produce clinical benefits in humans. Because the FDA must agree that data derived from animal studies may be extrapolated to establish safety and effectiveness in humans, seeking approval under the Animal Rule may add significant time, complexity and uncertainty to the testing and approval process. In addition, products approved under the Animal Rule are subject to additional requirements including post-marketing study requirements, restrictions imposed on marketing or distribution or requirements to provide information to patients.

Patent term restoration and extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act"), which permits a patent restoration of up to five years for the patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of a BLA, plus the time between the submission date of a BLA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of fourteen years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Biosimilars and reference product exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "ACA"), which was signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-approved reference biological product.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law. The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, recent government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and meaning of the BPCIA remains subject to significant uncertainty.

Review and Approval of Drug Products Outside the European Union and the United States

In addition to the above regulations, we must obtain approval of a product by the comparable regulatory authorities of foreign countries outside of the European Union and the United States before we can commence clinical trials or marketing of NexoBrid in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA or EMA approval. In addition, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country. In all cases, clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we obtain regulatory approval. In the United States, EU and other markets, sales of any products for which we receive regulatory approval for commercial sale will depend to a large extent on the availability of reimbursement from third-party payors. Third-party payors include governments, government health administrative authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the drug products approved for a particular indication by the FDA, European Commission or National Ministries of Health. Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of NexoBrid, in addition to the costs required to obtain the FDA or other Ministry of Health approvals. Additionally, NexoBrid may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a drug product does not guarantee that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

In the United States, the ACA substantially changed the way healthcare is financed by both governmental and private insurers and significantly impacted the pharmaceutical industry. The ACA contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse provisions, which will impact existing government healthcare programs and will result in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program. Additionally, the ACA:

- increases the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%;
- requires collection of rebates for drugs paid by Medicaid managed care organizations; and
- imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs.

Since its enactment, there have been judicial, executive and congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace from February 15, 2021 through August 15, 2021. The executive order 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.

There has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which have resulted in several Congressional inquiries and proposed bills 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. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our products or additional pricing pressures. 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.

In the EU, pricing and reimbursement schemes vary widely from country to country and often within regions or provinces of countries. Some countries may limit the annual budget of coverage or request that the company participate in the cost above certain use levels or for treatments perceived as unsuccessful and impose monitoring processes on the use of the product. Some countries and hospitals may require inclusion into the hospital formulary for payment from the hospital budget. Some countries and hospitals may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies. For example, the EU provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Law and Regulation; Data Privacy and Security Laws

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with healthcare providers, third-party payors and other customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations. Such restrictions under applicable federal, state and foreign healthcare laws and regulations, include the following:

- the federal healthcare Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by HITECH and its implementing regulations, also imposes obligations, including mandatory contractual terms, on covered entities and their respective business associates with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits 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 federal physician payment transparency requirements under the Affordable Care Act require certain manufacturers of drugs, devices and medical supplies to report to Centers for Medicare & Medicaid Services information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other healthcare professionals, and teaching hospitals and physician ownership and investment interests;

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and

- similar healthcare laws and regulations in the E.U. and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of personal data, including the General Data Protection Regulation (“GDPR”), which imposes obligations and restrictions on the collection and use of personal data relating to individuals located in the E.U. and EEA (including with regard to health data).

Violations of any of these laws or any other governmental laws and regulations that may apply include, without limitation, significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, certain state and local laws require the registration of pharmaceutical sales representatives. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. For example, the California Consumer Privacy Act, or CCPA, which went into effect on January 1, 2020, among other things, creates new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. Although the law includes limited exceptions, including for "protected health information" maintained by a covered entity or business associate, it may regulate or impact our processing of personal information depending on the context. Further, the California Privacy Rights Act (CPRA), recently passed in California. The CPRA will impose additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It will also create a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required.

Environmental, Health and Safety Matters

We are subject to extensive environmental, health and safety laws and regulations in a number of jurisdictions, primarily Israel, governing, among other things: the use, storage, registration, handling, emission and disposal of chemicals, waste materials and sewage; chemicals, air, water and ground contamination; air emissions and the cleanup of contaminated sites, including any contamination that results from spills due to our failure to properly dispose of chemicals, waste materials and sewage. Our operations at our Yavne manufacturing facility use chemicals and produce waste materials and sewage. Our activities require permits from various governmental authorities including, local municipal authorities, the Ministry of Environmental Protection and the Ministry of Health. The Ministry of Environmental Protection and the Ministry of Health, local authorities and the municipal water and sewage company conduct periodic inspections in order to review and ensure our compliance with the various regulations.

These laws, regulations and permits could potentially require the expenditure by us of significant amounts for compliance or remediation. If we fail to comply with such laws, regulations or permits, we may be subject to fines and other civil, administrative or criminal sanctions, including the revocation of permits and licenses necessary to continue our business activities. In addition, we may be required to pay damages or civil judgments in respect of third-party claims, including those relating to personal injury (including exposure to hazardous substances we use, store, handle, transport, manufacture or dispose of), property damage or contribution claims. Some environmental, health and safety laws allow for strict, joint and several liability for remediation costs, regardless of comparative fault. We may be identified as a responsible party under such laws. Such developments could have a material adverse effect on our business, financial condition and results of operations.

In addition, laws and regulations relating to environmental, health and safety matters are often subject to change. In the event of any changes or new laws or regulations, we could be subject to new compliance measures or to penalties for activities which were previously permitted. For instance, new Israeli regulations were promulgated in 2012 relating to the discharge of industrial sewage into the sewer system. These regulations establish new and potentially significant fines for discharging forbidden or irregular sewage into the sewage system.

Properties

Our principal executive offices are located at 42 Hayarkon Street, Yavne 8122745, Israel. We lease these facilities from our largest shareholder, Clal Life Sciences, L.P. ("CLS"), pursuant to a sub-lease agreement, as amended, that expires on October 30, 2025. The facilities consist of approximately 32,300 square feet of space, and the yearly lease fee is approximately $469,000. These facilities house our administrative headquarters, our research and development laboratories and our manufacturing plant. The sub-lease agreement includes an option to extend the lease period for additional 3 years at our sole discretion.

C. Organizational Structure

The legal name of our company is MediWound Ltd. and we are organized under the laws of the State of Israel. Our corporate structure consists of MediWound Ltd., our Israeli parent company, (i) MediWound Germany GmbH, our active wholly-owned subsidiary, which was incorporated on April 16, 2013 under the laws of the Federal Republic of Germany (ii) MediWound US, Inc., which was incorporated on December 8, 2020 under the laws of the State of Delaware and (iii) MediWound UK Limited, our inactive wholly-owned subsidiary, which was incorporated on July 26, 2004 under the laws of England.

D. Property, Plants and Equipment

See "ITEM 4.B. Business Overview—Properties", "ITEM 4.B. Business Overview—Manufacturing, Supply and Production" and "ITEM 4.B. Business Overview—Environmental, Health and Safety Matters".

Item 4A. UNRESOLVED STAFF COMMENTS

None.

Item 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

A. Operating Results

The information contained in this section should be read in conjunction with our consolidated financial statements for the year ended December 31, 2021 and related notes, and the information contained elsewhere in this annual report. Our financial statements have been prepared in accordance with IFRS, as issued by the IASB.

Company Overview

We are a biopharmaceutical company that develops, manufactures and commercializes novel, cost effective, bio-therapeutic solutions for tissue repair and regeneration. Our strategy is centered around our validated enzymatic platform technology, focused on next-generation protein-based therapies for burn and wound care, and for tissue repair.

Our first innovative biopharmaceutical product, NexoBrid, received marketing authorization from the European Commission and the Israeli, Argentinean, South Korean, Russian, Ukrainian, Eurasian economic union (Armenia, Kyrgyzstan, Belarus, Kazakhstan), Peruvian, Chilean, Taiwanese and United Arab Emirates Ministries of Health for removal of dead or damaged tissue, known as eschar, in adults with deep partial- and full-thickness thermal burns, also referred to as severe burns. In September 2020, the FDA accepted for review our BLA, which was based on acute data, including primary, secondary and safety endpoints, as well as 12-month safety follow-up data derived from our Phase 3 pivotal study. In June 2021, we received a Complete Response letter from the FDA stating that our BLA was not approved. We had a Type A meeting with the FDA in October 2021 to discuss a path forward for resubmission, in which we gained clarity on a path forward for resubmission of the BLA, and we plan to resubmit our BLA for NexoBrid in mid-2022. NexoBrid, a concentrated mixture of proteolytic enzymes enriched in bromelain, represents a new paradigm in burn care management and our clinical trials have demonstrated, with statistical significance, its ability to non-surgically and rapidly remove the eschar earlier relative to existing standard of care upon patient admission, without harming viable tissues.

We commercialize NexoBrid globally via multiple sales channels. We sell NexoBrid to burn centers in Europe and Israel, primarily through our sales force, focusing on leading burn centers and key opinion leader management, and are establishing additional distribution channels in the European Union to extend the product's outreach. We have signed distribution agreements with local distributors in multiple international markets, which are responsible for obtaining local marketing authorization within the relevant territory. In the United States, we entered into exclusive license and supply agreements with Vericel to commercialize NexoBrid in North America upon FDA's approval. For additional information on the commercialization of NexoBrid See ITEM 4.B. "Information on the Company - Marketing, Sales and Distribution."

We are conducting an expanded access treatment protocol (NEXT) for NexoBrid to treat burn patients with deep partial- and full-thickness burns in the U.S., which is funded by BARDA and which will continue to take place during the review of our upcoming BLA by the FDA. We are also conducting a pediatric study to broaden the approved indication of NexoBrid, which is also being funded by BARDA, in which we reported positive topline results in July 2021.

An additional product candidate is EscharEx, a topical bioactive drug candidate designed to enzymatically debride chronic and other hard-to-heal wounds.

In January 2022 we announced positive topline results from our ongoing Phase 2 study for the treatment of VLUs. These topline results suggest that the study met its primary endpoint, demonstrating that patients treated with EscharEx had a statistically significant higher incidence of complete debridement compared to the gel vehicle, with a p-value of 0.004.

Our third innovative product candidate, MW005, is a topically applied biological drug candidate for the treatment of non-melanoma skin cancers, based on the same active substance of NexoBrid and EscharEx products, a concentrated mixture of proteolytic enzymes enriched in bromelain.

We manufacture NexoBrid and our product candidates in our state-of-the-art, EMA-certified, cGMP-compliant, sterile pharmaceutical products manufacturing facility at our headquarters in Yavne, Israel. Our securities are listed for trading on Nasdaq since March 2014 following our Initial Public Offering.

As of December 31, 2021, we had cash and cash equivalents of $11.0 million. Our revenues were $21.8 million and $23.8 million in 2020 and 2021, respectively. Our net operating loss was $8.8 million and $11.2 million in 2020 and 2021, respectively. We had an accumulated deficit of $148.5 million as of December 31, 2021. We expect to incur significant expenses and operating losses for the foreseeable future, as research and development activities are central to our operations, which will offset by cash inflows from NexoBrid.

We expect to continue to invest in our research and development efforts, including in respect of our NexoBrid ongoing clinical trials which are fully funded by BARDA, as well as the clinical development and trials of EscharEx, MW005 and our other pipeline product candidates. In addition, we expect to continue to advance NexoBrid as a standard of care, and expand its commercial reach in international markets, including for potential use as a medical countermeasure during mass casualty events.

Key Components of Statements of Operations

Revenues

Sources of revenues. We derive revenues from sales of NexoBrid to burn centers and hospitals burn units in Europe and Israel as well as to local distributors in other countries in accordance with distribution agreements we have in place, which also include revenues from licenses. We generate revenues from BARDA procurement of NexoBrid for emergency stockpile pursuant to BARDA contract.

We generate revenues from development services provided to BARDA. Our ability to generate additional, more significant revenues will depend on the successful commercialization of NexoBrid, which itself will be dependent in part upon receipt of approval from the FDA.

Cost of Revenues

Our total cost of revenues includes expenses for the manufacturing of NexoBrid, including: the cost of raw materials; employee-related expenses, including salaries, equity based-compensation and other benefits and related expenses, lease payments, utility payments, depreciation, changes in inventory of finished products, royalties and other manufacturing expenses. These expenses are partially reduced by an allotment of manufacturing costs associated with research and development activities to research and development expenses.

Cost of revenues also includes costs associated with the research and development services provided to BARDA, including salaries and related expenses, clinical trials, sub-contractors and external advisors. We expect that our cost of revenues from sale of products will continue to increase as we expand the sale of NexoBrid throughout the European Union, the United States and other international markets.

Operating Expenses

Research and Development Expenses

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as EscharEx progresses in its clinical program in the U.S. and our other pipeline product candidates' progress in clinical trials. However, we do not believe that it is possible at this time to accurately project total program-specific expenses to reach commercialization. There are numerous factors associated with the successful development of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will affect our clinical development programs and plans. Our actual spending could differ as our plans change and we invest in other drugs or potentially reduce our anticipated funding on research for existing products.

Research and development expenses consist primarily of compensation for employees engaged in research and development activities, including salaries, equity-based compensation, benefits and related expenses, clinical trials, contract research organization sub-contractors, development materials, external advisors and the allotted cost of our manufacturing facility for research and development purposes.

Selling and Marketing Expenses

Selling and marketing expenses consist primarily of compensation expenses for personnel engaged in sales and marketing, including salaries, equity based-compensation and benefits and related expenses, as well as promotion, marketing, market access, medical, and sales and distribution activities. These expenses also include costs related to our subsidiary in Germany, which is focused primarily on marketing NexoBrid, and cost related to maintain marketing authorization.

General and Administrative Expenses

General and administrative expenses consist principally of compensation for employees in executive and administrative functions, including salaries, equity-based compensation, benefits and other related expenses, professional consulting services, including legal and audit fees, as well as costs of office and overhead. We expect general and administrative expenses to remain stable.

Financial Income/Financial Expense

Financial income includes interest income, revaluation of financial instruments and exchange rate differences. Financial expense consists primarily of revaluation of financial instruments, financial expenses in respect of deferred revenue, revaluation of lease liabilities and exchange rate differences. The market interest due on government grants received from the IIA is also considered a financial expense, and is recognized beginning on the date we receive the grant until the date on which the grant is expected to be repaid as part of the revaluation to fair value of liabilities in respect of government grants.

Discontinued Operation

Following the expiration of our PolyHeal license in 2013, we accounted for our operation related to PolyHeal as a discontinued operation in accordance with IFRS accounting standard 5, “Non-current Assets Held for Sale and Discontinued Operations.” Accordingly, the results of any legal process profit or loss are reported separately as a discontinued operation in our statement of operations for the periods presented below.

Taxes on Income

The standard corporate tax rate in Israel is 23%.

We do not generate taxable income in Israel, as we have historically incurred operating losses resulting in carry forward tax losses totaling approximately $148 million as of December 31, 2021. We anticipate that we will be able to carry forward these tax losses indefinitely to future tax years. Accordingly, we do not expect to pay taxes in Israel until we have taxable income after the full utilization of our carry forward tax losses.

Under the Law for the Encouragement of Capital Investments, 5719-1959 (the "Investment Law"), we have been granted "Beneficiary Enterprise" status, which provides certain benefits, including tax exemptions and reduced corporate tax rates. Income not eligible for Beneficiary Enterprise benefits is taxed at the regular corporate tax rate. The benefit entitlement period starts from the first year that the Beneficiary Enterprise first earns taxable income, and is limited to 12 years from the year in which the company requested to have tax benefits apply.

Comparison of Period to Period Results of Operations

We are providing within this section a supplemental discussion that compares our historical statement of operations data in accordance with IFRS, as issued by the IASB. The below table and the below discussion provides data for each of the years ended December 31, 2020 and 2021. The below discussion of our results of operations omits a comparison of our results for the years ended December 31, 2019 and 2020. In order to view that discussion, please see "Item 5. Operating and Financial Review and Prospects—A. Operating Results— Comparison of Period to Period Results of Operations— Year Ended December 31, 2019 Compared to Year Ended December 31, 2020" in our Annual Report on Form 20-F for the year ended December 31, 2020, which we filed with the SEC on February 25, 2021.

	Years Ended December 31,	
	2020	**2021**
	(*in thousands*)	
condensed statements of operations data:		
Revenues	$ 21,763	$ 23,763
Cost of revenues	14,218	14,992
Gross profit	7,545	8,771
Operating expenses:		
Research and development	7,698	10,256
Selling and marketing	3,228	3,388
General and administrative	5,459	6,348
Operating loss	**(8,840)**	**(11,221)**
Financial expenses, net	(436)	(2,303)
Loss from continuing operations	(9,276)	(13,524)
Profit from discontinued operation	80	-
Tax expenses	-	(27)
Net loss	$ (9,196)	$ (13,551)

Year Ended December 31, 2020 Compared to Year Ended December 31, 2021

Revenues

	Years Ended December 31,	
	2020	2021
	(*in thousands*)	
Revenues from sale of products	$ 7,445	$ 9,613
Revenues from development services	13,935	12,372
Revenues from license agreements	383	1,778
	21,763	23,763

We generated total revenues of approximately $23.8 million for the year ended December 31, 2021 compared to approximately $21.8 million for the year ended December 31, 2020. The increase in total revenues was a result of an increase in sale of products of $2.1 mainly derived from BARDA emergency stockpile procurement of $1.6 million and an increase in license sales of $1.4 million, partially offset by a decrease in development services to BARDA of $1.6 million.

Revenues from sale of products

Revenues from sales of products in 2021 increased $2.2 million, or 29%, in comparison to 2020, primarily as a result of BARDA's procurement of NexoBrid for emergency stockpile of approximately $5.5 million net in 2021, versus approximately $3.8 million net during 2020. Revenues from BARDA's procurement were recognized net of Vericel's share pursuant to gross profit split.

Revenues from development services

Revenues from development services decreased 11% from $13.9 million in 2020 to $12.4 million in 2021, as a result of completion of NexoBrid clinical studies.

Revenues from license agreement

In 2021, we recognized $1.8 million, of license revenues, driven by new distribution agreements and achieving certain milestones with current distributors agreements, compared to $0.4 million in 2020.

Our revenues, as reported in our consolidated financial statements, are based on the location of the customers, as shown in the below table:

	Years Ended December 31,	
	2020	2021
	(*in thousands*)	
International (excluding U.S.)	$ 3,733	$ 5,649
U.S.	18,030	18,069
	21,763	23,718

BARDA contributed 83% and 76% of our total revenues in 2020 and 2021, respectively.

Costs and Expenses

Cost of revenues

	Years Ended December 31,	
	2020	2021
	(*in thousands*)	
Cost of revenues from sales of products	$ 3,151	$ 4,983
Cost of revenues from development services	11,067	9,907
Cost of revenues from license agreements	-	102
	14,218	14,992

Cost of revenues as a percentage of total revenues decreased from 65% for 2020 to 63% for 2021.

Cost of revenues from sales of products as a percentage of revenues from sales of products increased to approximately 52% for the year ended December 31, 2021 from approximately 42% in the year ended December 31, 2020. The increase of cost of revenues from sales of product is primarily driven by BARDA procurement for emergency response preparedness.

Cost of revenues from development services as a percentage of revenues from development services was approximately 80% in the year ended December 31, 2021 compared to approximately 79% in the year ended December 31, 2020.

Cost of revenues from license agreements as a percentage of revenues from license agreements were 6% in the year ended December 31, 2021, due to costs associated with the support of our distributors to achieve their marketing authorizations.

Research and development expenses,

Research and development expenses, increased by 34% from approximately $7.7 million in the year ended December 31, 2020 to approximately $10.3 million in the year ended December 31, 2021. The increase was primarily related to EscharEx clinical development program.

Selling and marketing expenses

Selling and marketing expenses increased by 6% in 2021 compared to 2020, from approximately $3.2 million in the year ended December 31, 2020 to approximately $3.4 million in the year ended December 31, 2021.

General and administrative expenses

General and administrative expenses increased 15% in 2021 compared to 2020 from approximately $5.5 million in the year ended December 31, 2020 to approximately $6.3 million in the year ended December 31, 2021. The increase in general and administrative expenses was primarily due to rent and maintenance allocation and legal consultation.

Financial income, net

	Years Ended December 31,	
	2020	2021
	(*in thousands*)	
Financial income	$ 843	$ 11
Financial expenses	(1,279)	(2,314)
	(436)	(2,303)

Financial income

Financial income decreased from $0.8 million in the year ended December 31, 2020 to $0 million in the year ended December 31, 2021. The decrease was primarily driven by the Teva contingent liability revaluation and interest on deposits.

Financial expense

Financial expense increased from approximately $1.3 million in the year ended December 31, 2020 to approximately $2.3 million in the year ended December 31, 2021. The increase in financial expenses in 2021 was primarily driven by the Teva contingent liability revaluation, described below under “Application of Critical Accounting Policies and Estimates - Contingent Consideration for Purchase of Shares”, the Israeli innovation authority grant interest, currency exchange fluctuations and lease revaluations.

Profit from Discontinued operations

Profit from discontinued operations was $0 million for the year ended December 31, 2021 compared with $0.1 million for the year ended December 31, 2020. The profit from discontinued operations in 2020 was as a result of the Polyheal settlement of the litigation with certain PolyHeal Ltd.'s ("PolyHeal") shareholders. See “ITEM 8.A. Consolidated Statements and Other Financial Information—Legal Proceedings”.

B. Liquidity and Capital Resources

Our primary uses of cash are to fund working capital requirements, manufacturing costs, research and development expenses of EscharEx and other products candidates, as well as sales and marketing activities associated with the commercialization of NexoBrid in Europe.

We completed an underwritten follow-on offering in September 2017, whereby we issued and sold 5,037,664 ordinary shares and received net proceeds of approximately $22.7 million (after deducting the underwriting discount and offering expenses payable by us), pursuant to our previous shelf registration statement on Form F-3. We will continue to use the net proceeds from the sale of securities offered by us pursuant to that follow-on offering to fund our research and development activities, primarily the clinical development of EscharEx, and the remainder, if any, for working capital and other general corporate purposes. The timing and amount of our actual expenditures will be based on many factors, including cash flows from operations and the anticipated growth of our business. Under our current shelf registration statement on Form F-3 declared effective by the SEC on April 22, 2019, we may offer from time to time up to $125 million in the aggregate of our ordinary shares, warrants and/or debt securities in one or more series or issuances. In February 2020, we entered into an Open Market Sales Agreement with Jefferies LLC to issue and sell our ordinary shares with gross sales proceeds of up to $15 million, from time to time, through an at the market offering under which Jefferies LLC will act as our sales agent. As of the date hereof, we have not issued or sold any ordinary shares pursuant to the Open Market Sales Agreement.

Funding under the BARDA contracts is classified under cash use for continuing operating activities.

As of December 31, 2021, we had $11.0 million of cash, cash equivalents and short-term deposits. Our net operating loss was $8.8 million and $11.2 million for the years ended December 31, 2020 and 2021, respectively. As of December 31, 2021, we had an accumulated deficit of $148.5 million. We expect to incur significant expenses and operating losses for the foreseeable future. The net losses we will incur may fluctuate from quarter to quarter.

Our capital expenditures for fiscal years 2020 and 2021 amounted to $0.9 million and $0.5 million, respectively. Capital expenditures consist primarily of investments in manufacturing equipment and leasehold improvements.

In March 2022, we entered into an underwriting agreement with Oppenheimer & Co., Inc., a representative of the several underwriters (the “Underwriters”), relating to the issuance and sale of an aggregate of 5,208,333 of our ordinary shares at a price per share equal to $1.92. Total gross proceeds of the offering was approximately $10.0 million. The offering closed on March 7, 2022 and we received approximately $8.7 million in net proceeds, after deducting underwriting discounts and commissions and estimated offering expenses. Certain entities affiliated with CBI purchased approximately $2.8 million of ordinary shares in the offering at the public offering price. The Underwriters received the same underwriting discount on the shares purchased by these entities as they will on any other shares sold to the public in this offering. The securities purchased by these entities are subject to lock-up agreements with the Underwriters. We also granted the underwriters a 30-day option to purchase up to an additional 781,249 ordinary shares at the public offering price, less underwriting discounts and commissions.

Our future capital requirements will depend on many factors, including our revenue growth, timing of milestone payments, the timing and extent of our spending on research and development efforts, and international expansion. We may also seek to invest in or acquire complementary businesses or technologies. To the extent that existing cash and cash from operations are insufficient to fund our future activities, we may need to raise additional funding through debt and equity financing. Additional funds may not be available on favorable terms or at all. We believe our existing cash, cash equivalents and short-term bank deposits will be sufficient to satisfy our liquidity requirements for at least the next 24 months.

Cash Flows

The following table summarizes our consolidated statement of cash flows for the periods presented. The below discussion beneath the table omits a description of our cash flows for the year ended December 31, 2019. In order to view that discussion, please see "Item 5. Operating and Financial Review and Prospects—B. Liquidity and Capital Resources—Cash Flows" in our Annual Report on Form 20-F for the year ended December 31, 2020, which we filed with the SEC on February 25, 2021:

	Year Ended December 31,	
	2020	**2021**
Net cash provided by (used in):		
Continuing operating activities	$ (6,700)	$ (8,916)
Continuing investing activities	17,385	3,548
Continuing financing activities	(629)	(1,050)
Discontinued operating activities	(195)	-

Net cash used in continuing operating activities

Net cash used in all periods resulted primarily from our net loss adjusted for non-cash charges and measurements and changes in components of working capital. Adjustments for non-cash items include depreciation and amortization, equity-based compensation, revaluation of contingent liabilities and lease liability, and changes in assets and liabilities items.

Net cash used in continuing operating activities increased to approximately $8.9 million in the year ended December 31, 2021 compared to net cash used by continuing operating activities of approximately $6.7 million in the year ended December 31, 2020, primarily as a result of the operational net loss, partially offset by various non-cash items such as depreciation, shared based compensation and revaluation of contingent consideration for the purchase of shares.

Net cash used in discontinued operating activities

Net cash used in discontinued operating activities was $0 million in the year ended December 31, 2021, compared to approximately $0.2 million in the year ended December 31, 2020. The cash used in 2020 was primarily attributable to the consideration paid to PolyHeal's shareholders following the settlement of the litigation with certain PolyHeal's shareholders. See "ITEM 8.A. Consolidated Statements and Other Financial Information—Legal Proceedings".

Net cash provided by continuing investing activities

Net cash provided by continuing investing activities primarily resulted from proceeds of investments in short-term banks deposits offset by purchases of property and equipment. Net cash provided by investing activities was $3.5 million in the year ended December 31, 2021, compared to $17.4 million provided during the year ended December 31, 2020.

Net cash used in continuing financing activities

Net cash provided by continuing financing activities primarily resulted from payments of lease liabilities and repayment to IIA. Net cash used in continuing financing activities was $1.1 million during the year ended December 31, 2021 compared to $0.6 million during the year ended December 31, 2020.

Israeli Corporate-Level Tax Considerations and Government Programs

The following is a brief summary of the material Israeli tax laws applicable to us, and certain Israeli Government programs that benefit us and therefore impact our results of operations and financial condition. To the extent that the discussion is based on new tax legislation that has not yet been subject to judicial or administrative interpretation, we cannot assure you that the appropriate tax authorities or the courts will accept the views expressed in this discussion. The discussion below is subject to change, including due to amendments under Israeli law or changes to the applicable judicial or administrative interpretations of Israeli law, which change could affect the tax consequences described below.

General Corporate Tax Structure in Israel

Generally, Israeli companies are subject to a corporate tax on their taxable income. Effective January 1, 2018 and thereafter, the corporate tax rate is 23%. However, the effective tax rate payable by a company that derives income from an Approved Enterprise, a Beneficiary Enterprise, a Preferred Enterprise or Technology Enterprise (as discussed below) may be considerably less. Capital gains derived by an Israeli company are generally subject to the prevailing regular corporate tax rate.

Law for the Encouragement of Industry (Taxes), 5729-1969

The Law for the Encouragement of Industry (Taxes), 5729-1969 (the "Industry Encouragement Law"), provides several tax benefits for "Industrial Companies."

The Industry Encouragement Law defines an "Industrial Company" as an Israeli resident-company which was incorporated in Israel, of which 90% or more of its income in any tax year, other than income from certain government loans, is derived from an "Industrial Enterprise" owned by it and located in Israel. An "Industrial Enterprise" is defined as an enterprise whose principal activity in a given tax year is industrial production.

The following tax benefits, among others, are available to Industrial Companies:

- amortization of the cost of purchased a patent, rights to use a patent, and know-how, which are used for the development or advancement of the Industrial Enterprise, over an eight-year period, commencing on the year in which such rights were first exercised;
- under limited conditions, an election to file consolidated tax returns with related Israeli Industrial Companies controlled by it; and
- expenses related to a public offering are deductible in equal amounts over a three years period commencing on the year of the offering.

Eligibility for benefits under the Industry Encouragement Law is not contingent upon approval of any governmental authority.

We believe that we currently qualify as an Industrial Company within the meaning of the Industry Encouragement Law. However, there can be no assurance that we will continue to qualify as an Industrial Company or that the benefits described above will be available in the future.

Law for the Encouragement of Capital Investments, 5719-1959

The Investment Law provides certain incentives for capital investments in production facilities (or other eligible assets).

The Investment Law was significantly amended several times during recent years, with the three most significant changes effective as of April 1, 2005 (the "2005 Amendment"), as of January 1, 2011 (the "2011 Amendment"), and as of January 1, 2017 (the "2017 Amendment"). Pursuant to the 2005 Amendment, tax benefits granted in accordance with the provisions of the Investment Law prior to its revision by the 2005 Amendment remain in force but any benefits granted subsequently are subject to the provisions of the amended Investment Law. Similarly, the 2011 Amendment introduced new benefits to replace those granted in accordance with the provisions of the Investment Law in effect prior to the 2011 Amendment. However, companies entitled to benefits under the Investment Law as in effect prior to January 1, 2011 were entitled to choose to continue to enjoy such benefits, provided that certain conditions are met, or elect instead, irrevocably, to forego such benefits and have the benefits of the 2011 Amendment apply. The 2017 Amendment introduces new benefits for Technological Enterprises, alongside the existing tax benefits. Prior to 2011, we did not utilize any of the benefits for which we were eligible under the Investment Law.

The following is a summary of the Investment Law subsequent to its amendments as well as the relevant changes contained in the new legislation.

Tax Benefits Subsequent to the 2005 Amendment

The 2005 Amendment applies to new investment programs and investment programs commencing after 2004, but does not apply to investment programs approved prior to April 1, 2005 ("Approved Enterprise"). The 2005 Amendment provides that terms and benefits included in any certificate of approval that was granted before the 2005 Amendment became effective (April 1, 2005) will remain subject to the provisions of the Investment Law as in effect on the date of such approval. Pursuant to the 2005 Amendment, the Israeli Authority for Investments and Development of the Israeli Ministry of Economy (the "Investment Center") will continue to grant Approved Enterprise status to qualifying investments. The 2005 Amendment, however, limits the scope of enterprises that may be approved by the Investment Center by setting criteria for the approval of a facility as an Approved Enterprise.

The 2005 Amendment provides that Approved Enterprise status will only be necessary for receiving cash grants. As a result, it is no longer necessary for a company to obtain the advance approval of the Investment Center in order to receive the tax benefits previously available under the alternative benefits track. Rather, a company may claim the tax benefits offered by the Investment Law directly in its tax returns, provided that its facilities meet the criteria for tax benefits set forth in the 2005 Amendment. Companies or programs under the new provisions receiving these tax benefits are referred to as Beneficiary Enterprises. Companies that have a Beneficiary Enterprise, are entitled to approach the Israel Tax Authority for a pre-ruling regarding their eligibility for tax benefits under the Investment Law, as amended.

Tax benefits are available under the 2005 Amendment to production facilities (or other eligible facilities), which are generally required to derive more than 25% of their business income from export to specific markets with a population of at least 14 million in 2012 (such export criteria will further increase in the future by 1.4% per annum). In order to receive the tax benefits, the 2005 Amendment states that a company must make an investment which meets certain conditions, including exceeding a minimum investment amount specified in the Investment Law. Such investment allows a company to receive "Beneficiary Enterprise" status, and may be made over a period of no more than three years from the end of the year in which the company chose to have the tax benefits apply to its Beneficiary Enterprise. Where the company requests to apply the tax benefits to an expansion of existing facilities, only the expansion will be considered to be a Beneficiary Enterprise and the company's effective tax rate will be the weighted average of the applicable rates. In this case, the minimum investment required in order to qualify as a Beneficiary Enterprise is required to exceed a certain percentage of the value of the company's production assets before the expansion.

The extent of the tax benefits available under the 2005 Amendment to qualifying income of a Beneficiary Enterprise depends on, among other things, the geographic location in Israel of the Beneficiary Enterprise. The location will also determine the period for which tax benefits are available. Such tax benefits include an exemption from corporate tax on undistributed income for a period of between two to ten years, depending on the geographic location of the Beneficiary Enterprise in Israel, and a reduced corporate tax rate of between 10% to 25% for the remainder of the benefits period, depending on the level of foreign investment in the company in each year. A company qualifying for tax benefits under the 2005 Amendment which pays a dividend out of income attributed to its Beneficiary Enterprise during the tax exemption period will be subject to corporate tax in respect of the amount of the dividend distributed (grossed-up to reflect the pre-tax income that it would have had to earn in order to distribute the dividend) at the corporate tax rate that would have otherwise been applicable. Dividends paid out of income attributed to a Beneficiary Enterprise (or out of dividends received from a company whose income is attributed to a Beneficiary Enterprise) are generally subject to withholding tax at source at the rate of 15% or such lower rate as may be provided in an applicable tax treaty, applicable to dividends and distributions out of income attributed to a Beneficiary Enterprise. The reduced rate of 15% is limited to dividends and distributions out of income attributed to a Beneficiary Enterprise during the benefits period and actually paid at any time up to 12 years thereafter, except with respect to a qualified Foreign Investment Company (as such term is defined in the Investment Law), in which case the 12-year limit does not apply.

The benefits available to a Beneficiary Enterprise are subject to the fulfillment of conditions stipulated in the Investment Law and its regulations. If a company does not meet these conditions, it would be required to refund the amount of tax benefits, as adjusted by the Israeli consumer price index, and interest, or other monetary penalties.

We currently have Beneficiary Enterprise programs under the Investment Law, which we believe will entitle us to certain tax benefits. The majority of any taxable income from our Beneficiary Enterprise programs (once generated) would be tax exempt for a period of ten years commencing in the year in which we will first earn taxable income relating to such enterprises, subject to the 12-year limitation from the year the company chose to have its tax benefits apply.

Tax Benefits Under the 2011 Amendment

The 2011 Amendment canceled the availability of the tax benefits granted under the Investment Law prior to 2011 and, instead, introduced new tax benefits for income generated by a "Preferred Company" through its "Preferred Enterprise" (as such terms are defined in the Investment Law) as of January 1, 2011. The definition of a Preferred Company includes a company incorporated in Israel that is not fully owned by a governmental entity, and that has, among other things, Preferred Enterprise status and is controlled and managed from Israel.

The tax benefits under the 2011 Amendment for a Preferred Company meeting the criteria of the law include, among others, a reduced corporate tax rate of 15% for preferred income attributed to a Preferred Enterprise in 2011 and 2012, unless the Preferred Enterprise was located in a specified development zone, in which case the rate was 10%. Under the 2011 Amendment, such corporate tax rate was reduced in 2013 from 15% and 10%, respectively, to 12.5% and 7%, respectively, and then increased to 16% and 9%, respectively, in 2014 and thereafter until 2016. Pursuant to the 2017 Amendment, in 2017 and thereafter, the corporate tax rate for Preferred Enterprise which is located in a specified development zone was decreased to 7.5%, while the reduced corporate tax rate for other development zones remains 16%. Income attributed to a Preferred Company from a "Special Preferred Enterprise" (as such term is defined in the Investment Law) would be entitled, during a benefits period of 10 years, to reduced tax rates of 8%, or 5% if the Special Preferred Enterprise is located in a certain development zone. As of January 1, 2017, the definition of "Special Preferred Enterprise" includes less stringent conditions. Dividends paid out of preferred income attributed to a Preferred Enterprise or to a Special Preferred Enterprise are generally subject to withholding tax at source at the rate of 20% or such lower rate as may be provided in an applicable tax treaty (subject to the receipt in advance of a valid certificate from the Israel Tax Authority allowing for a reduced tax rate). However, if such dividends are paid to an Israeli company, no tax is required to be withheld (although, if such dividends are subsequently distributed to individuals or a non-Israeli company, withholding tax at a rate of 20% or such lower rate as may be provided in an applicable tax treaty will apply).

The 2011 Amendment also provided transitional provisions to address companies already enjoying existing tax benefits under the Investment Law. These transitional provisions provide, among other things, that: unless an irrevocable request is made to apply the provisions of the Investment Law as amended in 2011 with respect to income to be derived as of January 1, 2011, a Beneficiary Enterprise can elect to continue to benefit from the benefits provided to it before the 2011 Amendment came into effect, provided that certain conditions are met.

We have examined the possible effect, if any, of these provisions of the 2011 Amendment on our financial statements and have decided, at this time, not to opt to apply the new benefits under the 2011 Amendment. There can be no assurance that we will comply with the conditions required to remain eligible for benefits under the Investment Law in the future or that we will be entitled to any additional benefits thereunder.

New Tax benefits under the 2017 Amendment that became effective on January 1, 2017.

The 2017 Amendment was enacted as part of the Economic Efficiency Law that was published on December 29, 2016, and is effective as of January 1, 2017. The 2017 Amendment provides new tax benefits for two types of "Technology Enterprises," as described below, and is in addition to the other existing tax beneficial programs under the Investment Law.

The 2017 Amendment provides that a technology company satisfying certain conditions will qualify as a "Preferred Technology Enterprise" and will thereby enjoy a reduced corporate tax rate of 12% on income that qualifies as "Preferred Technology Income," as defined in the Investment Law. The tax rate is further reduced to 7.5% for a Preferred Technology Enterprise located in development zone A. In addition, a Preferred Technology Company will enjoy a reduced corporate tax rate of 12% on capital gain derived from the sale of certain "Benefitted Intangible Assets" (as defined in the Investment Law) to a related foreign company if the Benefitted Intangible Assets were acquired from a foreign company on or after January 1, 2017 for at least NIS 200 million, and the sale receives prior approval from the Israeli Innovation Authority.

The 2017 Amendment further provides that a technology company satisfying certain conditions will qualify as a "Special Preferred Technology Enterprise" and will thereby enjoy a reduced corporate tax rate of 6% on "Preferred Technology Income" regardless of the company's geographic location within Israel. In addition, a Special Preferred Technology Enterprise will enjoy a reduced corporate tax rate of 6% on capital gain derived from the sale of certain "Benefitted Intangible Assets" to a related foreign company if the Benefitted Intangible Assets were either developed by Special Preferred Technology Enterprise or acquired from a foreign company on or after January 1, 2017, and the sale received prior approval from IIA. A Special Preferred Technology Enterprise that acquires Benefitted Intangible Assets from a foreign company for more than NIS 500 million will be eligible for these benefits for at least ten years, subject to certain approvals as specified in the Investment Law.

Dividends distributed by a Preferred Technology Enterprise or a Special Preferred Technology Enterprise, paid out of Preferred Technology Income, are generally subject to withholding tax at source at the rate of 20% or such lower rate as may be provided in an applicable tax treaty (subject to the recipient in advance of a valid certificate from the Israeli Tax Authority allowing for reduced tax rate). However, if such dividends are paid to an Israeli company, no tax is required to be withheld. If such dividends are distributed to a foreign company and other conditions are met, the withholding tax rate will be 4% (or a lower under the tax treaty, if applicable, subject to the receipt in advance of a valid certificate from the Israeli Tax Authority allowing for a reduced tax rate).

C. Research and Development, Patents and Licenses, etc.

Our research and development strategy is centered on developing our patented proteolytic enzyme technology, which underlies NexoBrid and EscharEx, into additional products for high-value indications. Our research and development team is located at our facilities in Yavne, Israel, and consists of 25 employees as of December 31, 2021 and is supported by highly experienced consultants in various research and development disciplines.

We have received government grants (subject to our obligation to pay royalties) as part of the NexoBrid and EscharEx research and development programs approved by the IIA. The total gross amount of grants actually received by us from the IIA, including accrued LIBOR interest and net of royalties actually paid, totaled approximately $13.8 million as of December 31, 2021 and the amortized cost (using the interest method) of the liability totaled approximately $7.3 million and $8.1 million as of December 31, 2020 and 2021, respectively. Because the repayment of IIA grants is in the form of future royalties, the balance of the commitments to the IIA is presented as an amortized liability on our balance sheet. As of December 31, 2021, we had accrued and paid royalties to the IIA totaling $1.3 million.

We received funds from BARDA in accordance with the terms of our BARDA contracts. As of December 31, 2021 we had accrued $70 million of BARDA's participation in NexoBrid's research and development programs.

For a description of our research and development policies for the last three years, see "ITEM 4.B. Business Overview—Research and Development."

D. Trend Information

The COVID-19 pandemic has impacted companies in Israel and around the world, and as its trajectory remains highly uncertain, we cannot predict the duration and severity of the outbreak, its containment measures or the nature, timing and strength of recovery from it. Further, we cannot predict impacts, trends and uncertainties involving the pandemic's effects on economic activity, the size of our labor force, our third-party partners, our investments in marketable securities, and the extent to which our revenue, income, profitability, liquidity, or capital resources may be materially and adversely affected prospectively. See also "ITEM 3.D. – Risk Factors – "The coronavirus (COVID-19) outbreak could adversely impact our business, financial condition and results of operations." and – "We depend on a sole supplier to obtain our intermediate drug substance, bromelain SP, which is necessary for the production of our products."

Other than the foregoing and as disclosed elsewhere in this annual report, we are not aware of any trends, uncertainties, demands, commitments or events for the period from January 1, 2021 to the present time that are reasonably likely to have a material adverse effect on our net revenue, income, profitability, liquidity or capital resources, or that would cause the disclosed financial information to be not necessarily indicative of future operating results or financial condition.

E. Critical Accounting Estimates

Our consolidated financial statements are prepared in conformity with IFRS, as issued by the IASB. The preparation of these historical financial statements in conformity with IFRS requires management to make estimates, assumptions and judgments in certain circumstances that affect the reported amounts of assets, liabilities and contingencies as of the date of the financial statements and the reported amounts of revenue and expenses during the reporting periods. We evaluate our assumptions and estimates on an ongoing basis. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. Our critical accounting estimates are described in Notes 2 and 3 to our consolidated financial statements included elsewhere in this annual report.

Item 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and Senior Management

The following table sets forth the name, age and position of each of our executive officers and directors as of March 15, 2022:

Name	Age	Position
Executive Officers		
Sharon Malka	50	Chief Executive Officer
Boaz Gur-Lavie	48	Chief Financial Officer
Lior Rosenberg, M.D.	76	Chief Medical Technology Officer
Ety Klinger Ph.D.	60	Chief Research and Development Officer
Yaron Meyer	43	Executive Vice President, General Counsel and Corporate Secretary
Directors		
Stephen Wills	65	Executive Chairman of the Board of Directors
Ofer Gonen	49	Director
Assaf Segal	50	Director
Vickie R. Driver, M.D[(1)(3)]	68	Director
Nissim Mashiach[(1)(2)(3)(4)]	61	Director
Sharon Kochan[(1)(2)(3)(4)]	53	Director
Samuel Moed [(2)(3)]	59	Director
David Fox[(3)]	64	Director

(1) Member of our audit committee.

(2) Member of our compensation committee.

(3) Independent director under the listing rules of the Nasdaq Stock Market.

(4) External director under the Companies Law.

Executive Officers

Sharon Malka has served as our Chief Executive Officer since May 2019. Prior to that time, he served as our Chief Financial and Operations Officer, beginning in April 2007. From 2002 to 2007, Mr. Malka was a partner at Variance Economic Consulting Ltd., a multi-disciplinary consulting boutique that specializes in financial and business services. Mr. Malka also served as a Senior Manager at Kesselman Corporate Finance, a division of PricewaterhouseCoopers Global Network, from 1998 to 2002. Mr. Malka holds a B.Sc. in Business Administration from the Business Management College in Israel and an M.B.A. from Bar Ilan University, Israel.

Boaz Gur-Lavie has served as our Chief Financial Officer since June 2019. Prior to joining MediWound, Mr. Gur-Lavie co-founded in 2015 the Center for Digital Innovation (CDI), a non-profit organization determined to improve the quality of lives by creating innovative new solutions for challenges in the space of healthy aging and digital health, while focusing on senior citizens. In early 2015, he also co-founded MDClone, which introduced the world's first Healthcare Data Sandbox, unlocking healthcare data to enable exploration, discovery and collaboration. Previously, he served as the chief financial officer of the Nasdaq-listed company, Pluristem Therapeutics, a stem-cell development company, from 2013 to 2015. He also served as the chief financial officer of STARLIMS, a Nasdaq listed company, until it was acquired by Abbott Laboratories in 2010, after which he served as the chief financial officer of Abbott's informatics division until 2013. Mr. Gur-Lavie is a certified public accountant and received his B.A. in economics and M.B.A. in finance from the Ben-Gurion University in Israel.

Lior Rosenberg is one of our co-founders and has served as our Chief Medical Technology Officer since 2001 and served as a member of our board of directors from 2001 to 2013. Since 2001, Dr. Rosenberg has headed the unit for Cleft Lip Palate and Craniofacial Deformities at Soroka University Medical Center and Meir Medical Centers in Beer Sheva and Kfar Saba, Israel, respectively. Since 1987, he has served as a Full Professor of plastic surgery at the Ben-Gurion University Medical School in Beer Sheva, Israel. He also serves as the Chairman of the Burn Disaster Committee for the International Society of Burn Injuries and the Israeli Ministry of Health. From 1987 to 2012, Dr. Rosenberg served as the chairman of the Department of Plastic Surgery and Burn Unit at Soroka University Medical Center in Beer Sheva, Israel. He is a founding member of the Israeli Burn Association and the Mediterranean Burn Council, a member of the American Burn Association and a national representative at the European Burn Association. Dr. Rosenberg holds a M.D. degree from Tel-Aviv University, Israel and a Professor of Plastic Surgery degree from the Ben Gurion University, Israel.

Ety Klinger has served as our Chief Research and Development Officer since May 2014. Prior to joining MediWound, Dr. Klinger was Vice President of Research and Development at Proteologics Ltd since July 2011, where she was responsible for discovery projects in the ubiquitin system, conducted in collaboration with GlaxoSmithKline plc and Teva. Prior to this, Dr. Klinger served for 17 years in numerous leadership positions at Teva's global innovative R&D division and served as Teva's Board representative at various biotechnology companies. Dr. Klinger was a key member of the Copaxone® development team. As a project leader she led the chemistry, manufacture and control, preclinical, clinical and post-marketing R&D activities of various innovative treatments for multiple sclerosis (MS), autoimmune and neurological diseases. From 2006 to 2011, as a Senior Director at Teva, Dr. Klinger was a member of Teva's global innovative R&D management team. From 2006 to 2008, she served as the Head of MS and Autoimmune Diseases at Teva, and led the Life Cycle Management (LCM) of innovative R&D. Dr. Klinger holds a B.Sc. in Biology from the Hebrew University in Jerusalem, a M.S. and a Ph.D. in Biochemistry from Tel-Aviv University and an MBA degree from Tel Aviv University and Northwestern University.

Yaron Meyer has served as our Executive Vice President since March 2019 and as our General Counsel and Corporate Secretary since December 2013. From April 2008 to November 2013, he served as the Corporate Secretary of Clal Biotechnology Industries Ltd. (CBI). From November 2010 to November 2013, he served as the General Counsel and Corporate Secretary of D-Pharm Ltd. From April 2008 to May 2010, he served as a legal counsel of Clal Industries Ltd. From May 2005 to April 2008, he worked as an associate at Shibolet & Co. Advocates. Mr. Meyer holds an LL.B. degree from Haifa University, Israel.

Directors

Stephen T. Wills has served as a member of our board of directors since May 2017, as Chairman of our board since October 2017 and as Executive Chairman of our board since May 2019. Mr. Wills serves as Chief Financial Officer (since 1997) and Chief Operating Officer (since 2011) of Palatin Technologies, Inc. (NYSE: PTN), a biopharmaceutical company developing targeted, receptor-specific peptide therapeutics for the treatment of diseases with significant unmet medical need and commercial potential. Mr. Wills serve on the boards of Gamida Cell Ltd. (Nasdaq: GMDA), a leading cellular and immune therapeutics company since March 2019 (audit and finance committee member) and of Amryt Pharma, a biopharmaceutical company focused on developing and delivering treatments to help improve lives of patients with rare and orphan diseases since September 2019 (chairman of audit committee and member of the finance committee). Mr. Wills also serves on the board of trustees and executive committee of The Hun School of Princeton, a college preparatory day and boarding school since 2013, and its chairman since June 2018. Mr. Wills served on the board of directors of Caliper Corporation, a psychological assessment and talent development company since March 2016 and as chairman since December 2016 do December 2019, when Caliper was acquired by PSI. Mr. Wills serves as executive chairman and interim principal executive officer of Derma Sciences Inc. a provider of advanced wound care product from December 2015 to February 2017, when Derma Sciences was acquired by Integra Lifesciences (Nasdaq: IART). Previously, Mr. Wills served on the Board of Derma Sciences as the lead director and chairman of the audit committee from June 2000 to December 2015. Mr. Wills served as the Chief Financial Officer of Derma Sciences from 1997 to 2000. Mr. Wills served as the president and Chief Operating Officer of Wills, Owens & Baker, P.C., a public accounting firm from 1991 to 2000. Mr. Wills, a certified public accountant, earned his Bachelor of Science in accounting from West Chester University, and a Master of Science in taxation from Temple University.

Ofer Gonen has served as a member of our board of directors since September 2003. Mr. Gonen is the Chief Executive Officer of Clal Biotechnology Industries Ltd. (TASE: CBI) and Cactus Acquisition Corp. 1 (Nasdaq: CCTS). Mr. Gonen has more than 20 years of experience in managing life science investments and business collaborations in both the US and Israel. Mr. Gonen serves as a board member of several private and publicly-traded portfolio companies of CBI, including Gamida Cell (Nasdaq: GMDA), MediWound (Nasdaq: MDWD) and Cactus (Nasdaq: CCTS), as well as a managing partner at the Anatomy Medical Fund. Before joining CBI, Mr. Gonen was the General Manager of Biomedical Investments Ltd., a partner at Arte Venture Group, as well as a technology consultant to various Israeli venture capital funds. Mr. Gonen gained extensive experience in R&D and management of defense-oriented projects at the prestigious “Talpiot” program of the Israeli Defense Forces. He holds a B.Sc. in Physics, Mathematics and Chemistry from the Hebrew University of Jerusalem, and an M.A. in Economics and Finance from Tel Aviv University, with distinction.

*Assaf Segal*has served as a member of our board of directors since October 2017. Mr. Segal serves as a board member of several companies, including Biokine therapeutics Ltd., Campus Bio L.P., Clal Life Sciences L.P. and Clal Application Center Ltd. Prior to that time, Mr. Segal was a Partner at Variance Economic Consulting Ltd., from 2004 until June 2015, where he provided in-depth consulting for international and local clients in a wide range of industries, including telecommunications, internet, biotech, heavy industry and financial sectors. Previously, he founded a start-up software company. Mr. Segal also previously held a managerial position at PriceWaterhouseCoopers Corporate Finance and was an Economic Department manager at the North American division of Amdocs Inc. His experience also includes risk management and house account (“Nostro”) trading at the Union Bank of Israel, and serving as an economist for capital markets in the Research Department of the Bank of Israel. Mr. Segal also has many years of experience in economic consulting and company valuations, joint ventures and financial instruments for investments, M&A, and IPOs. He has 15 years of experience in economic consulting for international and local clients in the Bio-Tech sector as well as in Hi-Tech, financial and other sectors. He holds a B.A. in Economics and Statistics and an M.B.A. (Finance and Information Systems) from the Hebrew University of Jerusalem.

*Vickie R. Driver*has served as a member of our board of directors since May 2017. Dr. Driver is board certified in foot surgery by the American Board of Podiatric Surgery and is a Fellow at the American College of Foot and Ankle Surgeons, licensed in Rhode Island. Her career as a podiatric physician and surgeon has included a special emphasis on limb preservation and wound healing in her medical practice, as well as, research and education. Dr. Driver has been a Professor of Surgery in the Department of Orthopedics at Brown University (Clinical) since 2014. She has served for 9 years on the Board of Directors for the Association for the Advancement of Wound Care ("**AAWC**"), and recently completed her tenure as President for this international organization. Dr. Driver is also the chair of Wound Care Experts and U.S. Food and Drug Administration ("**FDA**") Clinical Endpoints Project. She has just been named to serve as member at large to the Board of Directors of the Wound Healing Society ("**WHS**") and Board Member to the Critical Limb Ischemia ("**CLI**") Global Society. In addition, she serves on multiple national and international clinical committees that focus on preventing limb loss and improving wound healing in the high-risk population. She has served as an investigator for more than 70 important multi-center randomized clinical trials, as well as developed and supervised multiple research fellowship training programs. She has served and chaired multiple committees for large national and international pivotal clinical trials and has authored over 120 publications and abstracts. Dr. Driver is credited with the development and directorship of multiple major multidisciplinary Limb Preservation– Wound Healing Centers of Excellence, including Military/VA, Hospital and University based programs. Since 2015, she has served as Director, Translational Medicine, Wound Healing at the Novartis Institute for Biomedical Research. From 2011 to 2014, she was Program Director, Inaugural Educational Committee at the American College of Wound Healing and Tissue Repair at University of Illinois School of Medicine. From 2011 to 2015, she was also Scientific Director, Colorado Prevention Center, Wound Care Laboratory at the University of Colorado. From 2012 to 2015, Dr. Driver held a number of positions at the Providence Veterans Administration Medical Center in Rhode Island, including Chief, Section of Podiatric Surgery and Director, Clinical Research, Limb Preservation and Wound Healing. Prior thereto, she held various positions at multiple major multidisciplinary Limb Preservation – Wound Healing Centers of Excellence. Dr. Driver received a Doctorate of Podiatric Medicine and Surgery from the California College of Podiatric Medicine and Surgery and a Masters in Medical Education from Samuel Merritt University.

Nissim Mashiach has served as a member of our board of directors since June 2017. Mr. Mashiach served as President and Chief Executive Officer of Macrocure Ltd., a Nasdaq-listed biotechnology company focused on the treatment of chronic and other hard-to-heal wounds, from June 2012 to January 2017. From 2009 to 2012, he served as General Manager at Ethicon, a Johnson & Johnson company. Prior to Ethicon, he served as President and Chief Operating Officer at Omrix Biopharmaceuticals, Inc., which was acquired by Johnson & Johnson in 2008. Prior to Omrix, Mr. Mashiach held leadership positions at several pharmaceutical companies. He holds an MBA from the University of Manchester in Manchester, England, an MPharmSc from the Hebrew University in Jerusalem, Israel, and a B.Sc, Chemical Engineering from the Technion-Israel Institute of Technology in Haifa, Israel.

Sharon Kochan has served as a member of our board of directors since June 2017. Mr. Kochan is the CEO of Padagis LLC. a leading specialty pharma company that was curved out of Perrigo Company PLC. On July 2021. Prior to such, Mr. Kochan has served as Executive Vice President & President Pharmaceuticals / International, for Perrigo Company Plc., a global, over-the-counter, consumer goods and specialty pharmaceutical company listed on the New York Stock Exchange, since 2012 and has been a member of the Perrigo Executive Committee since 2007. From March 2007 to July 2012, he served as Executive Vice President, General Manager of Prescription Pharmaceuticals for Perrigo and from 2005 to 2007, he was Senior Vice President of Business Development and Strategy for Perrigo. Mr. Kochan was Vice President, Business Development of Agis Industries (1983) Ltd. from 2001 until Perrigo acquired Agis in 2005. He completed the Senior Management Program at the Technion Institute of Management in Haifa, Israel, received a Master of Science in Operations Research & Management Science from Columbia University in New York City and received a Bachelor of Science in Industrial and Management Engineering from Tel-Aviv University in Tel-Aviv, Israel.

Mr. Samuel Moed has served as a member of our board of directors since April 2020. Prior to joining our board, Mr. Moed served as an executive at Bristol-Myers Squibb, a global biopharma company focused on innovative therapeutics. In his most recent capacity as Senior Vice President, Corporate Strategy, Mr. Moed led the strategic planning of the company in all major business activities worldwide. Previously, Mr. Moed oversaw strategy for BMS' Worldwide Pharmaceuticals Group, encompassing a range of global strategic initiatives, and managed a global portfolio of strategic alliances. Among other positions, he served as President of U.S. Pharmaceuticals and as President of Worldwide Consumer Healthcare. Mr. Moed received a BA in history from Columbia University in New York City.

Mr. David Fox has served as a member of our board of directors since April 2020. Mr. Fox was most recently a partner at Kirkland & Ellis LLP and served as a member of its Global Executive Management Committee until 2019. Prior to joining Kirkland, Mr. Fox was partner with Skadden, Arps, Slate, Meagher & Flom LLP, where he was a member of its top governing committee. Mr. Fox is a director of Israel Discount Bank of New York, a member of the borad of directors at the Park Avenue Armory and a member of the advisory board of New Alternatives for Children, for which he provides support to families caring for medically fragile children. In addition, Mr. Fox serves on the board of governors, and is an honorary fellow of the Hebrew University, Jerusalem. He holds an LL.B. degree from Jerusalem University, Israel.

B. Compensation

Compensation of Directors and Executive Officers

The table below reflects the compensation granted to our five most highly compensated officers during or with respect to the year ended December 31, 2021. All amounts reported in the table reflect the cost to the company, as recognized in our financial statements for the year ended December 31, 2021.

Name and Position	Salary & Social Benefits[1]	Bonus	Share-Based Payment[2]	Other Compensation[3]	Total
			(thousand U.S. dollars)[4]		
Sharon Malka, *Chief Executive Officer*	427	65	227	5	**724**
Lior Rosenberg, M.D., *Chief Medical Technology Officer*	334	39	81	25	**479**
Ety Klinger, *Chief Research & Development Officer*	292	32	73	20	**417**
Boaz Gur-Lavie, *Chief Financial Officer*	256	29	76	24	**385**
Yaron Meyer, *Executive Vice President, General Counsel & Corporate Secretary*	208[5]	27	61	5	**301**

(1) Represents the officer's gross salary plus payment of mandatory social benefits made by the company on behalf of such officer. Such benefits may include, to the extent applicable to the executive, payments, contributions and/or allocations for savings funds (e.g., Managers' Life Insurance Policy), education funds (referred to in Hebrew as "keren hishtalmut"), pension, severance, risk insurances (e.g., life or work disability insurance) and payments for social security.

(2) Represents the equity-based compensation expenses recorded in the company's consolidated financial statements for the year ended December 31, 2021 based on the options' grant date fair value in accordance with accounting guidance for equity-based compensation.

(3) Represents the other benefits to such officer, which includes either or both of (i) car expenses, including lease costs, gas and maintenance, provided to the officers, and (ii) vacation benefits.

(4) Converted (i) from NIS into U.S. dollars at the rate of NIS3.229 = U.S$1, based on the average representative rate of exchange between the NIS and the U.S. dollar in the year ended December 31, 2021 as reported by the Bank of Israel in the year ended December 31, 2021.

(5) Represents only 8 months' salary due to paternity leave.

The aggregate compensation paid and equity-based compensation and other payments expensed by us and our subsidiaries to our directors and executive officers with respect to the year ended December 31, 2021 was $3.5 million. As of December 31, 2021, options to purchase 1,811,319 ordinary shares, exercisable at a weighted average exercise price of $3.86 per share, and restricted share units ("RSUs") that may be settled for 55,002 ordinary shares, in each case granted to our directors and executive officers, were outstanding under our equity incentive plans. We do not have any written agreements with any director providing for benefits upon the termination of such director's relationship with our company or its subsidiaries.

Employment Agreements with Executive Officers

We have entered into written employment agreements with all of our executive officers, which include standard provisions for a company in our industry regarding non-competition/solicitation, confidentiality of information and assignment of inventions. Except for Prof. Rosenberg, our Chief Medical Officer, our executive officers will not receive benefits upon the termination of their respective employment with us, other than payment of salary and benefits (and limited accrual of vacation days) during the required notice period for termination of their employment, which varies for each individual. Upon termination of his employment, Prof. Rosenberg is entitled to a one-time termination payment of ten months of salary.

Directors' Service Contracts

Other than with respect to our directors that are also executive officers, there are no arrangements or understandings between us, on the one hand, and any of our directors, on the other hand, providing for benefits upon termination of their service as directors of our company.

2003 Israeli Share Option Plan

In November 2003, we adopted our 2003 Israeli Share Option Plan (the "2003 Plan"). The 2003 Plan provides for the grant of options to our and our subsidiaries' directors, employees, officers, consultants and service providers, among others.

The initial reserved pool under the 2003 Plan was 1,710,000 ordinary shares and subsequently increased to a total of 3,230,000 ordinary shares. The 2003 Plan expired on December 31, 2013. Options that remain outstanding under the 2003 Plan continue to be governed by the terms of the plan, notwithstanding that expiration. The 2003 Plan is administered by our board of directors or a committee designated by our board of directors, which determines, subject to Israeli law, the grantees of options, the terms of the options, including exercise prices, vesting schedules, acceleration of vesting, the type of option and the other matters necessary or desirable for, or incidental to the administration of the 2003 Plan. The 2003 Plan provides for the issuance of options under various tax regimes including, without limitation, pursuant to Sections 102 and 3(i) of the Israeli Income Tax Ordinance (New Version) 1961 (the "Ordinance").

Section 102 of the Ordinance allows employees, directors and officers who are not controlling shareholders and who are Israeli residents to receive favorable tax treatment for compensation in the form of shares or options. Section 102 of the Ordinance includes two alternatives for tax treatment involving the issuance of options or shares to a trustee for the benefit of the grantees and also includes an additional alternative for the issuance of options or shares directly to the grantee. Section 102(b)(2) of the Ordinance, which provides the most favorable tax treatment for grantees, permits the issuance to a trustee under the "capital gains track." In order to comply with the terms of the capital gains track, all options granted under a specific plan and subject to the provisions of Section 102 of the Ordinance, as well as the shares issued upon exercise of such options and other shares received following any realization of rights with respect to such options, such as share dividends and share splits, must be registered in the name of a trustee selected by the board of directors and held in trust for the benefit of the relevant employee, director or officer. The trustee may not release these options or shares to the relevant grantee before the second anniversary of the registration of the options in the name of the trustee. However, under this track, we are not allowed to deduct an expense with respect to the issuance of the options or shares.

The 2003 Plan provides that options granted to our employees, directors and officers who are not controlling shareholders and who are considered Israeli residents are intended to qualify for special tax treatment under the "capital gains track" provisions of Section 102(b)(2) of the Ordinance. Our Israeli non-employee service providers and controlling shareholders may only be granted options under Section 3(i) of the Ordinance, which does not provide for similar tax benefits.

Options granted under the 2003 Plan are subject to vesting schedules and generally expire ten years from approval of the option and vest over a four-year period commencing on the date of grant, such that 25% of the granted options vest annually on each of the first, second, third and fourth anniversaries of the date of grant. Under the 2003 Plan, in the event of termination of employment or services for reasons of disability or death, the grantee, or in the case of death, his or her legal successor, may exercise options that have vested prior to termination within a period of six months after the date of termination. If a grantee's employment or service is terminated for cause, all of the grantee's vested and unvested options expire on the date of termination. If a grantee's employment or service is terminated for any other reason, the grantee may exercise his or her vested options within 90 days after the date of termination. Any expired or unvested options are returned to the pool for reissuance.

The 2003 Plan provides that in the event of a merger or consolidation of our company or a sale of all, or substantially all, of our assets, the unexercised options outstanding may be assumed, or substituted for an appropriate number of shares of each class of shares or other securities as were distributed to our shareholders in connection with such transaction and the exercise price will be appropriately adjusted. If not so assumed or substituted, all non-vested and non-exercised options will expire upon the closing of the transaction. Our board of directors or its designated committee, as applicable, may provide in the option agreement that if the acquirer does not agree to assume or substitute the options, vesting of the options shall be accelerated so that any unvested option or any portion thereof will vest 10 days prior to the closing of the transaction. In the event that such consideration received in the transaction is not solely in the form of ordinary shares of another company, the board of directors or the designated committee, as applicable, may, with the approval of the acquirer, provide that in lieu of the assumption or substitution of the options, the options will be substituted by another type of asset or property, including cash.

2014 Equity Incentive Plan

In March 2014, we adopted and obtained shareholder approval for our 2014 Equity Incentive Plan, which was amended as of December 18, 2018 (the "2014 Plan"). The 2014 Plan provides for the grant of options, restricted shares, RSUs and other share-based awards to our and our subsidiaries' and affiliates' directors, employees, officers, consultants and advisors, among others and to any other person whose services are considered valuable to us or them, to continue as service providers, to increase their efforts on our behalf or behalf of a subsidiary or affiliate and to promote the success of our business. Following the approval of the 2014 Plan by the Israeli tax authorities, we are only granting options or other equity incentive awards under the 2014 Plan, although previously-granted options and awards will continue to be governed by our 2003 Plan and the shares underlying such options and awards will count against the reserved pool for the 2014 Plan. The initial reserved pool under the 2014 Plan was 3,032,742 ordinary shares, which will automatically increase on January 1 of each year by a number of ordinary shares equal to the lowest of (i) 2% of our outstanding shares, (ii) 600,000 shares and (iii) a number of shares determined by our board of directors, if so determined prior to January 1 of the year in which the increase will occur; provided that the pool of shares reserved under the Plan shall not exceed 15% (fifteen percent) of the then outstanding shares. Pursuant to an "evergreen" provision in the 2014 Plan, the reserved pool was increased by 431,006, 540,955, 543,577, 544,055 and 544,738 ordinary shares as of January 1, 2015, January 1, 2018, January 1, 2019, January 1, 2020 and January 1, 2021 , respectively, representing 2% of our outstanding shares as of each such date. We did not increase the reserved pool in 2016 or 2017.

The 2014 Plan is administered by our board of directors or by a committee designated by the board of directors, which determine, subject to Israeli law, the grantees of awards and the terms of the grant, including exercise prices, vesting schedules, acceleration of vesting and the other matters necessary in the administration of the 2014 Plan. The 2014 Plan enables us to issue awards under various tax regimes, including, without limitation, pursuant to Sections 102 and 3(i) of the Ordinance, as discussed under "—2003 Share Incentive Plan" above, and under Section 422 of the U.S. Internal Revenue Code of 1986, as amended (the "Code").

Options granted under the 2014 Plan to U.S. residents may qualify as "incentive stock options" within the meaning of Section 422 of the Code, or may be non-qualified. The exercise price for "incentive stock options" must not be less than the fair market value on the date on which an option is granted, or 110% of the fair market value if the option holder holds more than 10% of our share capital.

We currently intend to grant awards under the 2014 Plan under the capital gains track of Section 102(b)(2) of the Ordinance only to our employees, directors and officers who are not controlling shareholders and are considered Israeli residents.

Awards under the 2014 Plan may be granted until ten years from the date on which the 2014 Plan was approved by our board of directors.

Options granted under the 2014 Plan generally vest over three or four years commencing on the date of grant, such that 33% or 25%, respectively, vests annually on the anniversary of the date of grant. Options, other than certain incentive share options, that are not exercised within ten years from the grant date expire, unless otherwise determined by our board of directors or its designated committee, as applicable. Share options that qualify as "incentive stock options" and are granted to a person holding more than 10% of our voting power will expire within five years from the date of the grant. In the event of the death of a grantee while employed by or performing service for us or a subsidiary or within three months thereafter, or the termination of a grantee's employment or services for reasons of disability, the grantee, or in the case of death, his or her legal successor, may exercise options that have vested prior to termination within a period of one year from the date of disability or death. If we terminate a grantee's employment or service for cause, all of the grantee's vested and unvested options will expire on the date of termination. If a grantee's employment or service is terminated for any other reason, the grantee may exercise his or her vested options within three months of the date of termination. Any expired or unvested options return to the pool for reissuance.

In the event of a merger or consolidation of our company or a sale of all, or substantially all, of our shares or assets or other transaction having a similar effect on us, then without the consent of the option holder, our board of directors or its designated committee, as applicable, may but is not required to (i) cause any outstanding award to be assumed or an equivalent award to be substituted by such successor corporation, or (ii) in case the successor corporation refuses to assume or substitute the award (a) provide the grantee with the option to exercise the award as to all or part of the shares or (b) cancel the options against payment in cash in an amount determined by the board of directors or the committee as fair in the circumstances. Notwithstanding the foregoing, our board of directors or its designated committee may upon such event amend or terminate the terms of any award, including conferring the right to purchase any other security or asset that the board of directors shall deem, in good faith, appropriate. Our board of directors or its designated committee may, in its discretion, approve that any awards granted under the 2014 Plan shall be subject to additional conditions in the case of a merger or a consolidation.

Restricted share awards are ordinary shares that are awarded to a participant subject to the satisfaction of the terms and conditions established by the board of directors or a committee designated by the board of directors. Until such time as the applicable restrictions lapse, restricted shares are subject to forfeiture and may not be sold, assigned, pledged or otherwise disposed of by the participant who holds those shares. Generally, if a grantee's employment or service is terminated for any reason prior to the expiration of the time when the restrictions lapse, shares that are still restricted will be forfeited.

The following table provides information regarding the outstanding options to purchase our ordinary shares, and RSUs held by each of our directors and executive officers who beneficially owns greater than 1% of our ordinary shares (after including shares underlying options or RSUs) as of March 15, 2022:

Name	Number of Options	Number of RSUs	Grant Date	Exercise Price	Vested Options/RSU's as of March 15, 2022	Expiration Date
Sharon Malka, *Chief Executive Officer*	121,600		12/24/2013	$ 12.89	121,600	12/23/2023
	50,000		12/23/2015	$ 9.58	50,000	12/22/2025
	135,000		12/31/2018	$ 5.15	101,250	12/30/2028
		45,000	12/31/2018		33,750	
	40,000		05/02/2019	$ 4.92	30,000	5/1/2029
		20,000	05/02/2019		15,000	
	81,170		06/29/2020	$ 1.75	20,292	6/28/2030
	45,692		06/15/2021	$ 5.36	-	6/14/2031
		7,615	06/15/2021		-	6/14/3031
Lior Rosenberg, *Chief Medical Technology Officer*	76,000		12/24/2013	$ 12.89	76,000	12/23/2023
	25,000		12/23/2015	$ 9.58	25,000	12/22/2025
	20,000		12/31/2018	$ 5.15	15,000	12/30/2028
		6,667	12/31/2018		5,000	
	43,600		04/23/2020	$ 1.75	10,900	4/22/2030
	27,953		03/04/2021	$ 5.36	-	3/3/2031
		4,659	03/04/2021		1,165	3/3/2031

C. Board Practices

Board of Directors

Under the Israeli Companies Law, the management of our company is vested in our board of directors. Our board of directors may exercise all powers and may take all actions that are not specifically granted to our shareholders or to management. Our executive officers are responsible for our day-to-day management and have individual responsibilities established by our board of directors. Our Chief Executive Officer is appointed by, and serves at the discretion of, our board of directors, subject to the employment agreement that we have entered into with him. All other executive officers are also appointed by our board of directors, and are subject to the terms of any applicable employment agreements that we may enter into with them.

Under our articles of association, our board of directors must consist of at least five and not more than nine directors, including at least two external directors required to be appointed under the Israeli Companies Law. At any time the minimum number of directors (other than the external directors) shall not fall below three. Other than external directors, for whom special election requirements apply under the Israeli Companies Law, as detailed below, the Israeli Companies Law and our articles of association provide that directors are elected annually at the general meeting of our shareholders by a vote of the holders of a majority of the voting power represented present and voting, in person or by proxy, at that meeting. We have only one class of directors.

In accordance with the exemption available to foreign private issuers under Nasdaq rules, we are not required to comply with the requirements of the Nasdaq rules with regard to having a majority of independent directors on our board of directors, as long as we follow Israeli law and practice, in accordance with which our board of directors includes at least two external directors. Our board of directors has determined that four of our six current directors are independent under the Nasdaq Stock Market listing rules. The definition of "independent director" under the Nasdaq Stock Market listing rules and "external director" under the Israeli Companies Law overlap to a significant degree such that we would generally expect the two directors that serve as external directors to qualify as independent under the Nasdaq Stock Market listing rules. However, it is possible for a director to qualify as an "external director" under the Israeli Companies Law without qualifying as an "independent director" under the Nasdaq Stock Market listing rules, or vice-versa. The definition of external director under the Israeli Companies Law includes a set of statutory criteria that must be satisfied, including criteria whose aim is to ensure that there is no factor that would impair the ability of the external director to exercise independent judgment. The definition of independent director under the Nasdaq Stock Market listing rules specifies similar, although less stringent, requirements in addition to the requirement that the board of directors consider any factor which would impair the ability of the independent director to exercise independent judgment. In addition, external directors serve for a period of three years pursuant to the requirements of the Israeli Companies Law. However, external directors must be elected by a special majority of shareholders while independent directors may be elected by an ordinary majority. See "—External Directors" for a description of the requirements under the Israeli Companies Law for a director to serve as an external director.

In accordance with the exemption available to foreign private issuers under Nasdaq rules, we do not follow the requirements of the Nasdaq rules with regard to the process of nominating directors, and instead follow Israeli law and practice, in accordance with which our board of directors (or a committee thereof) is authorized to recommend to our shareholders director nominees for election.

Under the Israeli Companies Law and our articles of association, nominees for directors may also be proposed by any shareholder holding at least 1% of our outstanding voting power. However, any such shareholder may propose a nominee only if a written notice of such shareholder's intent to propose a nominee has been given to our Secretary (or, if we have no such Secretary, our Chief Executive Officer). Pursuant to our Articles of Association, any such notice must include certain information, including, among other things, a description of all arrangements between the nominating shareholder and the proposed director nominee(s) and any other person pursuant to which the nomination(s) are to be made by the nominating shareholder, the consent of the proposed director nominee(s) to serve as our director(s) if elected and a declaration signed by the nominee(s) declaring that there is no limitation under the Israeli Companies Law preventing their election, and that all of the information that is required under the Israeli Companies Law to be provided to us in connection with such election has been provided. Under the Israeli Companies Law regulations, any such shareholder nomination must be delivered to our registered Israeli office within seven days after we publish notice of our upcoming annual general meeting of shareholders (or within 14 days after we publish a preliminary notification of an upcoming annual general meeting).

In addition, our articles of association allow our board of directors to appoint directors to fill vacancies on our board of directors for a term of office equal to the remaining period of the term of office of the director(s) whose office(s) have been vacated. External directors are elected for an initial term of three years and may be elected for additional three-year terms under the circumstances described below. External directors may be removed from office only under the limited circumstances set forth in the Israeli Companies Law. See "—External Directors."

Under the Israeli Companies Law, our board of directors must determine the minimum number of directors who are required to have accounting and financial expertise. See "—External Directors" below. In determining the number of directors required to have such expertise, our board of directors must consider, among other things, the type and size of the company and the scope and complexity of its operations. Our board of directors has determined that the minimum number of directors of our company who are required to have accounting and financial expertise is one.

We are not a party to, and are not aware of, any voting agreements among our shareholders. In addition, there are no family relationships among our executive officers and directors.

Under regulations promulgated under the Israeli Companies Law, Israeli public companies whose shares are traded on certain U.S. stock exchanges, such as the Nasdaq Global Market, and that lack a controlling shareholder (as defined below) are exempt from the requirement to appoint external directors. Any such company is also exempt from the Israeli Companies Law requirements related to the composition of the audit and compensation committees of the Board. Eligibility for these exemptions is conditioned on compliance with U.S. stock exchange listing rules related to majority Board independence and the composition of the audit and compensation committees of the Board, as applicable to all listed domestic U.S. companies. Because we have a controlling shareholder (CBI), we are not eligible for these exemptions under these regulations.

External Directors

Under the Israeli Companies Law, our board of directors is required to include at least two members who qualify as external directors. Our current external directors are Nissim Mashiach and Sharon Kochan, each of whom serves on our audit committee and compensation committee.

The provisions of the Israeli Companies Law set forth special approval requirements for the election of external directors. External directors must be elected by a majority vote of the shares present and voting at a meeting of shareholders, provided that either:

- such majority includes at least a majority of the shares held by all shareholders who are not controlling shareholders and do not have a personal interest in the election of the external director (other than a personal interest not deriving from a relationship with a controlling shareholder) that are voted at the meeting, excluding abstentions, to which we refer as a disinterested majority; or

- the total number of shares voted by non-controlling shareholders and by shareholders who do not have a personal interest in the election of the external director against the election of the external director does not exceed 2% of the aggregate voting rights in the company.

The term "controlling shareholder" as used in the Israeli Companies Law for purposes of all matters related to external directors and for certain other purposes (such as the requirements related to appointment to the audit committee or compensation committee, as described below), means a shareholder with the ability to direct the activities of the company, other than by virtue of being an office holder. A shareholder is presumed to be a controlling shareholder if the shareholder holds 50% or more of the voting rights in a company or has the right to appoint the majority of the directors of the company or its general manager. With respect to certain matters (various related party transactions), a controlling shareholder is deemed to include a shareholder that holds 25% or more of the voting rights in a public company if no other shareholder holds more than 50% of the voting rights in the company, but excludes a shareholder whose power derives solely from his or her position as a director of the company or from any other position with the company.

The initial term of an external director is three years. Thereafter, an external director may be reelected by shareholders to serve in that capacity for up to two additional three-year terms, provided that either:

(i) his or her service for each such additional term is recommended by one or more shareholders holding at least 1% of the company's voting rights and is approved at a shareholders meeting by a disinterested majority, where the total number of shares held by non-controlling, disinterested shareholders voting for such reelection exceeds 2% of the aggregate voting rights in the company, subject to additional restrictions set forth in the Israeli Companies Law with respect to affiliations of external director nominee; or

(ii) his or her service for each such additional term is recommended by the board of directors and is approved at a meeting of shareholders by the same majority required for the initial election of an external director (as described above).

The term of office for external directors for Israeli companies traded on certain foreign stock exchanges, including the Nasdaq Global Market, may be extended indefinitely in increments of additional three-year terms, in each case provided that the audit committee and the board of directors of the company confirm that, in light of the external director's expertise and special contribution to the work of the board of directors and its committees, the reelection for such additional period(s) is beneficial to the company, and provided that the external director is reelected subject to the same shareholder vote requirements (as described above regarding the reelection of external directors). Prior to the approval of the reelection of the external director at a general meeting of shareholders, the company's shareholders must be informed of the term previously served by him or her and of the reasons why the board of directors and audit committee recommended the extension of his or her term.

External directors may be removed from office by a special general meeting of shareholders called by the board of directors, which approves such dismissal by the same shareholder vote percentage required for their election or by a court, in each case, only under limited circumstances, including ceasing to meet the statutory qualifications for appointment, or violating their duty of loyalty to the company.

If an external directorship becomes vacant and there are fewer than two external directors on the board of directors at the time, then the board of directors is required under the Israeli Companies Law to call a shareholders' meeting as soon as practicable to appoint a replacement external director. Each committee of the board of directors that exercises the powers of the board of directors must include at least one external director, except that the audit committee and the compensation committee must include all external directors then serving on the board of directors and an external director must serve as chair thereof. Under the Israeli Companies Law, external directors of a company are prohibited from receiving, directly or indirectly, any compensation from the company other than for their services as external directors pursuant to the Israeli Companies Law and the regulations promulgated thereunder. Compensation of an external director is determined prior to his or her appointment and may not be changed during his or her term subject to certain exceptions.

The Israeli Companies Law provides that a person is not qualified to be appointed as an external director if (i) the person is a relative of a controlling shareholder of the company, or (ii) if that person or his or her relative, partner, employer, another person to whom he or she was directly or indirectly subordinate, or any entity under the person's control, has or had, during the two years preceding the date of appointment as an external director: (a) any affiliation or other disqualifying relationship with the company, with any person or entity controlling the company or a relative of such person, or with any entity controlled by or under common control with the company; or (b) in the case of a company with no shareholder holding 25% or more of its voting rights, had at the date of appointment as an external director, any affiliation or other disqualifying relationship with a person then serving as chairman of the board or chief executive officer, a holder of 5% or more of the issued share capital or voting power in the company or the most senior financial officer.

The term "relative" is defined in the Israeli Companies Law as a spouse, sibling, parent, grandparent or descendant; spouse's sibling, parent or descendant; and the spouse of each of the foregoing persons. Under the Israeli Companies Law, the term "affiliation" and the similar types of disqualifying relationships include (subject to certain exceptions):

- an employment relationship;
- a business or professional relationship even if not maintained on a regular basis (excluding insignificant relationships);
- control; and
- service as an office holder, excluding service as a director in a private company prior to the initial public offering of its shares if such director was appointed as a director of the private company in order to serve as an external director following the initial public offering.

The term "office holder" is defined in the Israeli Companies Law as a general manager (i.e., chief executive officer), chief business manager, deputy general manager, vice general manager, any other person assuming the responsibilities of any of these positions regardless of that person's title, a director and any other manager directly subordinate to the general manager.

In addition, no person may serve as an external director if that person's position or professional or other activities create, or may create, a conflict of interest with that person's responsibilities as a director or otherwise interfere with that person's ability to serve as an external director or if the person is an employee of the Israel Securities Authority of an Israeli stock exchange. A person may furthermore not continue to serve as an external director if he or she received direct or indirect compensation from the company including amounts paid pursuant to indemnification or exculpation contracts or commitments and insurance coverage for his or her service as an external director, other than as permitted by the Israeli Companies Law and the regulations promulgated thereunder.

Following the termination of an external director's service on a board of directors, such former external director and his or her spouse and children may not be provided a direct or indirect benefit by the company, its controlling shareholder or any entity under its controlling shareholder's control. This includes engagement as an office holder of the company or a company controlled by its controlling shareholder or employment by, or provision of services to, any such company for consideration, either directly or indirectly, including through a corporation controlled by the former external director. This restriction extends for a period of two years with regard to the former external director and his or her spouse or child and for one year with respect to other relatives of the former external director.

If at the time at which an external director is appointed all members of the board of directors who are not controlling shareholders or relatives of controlling shareholders of the company are of the same gender, the external director to be appointed must be of the other gender. A director of one company may not be appointed as an external director of another company if a director of the other company is acting as an external director of the first company at such time.

According to the Israeli Companies Law and regulations promulgated thereunder, a person may be appointed as an external director only if he or she has professional qualifications or if he or she has accounting and financial expertise (each, as defined below); provided that at least one of the external directors must be determined by our board of directors to have accounting and financial expertise. However, if at least one of our other directors (i) meets the independence requirements under the Exchange Act, (ii) meets the standards of the Nasdaq Stock Market listing rules for membership on the audit committee and (iii) has accounting and financial expertise as defined under the Israeli Companies Law, then neither of our external directors is required to possess accounting and financial expertise as long as each possesses the requisite professional qualifications.

A director with accounting and financial expertise is a director who, due to his or her education, experience and skills, possesses an expertise in, and an understanding of, financial and accounting matters and financial statements, such that he or she is able to understand the financial statements of the company and initiate a discussion about the presentation of financial data. A director is deemed to have professional qualifications if he or she has any of (i) an academic degree in economics, business management, accounting, law or public administration, (ii) an academic degree or has completed another form of higher education in the primary field of business of the company or in a field which is relevant to his/her position in the company or (iii) at least five years of experience serving in one of the following capacities, or at least five years of cumulative experience serving in two or more of the following capacities: (a) a senior business management position in a company with a significant volume of business, (b) a senior position in the company's primary field of business or (c) a senior position in public administration or service. The board of directors is charged with determining whether a director possesses financial and accounting expertise or professional qualifications.

Our board of directors has determined that Sharon Kochan has accounting and financial expertise and possesses professional qualifications as required under the Israeli Companies Law, while Nissim Mashiach possesses professional qualifications.

Leadership Structure of the Board

In accordance with the Israeli Companies Law and our articles of association, our board of directors is required to appoint one of its members to serve as chairman of the board of directors. Our board of directors has appointed Stephen T. Wills to serve as executive chairman of the board of directors.

Audit Committee

Israeli Companies Law composition requirements

Under the Israeli Companies Law, we are required to have an audit committee comprised of at least three directors, including all of the external directors, one of whom must serve as chairman of the committee. The audit committee may not include the chairman of the board, a controlling shareholder of the company, a relative of a controlling shareholder, a director employed by or providing services on a regular basis to the company, to a controlling shareholder or to an entity controlled by a controlling shareholder, or a director who derives most of his or her income from a controlling shareholder. In addition, under the Israeli Companies Law, the audit committee of a publicly traded company must consist of a majority of unaffiliated directors. In general, an "unaffiliated director'' under the Israeli Companies Law is defined as either an external director or as a director who meets the following criteria:

- he or she meets the qualifications for being appointed as an external director, except for the requirement (i) that the director be an Israeli resident (which does not apply to companies such as ours whose securities have been offered outside of Israel or are listed for trading outside of Israel) and (ii) for accounting and financial expertise or professional qualifications; and

- he or she has not served as a director of the company for a period exceeding nine consecutive years. For this purpose, a break of less than two years in the service shall not be deemed to interrupt the continuation of the service.

Each member of our audit committee (each, as identified in the second paragraph under the sub-heading "Nasdaq listing rules composition requirements" below) is an unaffiliated director under the Israeli Companies Law, thereby fulfilling the foregoing Israeli law requirement for the composition of the audit committee.

Nasdaq listing rules composition requirements

Under the Nasdaq Stock Market listing rules, we are required to maintain an audit committee consisting of at least three independent directors, each of whom is financially literate and one of whom has accounting or related financial management expertise. If we choose to follow requirements under Israeli law in lieu of those Nasdaq requirements, we must disclose that fact in this annual report.

Our audit committee consists of Sharon Kochan (chairperson), Nissim Mashiach and Vickie R Driver, each of whom is an independent director in accordance with Rule 10A-3(b)(1) under the Exchange Act and satisfies the independent director requirements under the Nasdaq Stock Market listing rules. All members of our audit committee meet the requirements for financial literacy under the applicable listing rules of the Nasdaq Stock Market. Our board of directors has determined that Sharon Kochan is an "audit committee financial expert," as defined in the SEC regulations.

Audit committee role

Our board of directors has adopted an audit committee charter that sets forth the responsibilities of the audit committee consistent with the rules and regulations of the SEC and the Nasdaq Stock Market listing rules, as well as the requirements for such committee under the Israeli Companies Law, including the following:

- oversight of our independent registered public accounting firm and recommending the engagement, compensation or termination of engagement of our independent registered public accounting firm to the board of directors in accordance with Israeli law;
- recommending the engagement or termination of the person filling the office of our internal auditor; and
- recommending the terms of audit and non-audit services provided by the independent registered public accounting firm for pre-approval by our board of directors.

Our audit committee provides assistance to our board of directors in fulfilling its legal and fiduciary obligations in matters involving our accounting, auditing, financial reporting, internal control and legal compliance functions by pre-approving the services performed by our independent accountants and reviewing their reports regarding our accounting practices and systems of internal control over financial reporting. Our audit committee also oversees the audit efforts of our independent accountants and takes those actions that it deems necessary to satisfy itself that the accountants are independent of management.

Under the Israeli Companies Law, our audit committee is responsible for:

- determining whether there are deficiencies in the business management practices of our company, including in consultation with our internal auditor or the independent auditor, and making recommendations to the board of directors to improve such practices;
- determining whether to approve certain related party transactions (including transactions in which an office holder has a personal interest and whether such transaction is extraordinary or material under the Israeli Companies Law) (see "—Approval of Related Party Transactions Under Israeli Law");
- establishing the approval process (including, potentially, the approval of the audit committee and conducting a competitive procedure supervised by the audit committee) for certain transactions with a controlling shareholder or in which a controlling shareholder has a personal interest;
- where the board of directors approves the working plan of the internal auditor, examining such working plan before its submission to the board of directors and proposing amendments thereto;
- examining our internal audit controls and internal auditor's performance, including whether the internal auditor has sufficient resources and tools to fulfill his responsibilities;
- examining the scope of our auditor's work and compensation and submitting a recommendation with respect thereto to our board of directors or shareholders, depending on which of them is considering the appointment of our auditor; and
- establishing procedures for the handling of employees' complaints as to the management of our business and the protection to be provided to such employees.

Our audit committee may not approve any actions requiring its approval (see "—Approval of Related Party Transactions Under Israeli Law"), unless at the time of the approval a majority of the committee's members are present, which majority consists of unaffiliated directors including at least one external director.

Compensation Committee and Compensation Policy

Israeli Companies Law compensation committee composition requirements

Under the Israeli Companies Law, the board of directors of a public company must appoint a compensation committee. The compensation committee generally (subject to certain exceptions that do not apply to our company) must be comprised of at least three directors, including all of the external directors, who must constitute a majority of the members of, and include the chairperson of, the compensation committee. Each compensation committee member who is not an external director must be a director whose compensation does not exceed an amount that may be paid to an external director. The compensation committee is subject to the same Israeli Companies Law restrictions as the audit committee as to who may not be a member of the compensation committee. Each member of our compensation committee (each, as identified in the second paragraph under the sub-heading "Nasdaq listing rules compensation committee composition requirements" below) fulfills the foregoing Israeli law requirements related to the composition of the compensation committee.

Israeli Companies Law committee duties

The duties of the compensation committee include the recommendation to the company's board of directors of a policy regarding the terms of engagement of office holders, which we refer to as a compensation policy. That policy must be adopted by the company's board of directors, after considering the recommendations of the compensation committee, and must be approved by the company's shareholders, which approval requires what we refer to as a Special Majority Approval for Compensation. A Special Majority Approval for Compensation requires shareholder approval by a majority vote of the shares present and voting at a meeting of shareholders called for such purpose, provided that either (a) such majority includes at least a majority of the shares held by all shareholders who are not controlling shareholders and do not have a conflict of interest (referred to under the Israeli Companies Law as a "personal interest") in such compensation arrangement or (b) the total number of shares of non-controlling shareholders and shareholders who do not have a personal interest in the compensation arrangement and who vote against the arrangement does not exceed 2% of the company's aggregate voting rights.

Compensation policy requirements

We have adopted a compensation policy, most recently at the extraordinary general meeting of shareholders held on September 23, 2019, which policy serves as the basis for decisions concerning the financial terms of employment or engagement of office holders, including exculpation, insurance, indemnification or any monetary payment or obligation of payment or other benefit in respect of employment or engagement. Under the Israeli Companies Law, the compensation policy must relate to certain factors, including advancement of the company's objectives, the company's business plan and its long-term strategy, and creation of appropriate incentives for office holders. It must also consider, among other things, the company's risk management, size and the nature of its operations. The compensation policy must furthermore consider the following additional factors:

- the knowledge, skills, expertise and accomplishments of the relevant office holder;
- the office holder's roles and responsibilities and prior compensation agreements with him or her;
- the relationship between the terms offered and the average compensation of the other employees of the company, including those employed through manpower companies;
- the impact of disparities in salary upon work relationships in the company;
- the possibility of reducing variable compensation at the discretion of the board of directors;
- the possibility of setting a limit on the exercise value of non-cash variable equity-based compensation; and
- as to severance compensation, the period of service of the office holder, the terms of his or her compensation during such service period, the company's performance during that period of service, the person's contribution towards the company's achievement of its goals and the maximization of its profits, and the circumstances under which the person is leaving the company.

The compensation policy must also include the following principles:

- the link between variable compensation and long-term performance, which variable compensation shall, other than office holder who report to the CEO, be primarily based on measurable criteria;
- the relationship between variable and fixed compensation, and the ceiling for the value of variable compensation;

- the conditions under which an office holder would be required to repay compensation paid to him or her if it was later shown that the data upon which such compensation was based was inaccurate and was required to be restated in the company's financial statements;

- the minimum holding or vesting period for variable, equity-based compensation; and

- maximum limits for severance compensation.

The compensation committee is responsible for (a) recommending the compensation policy to the company's board of directors for its approval (and subsequent approval by its shareholders) and (b) duties related to the compensation policy and to the compensation of a company's office holders as well as functions previously fulfilled by a company's audit committee with respect to matters related to approval of the terms of engagement of office holders, including:

- recommending whether a compensation policy should continue in effect, if the then-current policy has a term of greater than three years (approval of either a new compensation policy or the continuation of an existing compensation policy must in any case occur every three years, other than following a company's initial public offering, in which case such approval must occur within 5 years of the initial public offering);

- recommending to the board of directors periodic updates to the compensation policy and assessing implementation of the compensation policy;

- approving compensation terms of executive officers, directors and employees that require approval of the compensation committee;

- determining whether the compensation terms of a chief executive officer nominee, which were determined pursuant to the compensation policy, will be exempt from approval of the shareholders because such approval would harm the ability to engage with such nominee; and

- determining, subject to the approval of the board and under special circumstances, whether to override a determination of the company's shareholders regarding certain compensation related issues.

A copy of our current compensation policy serves as an exhibit to this annual report on Form 20-F.

Nasdaq listing rules compensation committee composition requirements

Under Nasdaq corporate governance rules, we are required to maintain a wholly-independent compensation committee consisting of at least two independent directors or, if we choose to follow requirements under Israeli law, we must disclose that fact in this annual report. Each of the members of the compensation committee is required to be independent under the Nasdaq rules relating to compensation committee members and Rule 10C-1(b)(1) under the Exchange Act, which are different than the general test for independence of board members.

Our compensation committee consists of Nissim Mashiach (chairperson), Sharon Kochan and Samuel Moed, each of whom is an independent director under the Nasdaq Stock Market listing rules and each of whom satisfies the above-described additional requirements for compensation committee members under the Nasdaq rules and Exchange Act.

Compensation committee charter and role

Our board of directors has adopted a compensation committee charter setting forth the responsibilities of the compensation committee, which include:

- the responsibilities set forth in the compensation policy;

- reviewing and approving the granting of options and other incentive awards to the extent such authority is delegated by our board of directors; and

- reviewing, evaluating and making recommendations regarding the compensation and benefits for our non-employee directors.

Internal Auditor

Under the Israeli Companies Law, the board of directors of an Israeli public company must appoint an internal auditor recommended by the audit committee. An internal auditor may not be:

- a person (or a relative of a person) who holds 5% or more of the company's outstanding shares or voting rights;
- a person (or a relative of a person) who has the power to appoint a director or the general manager of the company (i.e., the chief executive officer);
- an office holder (including a director) of the company (or a relative thereof); or
- a member of the company's independent accounting firm, or anyone on its behalf.

The role of the internal auditor is to examine, among other things, our compliance with applicable law and orderly business procedures.

The audit committee is required to oversee the activities and to assess the performance of the internal auditor as well as to review the internal auditor's work plan. Our internal auditor is Mr. Yisrael Gewirtz.

Fiduciary Duties of Directors and Executive Officers

The Israeli Companies Law codifies the fiduciary duties that office holders owe to a company. Each person listed in the table under "—Executive Officers and Directors" is an office holder under the Israeli Companies Law.

An office holder's fiduciary duties consist of a duty of care and a duty of loyalty. The duty of care requires an office holder to act with the level of care with which a reasonable office holder in the same position would have acted under the same circumstances. The duty of loyalty requires that an office holder act in good faith and in the best interests of the company.

The duty of care includes a duty to use reasonable means to obtain:

- information on the advisability of a given action brought for his or her approval or performed by virtue of his or her position; and
- all other important information pertaining to any such action.

The duty of loyalty includes a duty to:

- refrain from any conflict of interest between the performance of his or her duties to the company and his or her other duties or personal affairs;
- refrain from any activity that is competitive with the business of the company;
- refrain from exploiting any business opportunity of the company to receive a personal gain for himself or herself or others; and
- disclose to the company any information or documents relating to the company's affairs which the office holder received as a result of his or her position as an office holder.

Disclosure of personal interests of an office holder and approval of certain transactions

The Israeli Companies Law requires that an office holder promptly disclose to the board of directors any personal interest that he or she may be aware of and all related material information or documents concerning any existing or proposed transaction with the company. An interested office holder's disclosure must be made promptly and in any event no later than the first meeting of the board of directors at which the transaction is considered. A personal interest includes an interest of any person in an act or transaction of a company, including a personal interest of such person's relative or of a corporate body in which such person or a relative of such person is 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, but excluding a personal interest stemming from one's ownership of shares in the company.

A personal interest furthermore includes the personal interest of a person for whom the office holder holds a voting proxy or the personal interest of the office holder with respect to his or her vote on behalf of a person for whom he or she holds a proxy even if such shareholder has no personal interest in the matter. An office holder is not, however, obliged to disclose a personal interest if it derives solely from the personal interest of his or her relative in a transaction that is not considered an extraordinary transaction. Under the Israeli Companies Law, an extraordinary transaction is defined as any of the following:

- a transaction other than in the ordinary course of business;
- a transaction that is not on market terms; or
- a transaction that may have a material impact on a company's profitability, assets or liabilities.

If it is determined that an office holder has a personal interest in a transaction which is not an extraordinary transaction, approval by the board of directors is required for the transaction, unless the company's articles of association provide for a different method of approval. Further, so long as an office holder has disclosed his or her personal interest in a transaction, the board of directors may approve an action by the office holder that would otherwise be deemed a breach of his or her duty of loyalty. However, a company may not approve a transaction or action that is not in the best interest of the company or that is not performed by the office holder in good faith. An extraordinary transaction in which an office holder has a personal interest requires approval first by the company's audit committee and subsequently by the board of directors. The compensation of, or an undertaking to indemnify or insure, an office holder who is not a director requires approval first by the company's compensation committee, then by the company's board of directors. If such compensation arrangement or an undertaking to indemnify or insure is inconsistent with the company's stated compensation policy, or if the office holder is the chief executive officer (apart from a number of specific exceptions), then such arrangement is further subject to a Special Majority Approval for Compensation. Arrangements regarding the compensation, indemnification or insurance of a director require the approval of the compensation committee, board of directors and shareholders by ordinary majority, in that order, and under certain circumstances, a Special Majority Approval for Compensation.

Generally, a person who 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 such a meeting or vote on that matter unless the chairman of the relevant committee or board of directors (as applicable) determines that he or she should be present in order to present the transaction that is subject to approval. If a majority of the members of the audit committee or the board of directors (as applicable) has a personal interest in the approval of a transaction, then all directors may participate in discussions of the audit committee or the board of directors (as applicable) on such transaction and the voting on approval thereof, but shareholder approval is also required for such transaction.

Disclosure of personal interests of controlling shareholders and approval of certain transactions

Pursuant to Israeli law, the disclosure requirements regarding personal interests that apply to directors and executive officers also apply to a controlling shareholder of a public company. In the context of a transaction involving a shareholder of the company, a controlling shareholder also includes a shareholder who holds 25% or more of the voting rights in the company if no other shareholder holds more than 50% of the voting rights in the company. For this purpose, the holdings of all shareholders who have a personal interest in the same transaction will be aggregated. The approval of the audit committee or the compensation committee, the board of directors and the shareholders of the company, in that order, is required for (a) extraordinary transactions with a controlling shareholder or in which a controlling shareholder has a personal interest, (b) the engagement with a controlling shareholder or his or her relative, directly or indirectly, including through a company under the control of the controlling shareholder, for the provision of services to the company, (c) the terms of engagement and compensation of a controlling shareholder or his or her relative who is an office holder or (d) the employment of a controlling shareholder or his or her relative by the company, other than as an office holder. In addition, the shareholder approval requires one of the following, which we refer to as a Special Majority:

- at least a majority of the shares held by all shareholders who do not have a personal interest in the transaction and who are present and voting at the meeting approves the transaction, excluding abstentions; or

- the shares voted against the transaction by shareholders who have no personal interest in the transaction and who are present and voting at the meeting do not exceed 2% of the voting rights in the company.

To the extent that any such transaction with a controlling shareholder is for a period extending beyond three years, approval is required once every three years, unless, with respect to certain transactions, the audit committee determines that the duration of the transaction is reasonable given the circumstances related thereto. Arrangements regarding the compensation, indemnification or insurance of a controlling shareholder in his or her capacity as an office holder require the approval of the compensation committee, board of directors and shareholders by a Special Majority, in that order, and the terms thereof may not be inconsistent with the company's stated compensation policy.

Pursuant to regulations promulgated under the Israeli Companies Law, certain transactions with a controlling shareholder or his or her relative, or with directors, that would otherwise require approval of a company's shareholders may be exempt from shareholder approval upon certain determinations of the audit committee and board of directors.

As of March 15, 2022, Clal Biotechnology Industries Ltd. beneficially owned or controlled, directly and indirectly, 33.8% of our issued and outstanding ordinary shares and (assuming that no other shareholder holds more than 50% of the voting rights in our company) should therefore be deemed a "controlling shareholder" for purposes of the approval of related party transactions under the Israeli Companies Law.

Shareholder duties

Pursuant to the Israeli Companies Law, a shareholder has a duty to act in good faith and in a customary manner toward the company and other shareholders and to refrain from abusing his or her power in the company, including, among other things, in voting at a general meeting and at shareholder class meetings with respect to the following matters:

- an amendment to the company's articles of association;
- an increase of the company's authorized share capital;
- a merger; or
- the approval of related party transactions and acts of office holders that require shareholder approval.

A shareholder also has a general duty to refrain from discriminating against other shareholders. In addition, certain shareholders have a duty of fairness toward the company. These shareholders include any controlling shareholder, any shareholder who knows that he or she has the power to determine the outcome of a shareholder vote and any shareholder who has the power to appoint or to prevent the appointment of an office holder of the company or other power towards the company. The Israeli Companies Law does not define the substance of the duty of fairness, except to state that the remedies generally available upon a breach of contract will also apply in the event of a breach of the duty to act with fairness.

Exculpation, Insurance and Indemnification of Directors and Officers

Under the Israeli Companies Law, a company may not exculpate an office holder from liability for a breach of the duty of loyalty. An Israeli company may exculpate an office holder in advance from liability to the company, in whole or in part, for damages caused to the company as a result of a breach of duty of care but only if a provision authorizing such exculpation is included in its articles of association. Our articles of association include such a provision. A company may not exculpate in advance a director from liability arising out of a prohibited dividend or distribution to shareholders.

Under the Israeli Companies Law, a company may indemnify an office holder in respect of the following liabilities and expenses incurred for acts performed by him or her as an office holder, either pursuant to an undertaking made in advance of an event or following an event, provided its articles of association include a provision authorizing such indemnification:

- financial liability imposed on him or her in favor of another person pursuant to a judgment, including a settlement or arbitrator's award approved by a court. However, if an undertaking to indemnify an office holder with respect to such liability is provided in advance, then such an undertaking must be limited to events which, in the opinion of the board of directors, can be foreseen based on the company's activities when the undertaking to indemnify is given, and to an amount or according to criteria determined by the board of directors as reasonable under the circumstances, and such undertaking shall detail the abovementioned foreseen events and amount or criteria;

- reasonable litigation expenses, including attorneys' fees, incurred by the office holder (1) as a result of an investigation or proceeding instituted against him or her by an authority authorized to conduct such investigation or proceeding, provided that (i) no indictment was filed against such office holder as a result of such investigation or proceeding, and (ii) no financial liability was imposed upon him or her as a substitute for the criminal proceeding as a result of such investigation or proceeding or, if such financial liability was imposed, it was imposed with respect to an offense that does not require proof of criminal intent; and (2) in connection with a monetary sanction; and

- reasonable litigation expenses, including attorneys' fees, incurred by the office holder or imposed by a court in proceedings instituted against him or her by the company, on its behalf, or by a third party, or in connection with criminal proceedings in which the office holder was acquitted, or as a result of a conviction for an offense that does not require proof of criminal intent.

Under the Israeli Companies Law, a company may insure an office holder against the following liabilities incurred for acts performed by him or her as an office holder, if and to the extent provided in the company's articles of association:

- a breach of the duty of loyalty to the company, provided that the office holder acted in good faith and had a reasonable basis to believe that the act would not harm the company;

- a breach of duty of care to the company or to a third party, to the extent such a breach arises out of the negligent conduct of the office holder; and

- a financial liability imposed on the office holder in favor of a third party.

Under the Israeli Companies Law, a company may not indemnify, exculpate or insure an office holder against any of the following:

- a breach of the duty of loyalty, except for indemnification and insurance for a breach of the duty of loyalty to the company to the extent that the office holder acted in good faith and had a reasonable basis to believe that the act would not harm the company;

- a breach of duty of care committed intentionally or recklessly, excluding a breach arising out of the negligent conduct of the office holder;

- an act or omission committed with intent to derive illegal personal benefit; or

- a fine or forfeit levied against the office holder.

Under the Israeli Companies Law, exculpation, indemnification and insurance of office holders in a public company must be approved by the compensation committee and the board of directors and, with respect to certain office holders or under certain circumstances, also by the shareholders. See "—Approval of Related Party Transactions Under Israeli Law."

Our articles of association permit us to exculpate, indemnify and insure our office holders to the fullest extent permitted or to be permitted by the Israeli Companies Law. We have obtained directors' and officers' liability insurance for the benefit of our office holders and intend to continue to maintain such coverage and pay all premiums thereunder to the fullest extent permitted by the Israeli Companies Law. In addition, we have entered into agreements with each of our directors and executive officers exculpating them from liability to us for damages caused to us as a result of a breach of duty of care and undertaking to indemnify them, in each case, to the fullest extent permitted by our articles of association and Israeli Law.

The maximum indemnification amount set forth in those agreements is limited to an amount equal to the greater of (i) 25% of our total shareholders' equity based on our most recently financial statements of the time of the actual payment of the indemnification; (ii) $50 million; (iii) 40% of our total market cap (which shall mean the average closing price of the Company's ordinary shares over the 30 trading days prior to the actual payment of indemnification multiplied by the total number of issued and outstanding shares of the Company as of the date of actual payment); and (iv) in connection with or arising out of a public offering of our securities, the aggregate amount of proceeds from the sale by us and/or any shareholder of ours securities in such offering. The maximum amount set forth in those agreements is in addition to amounts actually paid, if any, under insurance policies and/or by a third-party pursuant to an indemnification arrangement.

D. Employees

As of December 31, 2021, we had 77 employees, 67 of whom were based in Israel and 10 based throughout Europe and employed by our German subsidiary. The distribution of our employees according to main areas of activity is as follows: 9 employees in the administrative department, 25 employees in the research and development department, 33 employees in the manufacturing department and 10 employees in the sales and marketing department. As of December 31, 2021, we did not employ a significant number of temporary employees.

Israeli labor laws govern the length of the workday and workweek, minimum wages for employees, procedures for hiring and dismissing employees, determination of severance pay, annual leave, sick days, advance notice of termination, payments to the National Insurance Institute and other conditions of employment, and include equal opportunity and anti-discrimination laws. While none of our employees is party to any collective bargaining agreements, 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 in Israel by order of the Israeli Ministry of the Economy. These provisions primarily concern pension fund benefits for all employees, insurance for work-related accidents, recuperation pay and travel expenses. 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 relationships with our employees are good.

E. Share Ownership

For information regarding the share ownership of our directors and executive officers, see "ITEM 6.B. Compensation—2014 Equity Incentive Plan" and "ITEM 7.A. Major Shareholders."

Item 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major Shareholders

The following table sets forth information with respect to the beneficial ownership of our shares as of March 15, 2022 by:

- each person or entity known by us to own beneficially more than 5% of our outstanding shares;
- each of our directors and executive officers individually; and
- all of our executive officers and directors as a group.

The beneficial ownership of ordinary shares is determined in accordance with the rules of the SEC and generally includes any ordinary shares over which a person exercises sole or shared voting or investment power. The percentage of shares beneficially owned is based on 32,509,544 ordinary shares issued and outstanding as of March 15, 2022. Ordinary shares that are issuable under stock options or RSUs that are currently exercisable or exercisable within 60 days of March 15, 2022 are deemed to be outstanding and to be beneficially owned by the person holding the stock option for the purpose of computing the number of shares and percentage ownership of that person. Those shares are not deemed outstanding, however, for the purpose of computing the percentage ownership of any other person. The beneficial ownership does not include a 30 –day option to purchase up to an additional 781,249 ordinary shares that we gave to the Underwriters in relation with the public offering that we had in March 2022.

All of our shareholders, including the shareholders listed below, have the same voting rights attached to their ordinary shares. See "ITEM 10.B. Articles of Association." None of our principal shareholders nor our directors or executive officers possesses different or special voting rights with respect to their ordinary shares. Unless otherwise noted below, each shareholder's address is c/o MediWound Ltd., 42 Hayarkon Street, Yavne 8122745, Israel.

A description of any material relationship that our principal shareholders have had with us or any of our predecessors or affiliates within the past three years is included under "ITEM 7.B. Related Party Transactions."

Name of Beneficial Owner	Number of Shares Beneficially Held	Percentage of Class
Directors and Executive Officers		
Stephen T. Wills	*	*
Ofer Gonen	*	*
Assaf Segal	*	*
Vickie R. Driver	*	*
Nissim Mashiach	*	*
Sharon Kochan	*	*
David Fox	*	*
Samuel Moed	*	*
Sharon Malka	385,219	1.2%
Boaz Gur-Lavie	*	*
Lior Rosenberg(1)	1,983,637	6.1%
Ety Klinger	*	*
Yaron Meyer	*	*
All executive officers and directors as a group (13 persons)(2)	3,085,968	9.2%
Principal Shareholders (who are not Directors or Executive Officers)		
Clal Biotechnology Industries Ltd.(3)	10,980,805	33.8%

* Less than 1%.

(1) Shares beneficially owned consist of: (i) 146,532 ordinary shares held directly by Prof. Rosenberg; (ii) 126,900 ordinary shares issuable upon exercise of outstanding options held directly by Prof. Rosenberg that are currently exercisable or exercisable within 60 days of March 15, 2022; and (iii) 1,710,205 ordinary shares held by L.R. Research and Development Ltd. in trust for the benefit of Prof. Rosenberg. Prof. Rosenberg is the sole shareholder of L.R. Research and Development Ltd.

(2) Shares beneficially owned consist of 1,944,856 ordinary shares held directly or indirectly by such executive officers and directors and 1,141,113 ordinary shares issuable upon exercise of outstanding options and RSU's that are currently exercisable or exercisable within 60 days of March 15, 2022.

(3) Shares beneficially owned consist of: (i) 8,208,973 ordinary shares held by Clal Life Sciences, LP, whose managing partner is Clal Application Center Ltd., a wholly-owned subsidiary of CBI; (ii) 2,682,665 ordinary shares held by CBI and (iii) 89,167 ordinary shares issuable upon exercise of outstanding options held directly by CBI that are currently exercisable or exercisable within 60 days of March 15, 2022. As reported on a Schedule 13G/A filed on February 14, 2019 by Access Industries Holdings LLC, Access Industries Holdings LLC indirectly owns 100% of the outstanding shares of Clal Industries Ltd., which owns 47.17% of the outstanding shares of CBI. The address of Clal Industries Ltd. is the Triangular Tower, 3 Azrieli Center, Tel Aviv 67023, Israel and the address of Access Industries Holdings LLC is c/o Access Industries Inc., 40 West 57th Street, New York, New York 10019, United States.

Changes in Ownership of Major Shareholders

To our knowledge, other than as disclosed in the table above, our other filings with the SEC and this Annual Report, there has been no significant change in the percentage ownership held by any major shareholder since January 1, 2019. The major shareholders listed above do not have voting rights with respect to their ordinary shares that are different from the voting rights of other holders of our ordinary shares.

Controlling Shareholder

Because CBI (and its affiliates) beneficially owned or controlled, directly and indirectly, 34.6% of our issued and outstanding ordinary shares as of December 31, 2021, it is considered a "controlled shareholder" under the Israeli Companies Law.

Registered Holders

As of March 15, 2022, we had one holder of record of our ordinary shares in the United States, which is Cede & Co., the nominee of The Depository Trust Company. This shareholder held in the aggregate 64% of the 32,481,213 ordinary shares issued and outstanding as of March 15, 2022. The number of record holders in the United States is not representative of the number of beneficial holders nor is it representative of where such beneficial holders are resident since many of these ordinary shares were held by brokers or other nominees.

B. Related Party Transactions

Information Rights Agreement

We have entered into an information rights agreement with CBI which provides CBI with certain information rights relating to our financial information of the company and certain other information necessary for CBI to meet Israeli Securities Law requirements. CBI is not required to reimburse us for expenses we incur in providing such information.

Registration Rights Agreement

We are party to an amended and restated registration rights agreement, dated April 6, 2021, with certain of our shareholders (the "Registration Rights Agreement"). The Registration Rights Agreement, which was approved by our shareholders at our 2021 annual general meeting of shareholders, replaced the registration rights agreement, dated March 3, 2014 (the "Original Registration Rights Agreement"), that we had entered into in connection with our initial public offering with certain of our pre-IPO shareholders, which expired by its own terms on its seven-year anniversary. The ordinary shares held by most of our pre-IPO shareholders who were party to the Original Registration Rights Agreement were no longer entitled to registration rights under that agreement as of the time that it expired, given their ability to freely sell their shares in the open market under Rule 144 of the Securities Act. However, each of CBI and Professor Lior Rosenberg, and their affiliated entities that hold ordinary shares (consisting of Clal Life Sciences LP and L.R. Research & Development Ltd., respectively) remained entitled to registration rights as of the time of the expiration of the Original Registration Rights Agreement, and we therefore entered into the Registration Rights Agreement with them as a means of extending those rights. . The Registration Rights Agreement provides to the holders of our ordinary shares that are party to the agreement the right to demand that we file a registration statement or request that their ordinary shares be covered by a registration statement that we are otherwise filing. In March 2019, we filed, and the SEC declared effective, on April 22, 2019, a shelf registration statement on Form F-3 that registered the resale of the 11,240,827 shares that were then entitled to registration rights under the Original Registration Rights Agreement. That registration statement remains in effect as of the date of this Annual Report. The registration rights under the Registration Rights Agreement are described in more detail under "ITEM 10.B. Articles of Association" and in Exhibit 2.1 to this Annual Report, which is incorporated by reference in that ITEM 10.B.

Founders' and Shareholders' Agreement

In January 2001, we entered into a founders' and shareholders' agreement (the "Founders Agreement"), with CBI, Prof. Lior Rosenberg, our Chief Medical Technology Officer, and LR, a private company which is wholly-owned by Prof. Rosenberg. The Founders Agreement was amended in 2006. Pursuant to the Founders Agreement, in exchange for the issuance of ordinary shares and certain rights thereunder and the payment of certain fixed amounts, Prof. Rosenberg granted to us a perpetual, exclusive, non-revocable, royalty-free, sub-licensable, worldwide license for intellectual property relating to debridement using products based on our proteolytic enzyme technology. As of the date hereof, all of the payments under the Founders Agreement were paid by us to Prof. Rosenberg in accordance with the Founders Agreement. The Founders Agreement also provided for anti-dilution, pre-emptive rights, a right of first refusal on the sale of our ordinary shares and bring-along rights, all of which were subsequently terminated.

Sub-Lease Agreement

In January 2018, we entered into a sub-lease agreement (the "Sub-Lease Agreement"), with Clal Life Sciences, L.P. ("CLS"), a subsidiary of CBI, our controlling shareholder, which was amended in February 2019. Pursuant to the Sub-Lease Agreement, we currently sublease approximately 32,300 square feet of laboratory, office and clean room space from CLS and our yearly rent is $0.4 million. The Sub-Lease Agreement is scheduled to expire on October 30, 2025.

Agreements with Directors and Officers

Employment Agreements

We have entered into employment agreements with each of our executive officers, which include standard provisions for a company in our industry regarding non-competition/solicitation, confidentiality of information and assignment of inventions. However, the enforceability of the non-competition provisions may be limited under applicable law. Our executive officers will not receive benefits upon the termination of their respective employment with us, other than payment of salary and benefits (and limited accrual of vacation days) during the required notice period for termination of their employment, which varies for each individual.

Options

Since our inception, we have granted options to purchase our ordinary shares to our directors and executive officers. Such option agreements may contain acceleration provisions upon certain merger, acquisition or change of control transactions. We describe our option plans under "ITEM 6.B. Compensation—2003 Israeli Share Option Plan" and "ITEM 6.B. Compensation—2014 Equity Incentive Plan." If an executive officer is involuntarily terminated without cause or the executive officer voluntarily terminates his employment for good reason (as defined in the employment agreement), all options will immediately vest. Upon the consummation of a merger or acquisition transaction, an executive officer's options will be assumed or substituted by the surviving company, if applicable, or, in the compensation committee's sole discretion, will vest immediately or be amended, modified or terminated. Our compensation committee approved accelerated vesting in the case of a merger or an acquisition transaction for certain of our directors and executive officers with respect to the option agreements dated December 23, 2015, June 22, 2017, January 16, 2018, December 31, 2018, May 2, 2019, April 23, 2020 and March 4, 2021.

RSUs

Under the 2014 Plan, we have granted RSUs to our executive officers and our chairman of the board. The RSU agreements generally provide for vesting of RSUs over a four-year period of continuous employment or service, with 25% of the RSUs vesting at the lapse of one year following the vesting commencement date, and the remaining 75% of the RSUs vesting in three equal installments, at the lapse of each of the following three years. Absent a specific acceleration provision, if a grantee's service is terminated for any reason, all RSUs that have not vested will immediately terminate. RSUs that have vested but have not been settled yet for underlying ordinary shares may generally be settled within the three months following the termination of the service of the grantee, other than in the case of termination due to death or disability (in which case the grantee or his/her estate will have one year to settle the vested RSUs for underlying ordinary shares) or termination for cause (in which case all unsettled RSUs will immediately terminate). Upon the consummation of a merger or acquisition transaction, an executive officer's or the chairman's RSUs will be assumed or substituted by the surviving company, if applicable, or, in the compensation committee's sole discretion, will vest immediately or be amended, modified or terminated. The RSUs that we grant may contain acceleration provisions upon certain merger, acquisition or change of control transactions, if approved by our board of directors with respect to a specific grant. The RSUs are generally subject to the further terms of the 2014 Plan, which we describe under "ITEM 6.B. Compensation—2014 Equity Incentive Plan."

Exculpation, indemnification and insurance

Our articles of association permit us to exculpate, indemnify and insure each of our directors and office holders to the fullest extent permitted by the Israeli Companies Law. Additionally, we have entered into indemnification agreements with each of our directors and executive officers, undertaking to indemnify them to the fullest extent permitted by Israeli law, including with respect to liabilities resulting from a public offering of our shares, to the extent that these liabilities are not covered by insurance. We have also obtained Directors and Officers insurance for each of our executive officers and directors. See "ITEM 6.C. Board Practices—Exculpation, Insurance and Indemnification of Directors and Officers."

C. Interests of Experts and Counsel

Not applicable.

Item 8. FINANCIAL INFORMATION

A. Consolidated Statements and Other Financial Information

Consolidated Financial Statements

See Item 18. "Financial Statements".

Legal and Arbitration Proceedings

From time to time, we may be party to litigation or subject to claims incident to the ordinary course of business.

Settlement of Litigation Involving Our Company, PolyHeal Shareholders and Teva

In March 2019, we entered into settlement agreements and mutual general releases with respect to our previously-reported litigation arising under a series of agreements among PolyHeal, Teva and our company that we entered into in 2010 (collectively, the "2010 PolyHeal Agreements"). For a description of the history of the proceedings related to the 2010 PolyHeal Agreements and a dispute related to a collaboration agreement between Teva and our company that we entered into in 2007 (the "2007 Teva Agreement,") please see "ITEM 8. Financial Information— A. Consolidated Statements and Other Financial Information— Legal Proceedings" in our annual report on Form 20-F for the year ended December 31, 2018, filed with the SEC on March 25, 2019 (the "2018 Form 20-F").

As reported in the 2018 Form 20-F, on March 24, 2019, we entered into an initial settlement with the plaintiffs— certain shareholders of PolyHeal — which settlement was subsequently approved by the Israeli Supreme Court, which settled any and all debts, obligations or liabilities that we and the plaintiffs had to one another in connection with the transactions under the 2010 PolyHeal Agreements. Pursuant to the terms of this settlement agreement, the plaintiffs were to repay a non-material portion of the amount that was ruled in their favor under a November 2017 ruling, and the Israeli Supreme Court was to approve and accept the appeal that was filed by us in December, 2017, cancel the 2017 ruling that was issued by the Israeli District Court against us, and reject the PolyHeal shareholders' cross-appeal.

Also as reported in the 2018 Form 20-F, on March 24, 2019, we entered into a settlement agreement and mutual general release with Teva, which was contingent upon the Supreme Court's approval of the settlement with the PolyHeal plaintiffs (which approval was received), which settled any and all debts, obligations or liabilities that each party or any of its controlled affiliates had to the other party or any of its controlled affiliates in connection with certain transactions and collaboration agreements entered into between us and Teva from 2007 to 2012, which had terminated effective as of December 31, 2012 and September 2, 2013, as applicable, and which had related to NexoBrid and PolyHeal, including a milestone payment to PolyHeal and certain additional payments, which were primarily intended to serve as reimbursement for development and manufacturing costs, which we had believed were to be borne by Teva through the effective date of termination of those collaboration agreements in December 2012.

Pursuant to the terms of the Teva settlement agreement, Teva agreed to pay us $4.0 million in cash, and to reduce the contingent consideration that is payable to Teva pursuant to our repurchase of our shares from Teva in 2013, so that we are obligated to pay Teva annual payments at a reduced rate of 15% of its recognized revenues from the sale or license of NexoBrid after January 1, 2019, up to a reduced aggregate amount of $10.2 million. In addition, we also agreed to indemnify Teva and its controlled affiliates from and against claims relating to a certain milestone related to PolyHeal under an agreement associated with our collaboration agreements with Teva, for up to an amount of $10.2 million, if a notice of such claim has been received by us prior to December 31, 2023.

On December 13, 2020, we signed an amendment to the Teva settlement agreement that replaces the revenue-based payment mechanism with a fixed payment schedule. The aggregate amount paid to Teva of up to $10.2 million and the other terms, including with respect to our indemnification obligations, in the Teva settlement agreement are unchanged. Out of the $3 million already due to Teva we paid $1 million of the on December 2020 and the balance will be paid in twelve quarterly equal installments during the period commencing on January 1, 2021 and ending on December 31, 2023. In addition, commencing on January 1, 2021, we have agreed to pay Teva an aggregate annual amount of $1 million in four quarterly equal installments, unless we do not recognize any revenues generated from the sale or license of NexoBrid in any such quarter, up to an aggregate amount equal to $7.2 million regardless of the number of quarters required for purposes of the payment of such aggregate amount.

In September 2019, we entered into a series of additional settlement agreements and mutual general releases with certain shareholders of PolyHeal, including Clal Biotechnology Industries Ltd. (CBI), our controlling shareholder, which together constitute the majority of PolyHeal's shareholders. Those additional settlement agreements settle any and all debts, obligations or liabilities that each party or any of its affiliates had or has to the other party or any of its affiliates, in connection with or arising out of the series of 2010 PolyHeal Agreements. Pursuant to these settlement agreements, we paid an aggregate amount of approximately $2.8 million and received 14,473 shares of PolyHeal.

Dividend Policy

We have never declared or paid cash dividends to our shareholders and we do not intend to pay cash dividends in the foreseeable future. We intend to reinvest any earnings 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, our financial condition, operating results, contractual restrictions, capital requirements, business prospects, our strategic goals and plans to expand our business, applicable law and other factors that our board of directors may deem relevant.

B. Significant Changes

No significant changes have occurred since December 31, 2021, except as otherwise disclosed in this annual report.

Item 9. THE OFFER AND LISTING

A. Listing Details

Our ordinary shares trade on the Nasdaq Global Market under the symbol “MDWD”.

B. Plan of Distribution

Not applicable.

C. Markets

See “—Listing Details” above.

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. Articles of Association

A copy of our amended and restated articles of association is attached as Exhibit 1.1 to this Annual Report. Other than as disclosed below, the information called for by this Item is set forth in Exhibit 2.1 to our Annual Report on Form 20-F for the year ended December 31, 2019 and is incorporated by reference into this Annual Report.

Election of directors

Our ordinary shares do not have cumulative voting rights for the election of directors. As a result, the holders of a majority of the voting power represented at a meeting of shareholders have the power to elect each of our directors, subject to the special approval requirements for external directors described under "ITEM 6.C. Board Practices—External Directors." Under our articles of association, our board of directors must consist of at least five and not more than nine directors, including at least two external directors required to be appointed under the Israeli Companies Law. At any time the minimum number of directors (other than the external directors) shall not fall below three. Pursuant to our articles of association, each of our directors, other than the external directors, for whom special election requirements apply under the Israeli Companies Law, will be appointed by a simple majority vote of holders of our voting shares, participating and voting at an annual general meeting of our shareholders. Each director will serve until his or her successor is duly elected and qualified or until his or her earlier death, resignation or removal by a vote of the majority voting power of our shareholders at a general meeting of our shareholders or until his or her office expires by operation of law, in accordance with the Israeli Companies Law. Our articles of association allow our board of directors to appoint directors to fill vacancies on the board of directors to serve until the next annual general meeting of shareholders. External directors are elected for an initial term of three years, may be elected for additional terms of three years each under certain circumstances, and may be removed from office pursuant to the terms of the Israeli Companies Law. Under regulations promulgated under the Israeli Companies Law, Israeli public companies whose shares are traded on certain U.S. stock exchanges, such as the Nasdaq Global Market and that lack a controlling shareholder are exempt from the requirement to appoint external directors. See "ITEM 6.C. Board Practices—Board of Directors and External Directors."

C. Material Contracts

For a description of the registration rights that are subject to our Registration Rights Agreement, see "ITEM 7.B. Related Party Transactions—Registration Rights Agreement."

For a description of our contract with the U.S. Biomedical Advanced Research and Development Authority, see "ITEM 4.B. Our Focus—Burn Care—BARDA Contract."

For a description of our exclusive license and supply agreements with Vericel, see "ITEM 4.B. Business Overview— Marketing, Sales and Distribution — Vericel License and Supply Agreements."

For a description of our license agreement with Mark Klein, see "ITEM 4.B. Business Overview—Intellectual Property—Klein License Agreement."

We have entered into an agreement with Challenge Bioproducts Corporation Ltd. ("CBC"), a corporation organized and existing under the laws of the Republic of China, dated January 11, 2001, as amended on February 28, 2010, pursuant to which CBC uses proprietary methods to manufacture bromelain SP and supplies us with this intermediate drug substance in bulk quantities. According to the terms of the agreement, CBC shall not, and shall not permit related companies or a third party to, manufacture, use, supply or sell the raw materials for the use or production of a product directly or indirectly competing with any of our products. Our supply agreement with CBC has no fixed expiration date and can be voluntarily terminated by us, with at least six months' advance written notice, or by CBC, with at least 24 months' advance written notice.

D. Exchange Controls

In 1998, Israeli currency control regulations were liberalized significantly, so that Israeli residents generally may freely deal in foreign currency and foreign assets, and non-residents may freely deal in Israeli currency and Israeli assets. There are currently no Israeli currency control restrictions on remittances of dividends on the ordinary shares or the proceeds from the sale of the shares provided that all taxes were paid or withheld; however, legislation remains in effect pursuant to which currency controls can be imposed by administrative action at any time.

Non-residents of Israel may freely hold and trade our securities. Neither our articles of association nor the laws of the State of Israel restrict in any way the ownership or voting of ordinary shares by non-residents, except that such restrictions may exist with respect to citizens of countries which are in a state of war with Israel. Israeli residents are allowed to purchase our ordinary shares.

E. Taxation

The following description is not intended to constitute a complete analysis of all tax consequences relating to the acquisition, ownership and disposition of our ordinary shares. You should consult your own tax advisor concerning the tax consequences of your particular situation, as well as any tax consequences that may arise under the laws of any state, local, foreign or other taxing jurisdiction.

Israeli Tax Considerations for Our Shareholders

Capital gains taxes applicable to non-Israeli resident shareholders

A non-Israeli resident (whether an individual or a corporation) who derives capital gains from the sale of shares in an Israeli resident company that were purchased after the company was listed for trading on the Tel Aviv Stock Exchange or on a recognized stock exchange outside of Israel, will generally be exempt from Israeli capital gain tax so long as the shares were not held through a permanent establishment that the non-resident maintains in Israel (and with respect to shares listed on a recognized stock exchange outside of Israel, so long as the particular capital gain is otherwise subject to the Israeli Income Tax Law (Inflationary Adjustments) 5745-1985. These provisions dealing with capital gain are not applicable to a person whose gains from selling or otherwise disposing of the shares are deemed to be business income. However, non-Israeli corporations will not be entitled to the foregoing exemption if Israeli residents (i) have a controlling interest of more than 25% in such non-Israeli corporation or (ii) are the beneficiaries of, or are entitled to, 25% or more of the revenues or profits of such non-Israeli corporation, whether directly or indirectly.

Additionally, a sale of shares by a non-Israeli resident may also be exempt from Israeli capital gains tax under the provisions of an applicable tax treaty. For example, under 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, as amended (the “United States-Israel Tax Treaty”), the sale, exchange or other disposition of shares by a shareholder who is a United States resident (for purposes of the United States-Israel Tax Treaty) holding the shares as a capital asset and is entitled to claim the benefits afforded to such a resident by the United States-Israel Tax Treaty (a “Treaty U.S. Resident”) is generally exempt from Israeli capital gains tax unless: (i) the capital gain arising from such sale, exchange or disposition is attributed to real estate located in Israel; (ii) the capital gain arising from such sale, exchange or disposition is attributed to royalties; (iii) the capital gain arising from the such sale, exchange or disposition can be attributable to a permanent establishment of the shareholder maintained in Israel, under certain terms; (iv) such Treaty U.S. Resident holds, directly or indirectly, shares representing 10% or more of the voting capital of a company during any part of the 12-month period preceding such sale, exchange or disposition, subject to certain conditions; or (v) such Treaty U.S. Resident is an individual and was present in Israel for a period or periods aggregating to 183 days or more during the relevant taxable year. In each case, the sale, exchange or disposition of our ordinary shares would be subject to such Israeli tax, to the extent applicable; However, under the United States-Israel Tax Treaty, such Treaty U.S. Resident 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 in U.S. laws applicable to foreign tax credits.

In some instances where our shareholders may be liable for Israeli tax on the sale of their ordinary shares, the payment of the consideration may be subject to the withholding of Israeli tax at source. Shareholders may be required to demonstrate that they are exempt from tax on their capital gains in order to avoid withholding at source at the time of sale. Specifically, in transactions involving a sale of all of the shares of an Israeli resident company, in the form of a merger or otherwise, the Israel Tax Authority may require from shareholders who are not liable for Israeli tax to sign declarations in forms specified by this authority or obtain a specific exemption from the Israel Tax Authority to confirm their status as non-Israeli resident, and, in the absence of such declarations or exemptions, may require the purchaser of the shares to withhold taxes at source.

Taxation of non-Israeli shareholders on receipt of dividends

Non-Israeli residents (whether individuals or corporations) are generally subject to Israeli income tax on the receipt of dividends paid on our ordinary shares at the rate of 25% unless a relief is provided in a treaty between Israel and a shareholder's country of residence (provided that a certificate from the Israeli Tax Authority allowing for a reduced withholding tax rate is obtained in advance). With respect to a person who is a "substantial shareholder" at the time of receiving the dividend or on any time during the preceding 12 months, the applicable tax rate is 30%. A "substantial shareholder" is generally a person who alone or together with such person's relative or another person who collaborates with such person on a permanent basis, holds, directly or indirectly, at least 10% of any of the "means of control" of the corporation. "Means of control" generally include the right to vote, receive profits, nominate a director or an executive officer, receive assets upon liquidation, or order someone who holds any of the aforesaid rights how to act, regardless of the source of such right. Such dividends are generally subject to Israeli withholding tax at a rate of 25% so long as the shares are registered with a nominee company (whether or not the recipient is a substantial shareholder), unless relief is provided in a treaty between Israel and the shareholder's country of residence and provided that a certificate from the Israel Tax Authority allowing for a reduced withholding tax rate is obtained in advance. However, a distribution of dividends to non-Israeli residents is subject to withholding tax at source at a rate of 15% if the dividend is distributed from income attributed to a Beneficiary Enterprise, unless a reduced tax rate is provided under an applicable tax treaty, and provided that a certificate from the Israel Tax Authority allowing for a reduced withholding tax rate is obtained in advance. For example, under the United States-Israel Tax Treaty, the maximum rate of tax withheld at source in Israel on dividends paid to a holder of our ordinary shares who is a Treaty U.S. Resident is 25%. However, generally, the maximum rate of withholding tax on dividends, not generated by an Approved Enterprise or Beneficiary Enterprise, that are paid to a U.S. corporation holding 10% or more of the outstanding voting capital throughout the tax year in which the dividend is distributed as well as during the previous tax year, is 12.5%, provided that not more than 25% of the gross income for such preceding year consists of certain types of dividends and interest. Notwithstanding the foregoing, dividends distributed from income attributed to an Approved Enterprise or Beneficiary Enterprise are not entitled to such reduction under the tax treaty but are subject to a withholding tax rate of 15% for such a U.S. corporation, provided that the condition related to our gross income for the previous year (as set forth in the previous sentence) is met. If the dividend is attributable partly to income derived from an Approved Enterprise, Beneficiary Enterprise or Preferred Enterprise, and partly to other sources of income, the withholding rate will be a blended rate reflecting the relative portions of the two types of income. We cannot assure you that we will designate the profits that we may distribute in a way that will reduce shareholders' tax liability.

A non-Israeli resident who receives dividends from which tax was withheld, is generally exempt from the obligation to file tax returns in Israel with respect to such income, provided that (i) such income was not derived from a business conducted in Israel by the taxpayer, (ii) the taxpayer has no other taxable sources of income in Israel with respect to which a tax return is required to be filed and (iii) the tax payer is not obligated to pay the excess tax (as further explained below).

Excess Tax

Individuals who are subject to tax in Israel are also subject to an additional tax at a rate of 3% on annual income exceeding a certain level, which amount is linked to the annual change in the Israeli consumer price index, including but not limited to, dividends, interest and capital gain. In 2021, the additional tax was at a rate of 3% on annual income exceeding NIS 647,640.

United States Federal Income Taxation

The following is a description of the material U.S. federal income tax consequences of the ownership and disposition of our ordinary shares by a U.S. Holder that holds the ordinary shares as capital assets. This description does not address tax considerations applicable to holders that may be subject to special tax rules, including, without limitation:

- banks, financial institutions or insurance companies;
- real estate investment trusts, regulated investment companies or grantor trusts;
- dealers or traders in securities, commodities or currencies;
- tax-exempt entities or organizations, including an "individual retirement account" or "Roth IRA" as defined in Section 408 or 408A of the Code, respectively;
- certain former citizens or long-term residents of the United States;
- persons that received our shares as compensation for the performance of services;
- persons that holds our shares as part of a "hedging," "integrated" or "conversion" transaction or as a position in a "straddle" for U.S. federal income tax purposes;
- partnerships (including entities classified as partnerships for U.S. federal income tax purposes) or other pass-through entities, or holders that will hold our shares through such an entity;
- S corporations;
- holders that acquired ordinary shares as a result of holding or owning our preferred shares;
- U.S. Holders (as defined below) whose "functional currency" is not the U.S. dollar;
- persons that are residents of ordinarily resident in or have a permanent establishment in a jurisdiction outside the United States; or
- holders that own directly, indirectly or through attribution 10.0% or more of the voting power or value of our shares.

Moreover, this description does not address the U.S. federal estate, gift or alternative minimum tax consequences, Medicare consequences, or any state, local or foreign tax consequences, of the ownership and disposition of our ordinary shares.

This summary is based on the Internal Revenue Code of 1986, as amended (the "Code"), administrative pronouncements, judicial decisions and final, temporary and proposed Treasury regulations, all as currently in effect and available. These authorities are subject to change or differing interpretation, possibly with retroactive effect. U.S. Holders should consult their tax advisors concerning the U.S. federal, state, local and foreign tax consequences of owning and disposing of our ordinary shares in their particular circumstances.

For purposes of this summary, a "U.S. Holder" is a beneficial owner of our ordinary shares who is, for U.S. federal income tax purposes:

- an individual who is a citizen or individual resident of the United States;
- a corporation, or other entity taxable as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. Court and one or more U.S. persons that have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable Treasury regulations to be treated as a U.S. person.

If a partnership (or other entity treated as a partnership for U.S. federal income tax purposes) holds our ordinary shares, the tax treatment of a partner in such partnership generally will depend upon the status of the partner and upon the activities of the partnership. Investors who are partners in a partnership should consult their tax advisors as to the particular U.S. federal income tax consequences of owning and disposing of our ordinary shares in their particular circumstances.

A "Non-U.S. Holder" is a beneficial owner of our ordinary shares that is neither a U.S. Holder nor a partnership for U.S. federal income tax purposes.

Unless otherwise indicated, this discussion assumes that the company is not, and will not become, a "passive foreign investment company," or a PFIC, for U.S. federal income tax purposes. See "ITEM 10.E. Taxation—United States Federal Income Taxation—Passive Foreign Investment Company Considerations" below. Further, this summary does not address the U.S. federal estate and gift, state, local or non-U.S. tax consequences to U.S. Holders of owning and disposing of our ordinary shares. Investors should consult their own tax advisors regarding the U.S. federal, state and local, as well as non-U.S. income and other tax consequences of owning and disposing of our ordinary shares in their particular circumstances.

Distributions

If you are a U.S. Holder, the gross amount of any distribution made to you with respect to our ordinary shares before reduction for any Israeli taxes withheld therefrom, other than certain distributions, if any, of our ordinary shares distributed pro rata to all our shareholders, generally will be includible in your income as dividend income to the extent such distribution is paid out of our current or accumulated earnings and profits as determined under U.S. federal income tax principles. We do not expect to maintain calculations of our earnings and profits under U.S. federal income tax principles. Therefore, if you are a U.S. Holder you should expect that the entire amount of any distribution generally will be taxable as dividend income to you. Non-corporate U.S. Holders may qualify for the lower rates of taxation with respect to dividends on ordinary shares applicable to long-term capital gains (i.e., gains from the sale of capital assets held for more than one year), provided that certain conditions are met, including certain holding period requirements and the absence of certain risk reduction transactions. However, such dividends will not be eligible for the dividends received deduction generally allowed to corporate U.S. Holders.

If you are a U.S. Holder, dividends paid to you with respect to our ordinary shares will generally be treated as foreign source income, which may be relevant in calculating your foreign tax credit limitation. Subject to certain conditions and limitations, Israeli tax withheld on dividends may be deducted from your taxable income or credited against your U.S. federal income tax liability. The limitation on foreign taxes eligible for credit is calculated separately with respect to specific classes of income. For this purpose, dividends that we distribute generally should constitute "passive category income." A foreign tax credit for foreign taxes imposed on distributions may be denied if you do not satisfy certain minimum holding period requirements. The rules relating to the determination of the foreign tax credit are complex, and you should consult your tax advisor to determine whether and to what extent you will be entitled to this credit.

Subject to the discussion below under "—Backup Withholding Tax and Information Reporting Requirements," if you are a Non-U.S. Holder, you generally will not be subject to U.S. federal income (or withholding) tax on dividends received by you on your ordinary shares, unless you conduct a trade or business in the United States and such income is effectively connected with that trade or business (or, if required by an applicable income tax treaty, the dividends are attributable to a permanent establishment or fixed base that such holder maintains in the United States).

Sale, Exchange or Other Taxable Disposition of Ordinary Shares

If you are a U.S. Holder, you generally will recognize gain or loss on the sale, exchange or other taxable disposition of our ordinary shares equal to the difference between the amount realized on such sale, exchange or other taxable disposition and your adjusted tax basis in our ordinary shares, and such gain or loss will be capital gain or loss. The initial tax basis in an ordinary share generally will be equal to the cost of such ordinary share. Except with respect to foreign currency gain or loss, if you are a non-corporate U.S. Holder, capital gain from the sale, exchange or other taxable disposition of ordinary shares is generally eligible for a preferential rate of taxation applicable to capital gains, if your holding period for such ordinary shares exceeds one year (i.e., such gain is long-term capital gain). The deductibility of capital losses for U.S. federal income tax purposes is subject to limitations under the Code. Any such gain or loss that a U.S. Holder recognizes generally will be treated as U.S. source income or loss for foreign tax credit limitation purposes.

Subject to the discussion below under "—Backup Withholding Tax and Information Reporting Requirements," if you are a Non-U.S. Holder, you generally will not be subject to U.S. federal income or withholding tax on any gain realized on the sale or exchange of such ordinary shares unless:

- such gain is effectively connected with your conduct of a trade or business in the United States (or, if required by an applicable income tax treaty, the gain is attributable to a permanent establishment or fixed base that such holder maintains in the United States); or

- you are an individual and have been present in the United States for 183 days or more in the taxable year of such sale or exchange and certain other conditions are met.

Passive Foreign Investment Company Considerations

If we were to be classified as a "passive foreign investment company," or "PFIC," in any taxable year, a U.S. Holder would be subject to special rules generally intended to reduce or eliminate any benefits from the deferral of U.S. federal income tax that a U.S. Holder could derive from investing in a non-U.S. company that does not distribute all of its earnings on a current basis.

A non-U.S. corporation will be classified as a PFIC for federal income tax purposes in any taxable year in which, after applying certain look-through rules with respect to the income and assets of subsidiaries, either:

- at least 75% of its gross income is "passive income"; or

- at least 50% of the average quarterly value of its total gross assets (which may be determined in part by the market value of our ordinary shares, which is subject to change) is attributable to assets that produce "passive income" or are held for the production of passive income.

Passive income for this purpose generally includes dividends, interest, royalties, rents, gains from commodities and securities transactions, the excess of gains over losses from the disposition of assets which produce passive income, and includes amounts derived by reason of the temporary investment of funds raised in offerings of our ordinary shares. If a non-U.S. corporation owns at least 25% by value of the stock of another corporation, the non-U.S. corporation is treated for purposes of the PFIC tests as owning its proportionate share of the assets of the other corporation and as receiving directly its proportionate share of the other corporation's income. If we are classified as a PFIC in any year with respect to which a U.S. Holder owns our ordinary shares, we will continue to be treated as a PFIC with respect to such U.S. Holder in all succeeding years during which the U.S. Holder owns our ordinary shares unless we cease to be a PFIC and the U.S. holder has made a "deemed sale" election under the PFIC rules.

Based on our current estimates of our gross income and the estimated fair market value of our gross assets and the nature of our business, we do not believe we were classified as a PFIC for the taxable year ending December 31, 2021. However, we must determine our PFIC status annually based on tests which are factual in nature, and our status in future years will depend on our income, assets and activities in those years. Further, because the value of our gross assets is likely to be determined in large part by reference to our market capitalization, a decline in the value of our ordinary shares or an increase in the value of our passive assets (including cash and short term investments) may result in our becoming a PFIC. There can be no assurance that we will not be considered a PFIC for any taxable year. If we were a PFIC and you are a U.S. Holder, then unless you make one of the elections described below, a special tax regime will apply to both (a) any "excess distribution" by us to you (generally, your ratable portion of distributions in any year which are greater than 125% of the average annual distribution received by you in the shorter of the three preceding years or your holding period for our ordinary shares) and (b) any gain realized on the sale or other disposition of the ordinary shares. Under this regime, any excess distribution and realized gain will be treated as ordinary income and will be subject to tax as if (a) the excess distribution or gain had been realized ratably over your holding period, (b) the amount deemed realized in each year had been subject to tax in each year of that holding period at the highest marginal rate for such year (other than income allocated to the current period or any taxable period before we became a PFIC, which would be subject to tax at the U.S. Holder's regular ordinary income rate for the current year and would not be subject to the interest charge discussed below) and (c) the interest charge generally applicable to underpayments of tax had been imposed on the taxes deemed to have been payable in those years. In addition, dividend distributions made to you will not qualify for the lower rates of taxation applicable to long-term capital gains discussed above under "Distributions." Certain elections may be available that would result in an alternative treatment (such as mark-to-market treatment) of our ordinary shares.

If a U.S. Holder makes a valid mark-to-market election for the first tax year in which such U.S. Holder holds (or is deemed to hold) ordinary shares in a corporation and for which such corporation is determined to be a PFIC, the U.S. Holder generally will recognize as ordinary income any excess of the fair market value of the ordinary shares at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the ordinary shares over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. Holder makes the election, the U.S. Holder's tax basis in the ordinary shares will be adjusted to reflect these income or loss amounts. Any gain recognized on the sale or other disposition of ordinary shares in a year when we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). The mark-to-market election is available only if we are a PFIC and our ordinary shares are "regularly traded" on a "qualified exchange." Our ordinary shares will be treated as "regularly traded" in any calendar year in which more than a de minimis quantity of the ordinary shares, are traded on a qualified exchange on at least 15 days during each calendar quarter. Nasdaq is a qualified exchange for this purpose and, consequently, if the ordinary shares are regularly traded, the mark-to-market election will be available to a U.S. Holder.

If we are a PFIC, the general tax treatment for U.S. Holders described in this section would apply to indirect distributions and gains deemed to be realized by U.S. Holders in respect of any entity in which we hold equity that is also a PFIC (a "lower tier PFIC"). Because a mark-to-market election generally would not be available with respect to any lower-tier PFICs, a U.S. Holder may continue to be subject to the PFIC rules with respect to such holder's indirect interest in any investments held by us that are treated as an equity interest in such lower-tiers PFICs.

We do not intend to provide the information necessary for U.S. Holders to make qualified electing fund elections if we are classified as a PFIC. U.S. Holders should consult their tax advisors to determine whether any of these elections would be available and if so, what the consequences of the alternative treatments would be in their particular circumstances.

If a U.S. Holder owns ordinary shares during any year in which we are a PFIC, the U.S. Holder generally will be required to file an IRS Form 8621 (Information Return by a Shareholder of a Passive Foreign Investment Company or Qualified Electing Fund) or successor form with respect to the company, generally with the U.S. Holder's federal income tax return for that year. If the company was a PFIC for a given taxable year, then you should consult your tax advisor concerning your annual filing requirements.

U.S. Holders should consult their tax advisors regarding whether we are a PFIC and the potential application of the PFIC rules.

Backup Withholding Tax and Information Reporting Requirements

U.S. backup withholding tax and information reporting requirements may apply to certain payments to certain holders of stock. Information reporting generally will apply to payments of dividends on, and to proceeds from the sale, exchange or redemption of, our ordinary shares made within the United States, or by a United States payor or United States middleman, to a holder of our ordinary shares, other than an exempt recipient (including a payee that is not a United States person that provides an appropriate certification and certain other persons). Payments made (and sales or other dispositions effected at an office) outside the U.S. will be subject to information reporting in limited circumstances. A payor will be required to withhold backup withholding tax from any payments of dividends on, or the proceeds from the sale or redemption of, ordinary shares within the United States, or by a United States payor or United States middleman, to a holder, other than an exempt recipient, if such holder fails to furnish its correct taxpayer identification number or otherwise fails to comply with, or establish an exemption from, such backup withholding tax requirements, or to report dividends required to be shown on the holder's U.S. federal income tax returns. Back up withholding is not an additional tax. Any amounts withheld under the backup withholding rules will be allowed as a credit against the beneficial owner's U.S. federal income tax liability, if any, and any excess amounts withheld under the backup withholding rules may be refunded, provided that the required information is timely furnished to the IRS.

Foreign Asset Reporting

Certain U.S. Holders who are individuals and certain entities may be required to report information relating to an interest in our ordinary shares, subject to certain exceptions (including an exception for shares held in accounts maintained by certain financial institutions) by filing IRS Form 8938 (Statement of Specified Foreign Financial Assets) with their federal income tax return. U.S. Holders are urged to consult their tax advisors regarding their information reporting obligations, if any, with respect to their ownership and disposition of our ordinary shares.

F. Dividends and Paying Agents

Not applicable.

G. Statement by Experts

Not applicable.

H. Documents on Display

We are required to make certain filings with the SEC. The SEC maintains an internet website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the SEC. The address of that site is www.sec.gov.

We also make available on our website, free of charge, our annual reports on Form 20-F and the text of our reports on Form 6-K, including any amendments to these reports, as well as certain other SEC filings, as soon as reasonably practicable after they are electronically filed with or furnished to the SEC. Our website address is www.mediwound.com. The information contained on our website is not incorporated by reference in this document.

I. Subsidiary Information

Not applicable.

Item 11. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to a variety of risks, including foreign currency exchange fluctuations, changes in interest rates and inflation. We regularly assess currency, interest rate and inflation risks to minimize any adverse effects on our business as a result of those factors.

Foreign Currency Risk

The U.S. dollar is our functional and reporting currency. A significant portion of our operating expenses are denominated in Israeli shekels, accounting for approximately 40%, 44% and 45% of our operating expenses in the years ended December 31, 2019, 2020 and 2021, respectively. We also have expenses in other non-dollar currencies, in particular the Euro, and for the next few years, we expect that a substantial portion of our revenues will be denominated in U.S dollar. A devaluation of the shekel in relation to the U.S. dollar has the effect of reducing the U.S. dollar amount of our expenses or payables that are payable in shekels, unless those expenses or payables are linked to the U.S. dollar. Conversely, any increase in the value of the shekel in relation to the U.S. dollar has the effect of increasing the U.S. dollar value of our unlinked shekel expenses, which would have a negative impact on our profit margins.

Because exchange rates between the U.S. dollar and both the shekel and the Euro (as well as between the U.S. dollar and other currencies) fluctuate continuously, such fluctuations have an impact on our results and period-to-period comparisons of our results. The effects of foreign currency re-measurements are reported in our consolidated financial statements of operations.

The following table presents information about the changes in the exchange rates of the shekel against the U.S. dollar and changes in the exchange rates of the Euro against the U.S. dollar:

	Appreciation (Devaluation) of	
Period	**Shekel against the U.S. dollar (%)**	**Euro against the U.S. dollar (%)**
2019	7.8	(2.0)
2020	7.0	8.0
2021	3.3	(6.9)

A 10% increase (decrease) in the value of the NIS and Euro against the U.S. dollar would have increased (decreased) our net profit by (loss) approximately $0.74 million for the year ended December 31, 2021.

As we are marketing and selling NexoBrid in Europe and conducting clinical trials of outside the United States, we will continue to monitor exposure to currency fluctuations. We do not currently engage in currency hedging activities in order to reduce this currency exposure, but we may begin to do so in the future. Instruments that may be used to hedge future risks may include foreign currency forward and swap contracts. These instruments may be used to selectively manage risks, but there can be no assurance that we will be fully protected against material foreign currency fluctuations.

Other Market Risks

We do not believe that we have material exposure to interest rate risk due to the fact that we have no long-term debt.

We do not believe that we have any material exposure to inflationary risks. We do not believe that the rate of inflation in Israel has had a material impact on our business to date. However, our costs in Israel will increase if inflation in Israel exceeds the devaluation of the shekel against the U.S. dollar (to the extent that it devalues at all) or if the timing of such devaluation lags behind inflation in Israel.

Item 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

Not applicable.

PART II

Item 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

None.

Item 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS

None.

Item 15. CONTROLS AND PROCEDURES

(a) Disclosure Controls and Procedures

Our management, including our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2021. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2021, our disclosure controls and procedures were effective.

(b) Management 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 financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act.

Our management, including our Chief Executive Officer and Chief Financial Officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2021. In making this assessment, our management used the criteria established in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Our management has concluded, based on its assessment, that our internal control over financial reporting was effective as of December 31, 2021.

(d) Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the period covered by this annual report that have materially affected, or that 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 Sharon Kochan qualifies as an “audit committee financial expert,” as defined under the U.S. federal securities laws and has the requisite financial experience defined by the Nasdaq Marketplace Rules. In addition, Sharon Kochan is independent as such term is defined in Rule 10A-3(b)(1) under the Exchange Act and under the listing standards of the Nasdaq Global Market.

Item 16B. CODE OF ETHICS

We have adopted a code of business conduct and ethics applicable to our executive officers, directors and all other employees. A copy of the code is delivered to every employee of MediWound Ltd. and its subsidiaries and is available to our investors and others on our website http://ir.mediwound.com/ or by contacting our investor relations department. Information contained on, or that can be accessed through, our website does not constitute a part of this annual report and is not incorporated by reference herein. Any waivers of this code for executive officers or directors will be disclosed through the filing of a Form 6-K or on our website. We granted no waivers under our code of ethics in 2021.

Item 16C. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Principal Accountant Fees and Services

We paid the following fees for professional services rendered by Kost Forer Gabbay & Kasierer, a member of Ernst & Young Global, who was our independent registered public accounting firm until the April 28, 2021, and by Somekh Chaikin, a member firm of KPMG International Haifa, Israel, Auditor firm ID: 1057, who became our independent registered public accounting firm on June 15, 2021 for the year ended December 31, 2021:

	2020	2021
Audit Fees	$ 170,000	$ 245,000
Audit-Related Fees	33,500	—
Tax Fees	—	15,000
Total	$ 203,500	$ 260,000

"**Audit fees**" are the aggregate fees paid for the audit of our annual financial statements for the year 2021. This category also includes services that generally the independent accountant provides, such as consents and assistance with and review of documents filed with the SEC.

"**Audit-related fees**" are the aggregate fees paid for assurance and related services that are reasonably related to the performance of the audit and are not reported under audit fees. These fees primarily include accounting consultations regarding the accounting treatment of matters that occur in the regular course of business, implications of new accounting pronouncements and other accounting issues that occur from time to time.

"**Tax fees**" include fees for professional services rendered by our independent registered public accounting firm for tax compliance, transfer pricing and tax advice on actual or contemplated transactions.

The Audit Committee pre-approves all audit and non-audit services provided by the independent registered public accounting firm.

Item 16D. EXEMPTIONS FROM THE LISTING STANDARDS FOR AUDIT COMMITTEES

Not applicable.

Item 16E. PURCHASES OF EQUITY SECURITIES BY THE ISSUER AND AFFILIATED PURCHASERS

Not applicable.

Item 16F. CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT

The information required by this Item 16F was previously reported in our report of foreign private issuer on Form 6-K (File No. 001-36349) filed with the SEC on March 2, 2022.

Item 16G. CORPORATE GOVERNANCE

As a foreign private issuer, we are permitted to comply with Israeli corporate governance practices instead of the Nasdaq Stock Market requirements, provided that we disclose those Nasdaq Stock Market requirements with which we do not comply and the equivalent Israeli requirement that we follow instead. We currently rely on this "foreign private issuer exemption" with respect to the following requirements:

- *Quorum*. As permitted under the Israeli Companies Law pursuant to our articles of association, the quorum required for an ordinary meeting of shareholders will consist of at least two shareholders present in person, by proxy or by other voting instrument in accordance with the Israeli Companies Law, who hold at least 25% of the voting power of our shares (and in an adjourned meeting, with some exceptions, at least two shareholders), instead of 33 1/3% of the issued share capital required under the Nasdaq Stock Market listing rules.

- *Nomination of directors*. With the exception of external directors and directors elected by our board of directors due to vacancy, our directors are elected by an annual meeting of our shareholders to hold office until the next annual meeting following one year from his or her election. The nominations for directors, which are presented to our shareholders by our board of directors, are generally made by the entire board of directors itself, in accordance with the provisions of our articles of association and the Israeli Companies Law. Nominations need not be made by a nominating committee of our board of directors consisting solely of independent directors or otherwise, as required under the Nasdaq Stock Market listing rules.

- *Majority of independent directors*. Under the Israeli Companies Law, we are only required to appoint at least two external directors, within the meaning of the Israeli Companies Law, to our board of directors. Currently, four of our directors (of whom two are external directors, within the meaning of the Israeli Companies Law) qualify as independent directors under the rules of the U.S. federal securities laws and the Nasdaq Stock Market listing rules. If at any time we no longer have a controlling shareholder, we will no longer be required to have external directors, provided that we comply with the majority Board independence requirements and the audit and compensation committee composition requirements of the Nasdaq Stock Market.

- *Shareholder approval*. We do not intend to follow Nasdaq Stock Market rules which require shareholder approval in order to enter into any transaction, other than a public offering, involving the sale, issuance or potential issuance by the Company of ordinary shares (or securities convertible into or exercisable for ordinary shares) equal to 20% or more of the outstanding share capital of the Company or 20% or more of the voting power outstanding before the issuance for less than the greater of book or market value of the ordinary shares. We will follow Israeli law with respect to any requirement to obtain shareholder approval in connection with any private placements of equity securities.

Item 16H. MINE SAFETY DISCLOSURE

Not applicable.

Item 16I. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

[Not applicable.]

PART III

Item 17. FINANCIAL STATEMENTS

Not applicable.

Item 18. FINANCIAL STATEMENTS

See pages F-1 through F-49 of this annual report.

Item 19. EXHIBITS

Exhibit No.	Description
1.1	Amended and Restated Articles of Association of the Registrant, as amended
1.2	Memorandum of Association of the Registrant(1)
2.1	Description of Securities
4.1	Amended and Restated Registration Rights Agreement by and among the Registrant and certain shareholders of the Registrant(2)
4.2	Information Rights Agreement by and between Clal Biotechnology Industries Ltd. and the Registrant(1)
4.3	Founders and Shareholders Agreement, dated January 2001, by and among Clal Biotechnology Industries Ltd., L.R. R & D Ltd., Professor Lior Rosenberg and the Registrant(3)
4.4	Patent Purchase Agreement, dated November 24, 2010, by and between the Registrant and L.R. R & D Ltd.(3)
4.5	Form of Indemnification Agreement(2)
4.6	Supply Agreement, dated January 11, 2001, as amended, by and between the Registrant and Challenge Bioproducts Corporation Ltd.†(3)
4.7	License Agreement, dated September 22, 2000, as amended, by and between the Registrant and Mark Klein†(3)
4.8	2003 Israeli Share Option Plan(3)
4.9	2014 Equity Incentive Plan(4)
4.10	MediWound Ltd.'s Compensation Policy for Executive Officers and Directors(5)
4.11.1	BARDA Contract, dated September 29, 2015, by and between the Registrant and the U.S. Biomedical Advanced Research and Development Authority†(6)
4.11.2	Modification to the BARDA Contract, dated October 7, 2015, by and between the Registrant and the U.S. Biomedical Advanced Research and Development Authority(7)
4.11.3	Modification to the BARDA Contract, dated January 29, 2017, by and between the Registrant and the U.S. Biomedical Advanced Research and Development Authority†(8)
4.11.4	Modification to the BARDA Contract, dated July 9, 2017, by and between the Registrant and the U.S. Biomedical Advanced Research and Development Authority(9)
4.11.5	Modification to the BARDA Contract, dated May 24, 2019, by and between the Registrant and the U.S. Biomedical Advanced Research and Development Authority(4)
4.11.6	Modification to the BARDA Contract, dated February 28, 2020, by and between the Registrant and the U.S. Biomedical Advanced Research and Development Authority(6)
4.11.7	Modification to the BARDA Contract, dated February 9, 2022, by and between the Registrant and the U.S. Biomedical Advanced Research and Development Authority†
4.13	BARDA Contract, dated September 30, 2018, by and between the Registrant and the U.S. Biomedical Advanced Research and Development Authority†(10)
4.14.1	Unprotected Sub-Lease Agreement, dated March 18, 2018, by and between the Registrant and Clal Life Sciences L.P. (unofficial English translation of Hebrew original) (11)
4.14.2	Addendum to Sub-Lease Agreement, dated March 18, 2018, by and between the Registrant and Clal Life Sciences L.P. (unofficial English translation of Hebrew original) (12)
4.15	Settlement Agreement and Mutual General Release, dated as of March 24, 2019, by and among Teva Pharmaceuticals Ltd. and MediWound Ltd. and Certain Indemnity in connection with Settlement Agreement dated as of March 24, 2019 by MediWound Ltd.(13)
4.16	Amendment No. 1 to Settlement Agreement and Mutual General Release as of December 13, 2020, by and among Teva Pharmaceuticals Ltd. and MediWound Ltd.(6)
4.17	License Agreement, dated as of May 6, 2019, by and between the Registrant and Vericel Corporation† (14)
4.18	Supply Agreement, dated as of May 6, 2019, by and between the Registrant and Vericel Corporation† (15)
8.1	List of subsidiaries of the Registrant(6)
12.1	Certificate of Chief Executive Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to §302 of the Sarbanes-Oxley Act of 2002
12.2	Certificate of Chief Financial Officer pursuant to Securities Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to §302 of the Sarbanes-Oxley Act of 2002
13.1	Certificate of Chief Executive Officer pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, furnished herewith
13.2	Certificate of Chief Financial Officer pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, furnished herewith

15.1	Consent of Somekh Chaikin, a member firm of KPMG International, an independent registered public accounting firm
15.2	Consent of Kost Forer Gabbay & Kasierer, a member firm of Ernst & Young Global, an independent registered public accounting firm
101.INS	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (the cover page iXBRL tags are embedded within the Inline XBRL document)

† Portions of this exhibit have been omitted pursuant to Instruction 4(a) to Exhibits to Form 20-F because they are both (i) not material and (ii) the type that the Registrant treats as private or confidential.

(1) Previously filed with the SEC on March 3, 2014 pursuant to the Registrant's registration statement on Form F-1 (File No. 333-193856) and incorporated by reference herein.

(2) Previously furnished to the SEC on May 5, 2021 as Appendix B to the Registrant's proxy statement for its 2021 annual general meeting of shareholders held on June 15, 2021, attached as Exhibit 99.1 to the Registrant's report of foreign private issuer on Form 6-K (File No. 001-36349) and incorporated by reference herein.

(3) Previously filed with the SEC on February 10, 2014 pursuant to the Registrant's registration statement on Form F-1 (File No. 333-193856) and incorporated by reference herein.

(4) Previously filed with the SEC on February 25, 2020 pursuant to the Registrant's annual report on Form 20-F for the year ended December 31, 2019 (File No. 001-36349) and incorporated by reference herein.

(5) Previously furnished to the SEC on August 14, 2019 as Appendix A to the Registrant's proxy statement for its extraordinary general meeting of shareholders held on September 23, 2019, attached as Exhibit 99.1 to the Registrant's report of foreign private issuer on Form 6-K (File No. 001-36349) and incorporated by reference herein.

(6) Previously filed with the SEC on February 25, 2021 pursuant to the Registrant's annual report on Form 20-F for the year ended December 31, 2020 (File No. 001-36349) and incorporated by reference herein.

(7) Previously filed with the SEC on January 25, 2016 as Exhibit 4.14 to the Registrant's annual report on Form 20-F for the year ended December 31, 2015 (File No. 001-36349) and incorporated by reference herein.

(8) Previously filed with the SEC on February 21, 2017 as Exhibit 4.15 to the Registrant's annual report on Form 20-F for the year ended December 31, 2016 (File No. 001-36349) and incorporated by reference herein.

(9) Previously filed with the SEC on March 19, 2018 as Exhibit 4.16 to the Registrant's annual report on Form 20-F for the year ended December 31, 2017 (File No. 001-36349) and incorporated by reference herein.

(10) Previously filed with the SEC on March 25, 2019 as Exhibit 4.17 to the Registrant's annual report on Form 20-F for the year ended December 31, 2018 (File No. 001-36349) and incorporated by reference herein.

(11) Previously filed with the SEC on March 19, 2018 as Exhibit 4.17 to the Registrant's annual report on Form 20-F for the year ended December 31, 2017 (File No. 001-36349) and incorporated by reference herein.

(12) Previously filed with the SEC on March 25, 2019 as Exhibit 4.20 to the Registrant's annual report on Form 20-F for the year ended December 31, 2018 (File No. 001-36349) and incorporated by reference herein.

(13) Previously filed with the SEC on March 25, 2019 as Exhibit 4.21 to the Registrant's annual report on Form 20-F for the year ended December 31, 2018 (File No. 001-36349) and incorporated by reference herein.

(14) Previously filed with the SEC by Vericel Corporation on August 6, 2019 as Exhibit 10.9 to its quarterly report on Form 10-Q for the quarter ended June 30, 2019 (File No. 001-35280) and incorporated by reference herein.

(15) Previously filed with the SEC by Vericel Corporation on August 6, 2019 as Exhibit 10.10 to its quarterly report on Form 10-Q for the quarter ended June 30, 2019 (File No. 001-35280) and incorporated by reference herein

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.

MediWound Ltd.

Date: March 17, 2022

By: /s/ Boaz Gur-Lavie
Boaz Gur-Lavie
Chief Financial Officer

CONSOLIDATED FINANCIAL STATEMENTS

DECEMBER 31, 2021

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Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors
MediWound Ltd.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated statement of financial position of MediWound Ltd. and its subsidiaries (hereinafter – "the Company") as of December 31, 2021, the related consolidated statements of profit or loss and other comprehensive income (loss), changes in shareholders' equity (deficit), and cash flows for the year then ended, and the related notes (collectively, "the consolidated financial statements").

In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021, and the results of its operations and its cash flows for the year then ended, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audit, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audit 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 audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audit provides a reasonable basis for our opinion.

Critical Audit Matter

Israeli Innovation Authority grant liability

As discussed in Notes 3e and 14 to the consolidated financial statements, in previous years the Company received grants from the Israeli Innovation Authority ("IIA") to finance its research and development efforts. These grants were recognized as a liability to the extent the Company expected to refund them through royalties on its revenues derived from sales of products or services developed in whole or in part using the grants. The amount of the liability is reexamined each period using the Company's updated future revenue forecasts discounted to their present value. Any changes in the IIA grant liability are recognized in profit or loss. The IIA grant liability was $8,105 thousand as of December 31, 2021.

We identified the evaluation of the subsequent period end measurement of the IIA grant liability as a critical audit matter. Specifically, a high degree of subjective auditor judgment was involved in evaluating certain significant assumptions used by the Company to develop its future revenue forecasts, including the likelihood and timing of achievement of regulatory approvals and potential market demand and market share for the Company's products, which were based on external market research. These significant assumptions were forward-looking and could be affected by future economic and market conditions.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design of certain internal controls related to the Company's process for measuring the IIA grant liability, including controls related to the determination of the above referenced significant assumptions used to develop future revenue forecasts. We compared the Company's assumption of the likelihood and timing for obtaining regulatory approvals for its products, based on the specific phases of their development, to relevant data in industry research reports. We evaluated the Company's assumption of potential market demand and market share by evaluating the relevance and reliability of the external market research upon which the Company based its future revenue forecasts. We performed sensitivity analyses over these significant assumptions to assess the impact of changes in the assumptions on the period end IIA grant liability.

/s/ Somekh Chaikin
Somekh Chaikin
Member Firm of KPMG International

We have served as the Company's auditor since 2021.
Haifa, Israel
March 17, 2022

Building a better working world

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and
Board of Directors of

MEDIWOUND LTD. AND ITS SUBSIDIARIES

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheet of MediWound Ltd and subsidiaries (the "Company") as of December 31, 2020, the related consolidated statements of comprehensive or loss, shareholders' equity and cash flows for each of the two years in the period ended December 31, 2020, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company’s financial statements 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 audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. Our audits included performing procedures to assess the risks of material misstatement of the 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 financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter 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 matter below, providing a separate opinion on the critical audit matter or on the account or disclosure to which it relates.

Israel Innovation Authority (IIA) grant liability

Description of the matter	As described in Notes 3 and 17b to the consolidated financial statements, the Company's research and development efforts have been financed in part through grants from the Israeli Innovation Authority ("IIA"). Grants received from the IIA are recognized as a liability if future economic benefits are expected from the research and development activity that will result in royalty-bearing sales. The Company undertook to pay royalties of 3% on the revenues derived from sales of products or services developed in whole or in part using IIA grants, up to the amount of total grants received, plus LIBOR interest. The liability to the IIA is measured at amortized cost using the effective interest method and amounted as of December 31, 2020 to $7,529 thousands. Auditing the Company's IIA liability involved a high degree of subjectivity as it is based on assumptions about future revenue forecasts, such as long-term demand for the Company's products and licenses and revenue growth rates. These significant assumptions are forward-looking and could be affected by future economic and market conditions.
How we addressed the matter in our audit	Our substantive audit procedures included, among others, evaluating the significant assumptions and operating data used by management. For example, we compared the significant assumptions and operating data used by management to historical trends, we performed look-back analyses by comparing the Company's historical financial forecasted revenues with the actual results and we agreed future revenues to approved budgets. In addition, we considered the phases of development of the Company's products and the Company's ability of obtaining regulatory approvals. We also tested the completeness and accuracy of the relevant data used in management's calculation, tested the mathematical accuracy of management's calculations and performed sensitivity analyses over significant assumptions used by management related to revenue growth rates.

/s/ KOST FORER GABBAY & KASIERER
KOST FORER GABBAY & KASIERER
A Member of Ernst & Young Global

Tel-Aviv, Israel
February 25, 2021

We have served as the Company's auditor since 2001 to 2020

Consolidated Statements of Financial Positions

U.S. dollars in thousands

	Note	As of December 31 2021	2020
Cash and cash equivalents	4	**11,046**	17,376
Restricted deposits	5	**-**	184
Short-term bank deposits	5	**-**	4,024
Trade receivables	6	**1,779**	2,767
Inventories	7	**1,200**	1,380
Other receivables	8, 25	**927**	462
Total current assets		**14,952**	26,193
Other receivables	9	**469**	-
Property, plant and equipment, net	10	**2,478**	2,630
Right-of-use assets, net	11	**1,548**	1,884
Intangible assets, net	12	**297**	363
Total non-current assets		**4,792**	4,877
Total assets		**19,744**	31,070
Current maturities of long-term liabilities		**2,408**	2,417
Trade payables and accrued expenses		**4,693**	2,992
Other payables	13, 25	**3,620**	2,857
Total current liabilities		**10,721**	8,266
Deferred revenues		**119**	1,234
Liabilities in respect of IIA grants	14, 17b	**7,885**	7,267
Liabilities in respect of purchase of shares	17c	**3,922**	4,998
Lease liabilities	11	**1,391**	1,741
Severance pay liability, net	16	**288**	292
Total non-current liabilities		**13,605**	15,532
Total liabilities		**24,326**	23,798
Shareholders' equity:	19		
Ordinary shares of NIS 0.01 par value:			
Authorized: 50,000,000 shares as of December 31, 2021 and December 31, 2020; Issued and Outstanding 27,272,818 shares as of December 31, 2021 and 27,236,752 shares as of December 31, 2020		**75**	75
Share premium		**143,869**	142,193
Foreign currency translation reserve		**(19)**	(40)
Accumulated deficit		**(148,507)**	(134,956)
Total equity (deficit)		**(4,582)**	7,272
Total liabilities and equity		**19,744**	31,070

The accompanying notes are an integral part of the consolidated financial statements.

Consolidated Statements of Profit or Loss and Other Comprehensive Income or Loss

U.S. dollars in thousands (except of share and per share data)

	Note	Year Ended December 31		
		2021	2020	2019
Revenues from sale of products		**9,613**	7,445	3,393
Revenues from development services		**12,372**	13,935	10,678
Revenues from license agreements		**1,778**	383	17,718
Total revenues	23a	**23,763**	21,763	31,789
Cost of revenues	23b	**14,992**	14,218	11,849
Gross profit		**8,771**	7,545	19,940
Research and development, net of participations	23c	**10,256**	7,698	4,969
Selling and marketing	23d	**3,388**	3,228	4,064
General and administrative	23e	**6,348**	5,459	5,242
Other expenses	23f	**-**	-	1,172
Total operating expenses		**19,992**	16,385	15,447
Operating profit (loss)		**(11,221)**	(8,840)	4,493
Financial income	23g	**11**	843	556
Financial expense	23g	**(2,314)**	(1,279)	(2,983)
Financing expenses, net		**(2,303)**	(436)	(2,427)
Profit (loss) before taxes on income		**(13,524)**	(9,276)	2,066
Taxes on income		**(27)**	-	-
Profit (loss) from continuing operations		**(13,551)**	(9,276)	2,066
Profit from discontinued operations	17c,22	**-**	80	2,889
Net profit (loss) for the year		**(13,551)**	(9,196)	4,955
Other comprehensive income (loss):				
Foreign currency translation adjustments		**21**	(23)	8
Total comprehensive income (loss)		**(13,530)**	(9,219)	4,963
Earning (loss) per share data	24			
Basic and diluted net profit (loss) per share from continuing operations		**(0.50)**	(0.34)	0.08
Basic and diluted net profit per share from discontinued operations		**-**	-	0.10
Total Basic and diluted net profit (loss) per share - USD		**(0.50)**	(0.34)	0.18
Number of shares used in calculating basic and diluted profit (loss) per share		**27,244,475**	27,209,878	27,178,839

The accompanying notes are an integral part of the consolidated financial statements.

Consolidated Statements of Changes in Shareholders' Equity (Deficit)

U.S. dollars in thousands

	Share capital	Share premium	Foreign currency translation reserve	Accumulated deficit	Total equity (deficit)
Balance as of January 1, 2021	**75**	**142,193**	**(40)**	**(134,956)**	**7,272**
Net loss	-	-	-	**(13,551)**	**(13,551)**
Other comprehensive income	-	-	**21**	-	**21**
Total comprehensive loss	-	-	**21**	**(13,551)**	**(13,530)**
Exercise of options	**(*)**	**3**	-	-	**3**
Share-based compensation	-	**1,673**	-	-	**1,673**
Balance as of December 31, 2021	**75**	**143,869**	**(19)**	**(148,507)**	**(4,582)**
Balance as of January 1, 2020	**75**	**140,871**	**(17)**	**(125,760)**	**15,169**
Net loss	-	-	-	(9,196)	(9,196)
Other comprehensive loss	-	-	(23)	-	(23)
Total comprehensive loss	-	-	(23)	(9,196)	(9,219)
Exercise of options	(*)	(*)	-	-	(*)
Share-based compensation	-	1,322	-	-	1,322
Balance as of December 31, 2020	**75**	**142,193**	**(40)**	**(134,956)**	**7,272**
Balance as of January 1, 2019	**75**	**139,637**	**(25)**	**(130,715)**	**8,972**
Net profit	-	-	-	4,955	4,955
Other comprehensive income	-	-	8	-	8
Total comprehensive income	-	-	8	4,955	4,963
Exercise of options	(*)	(*)	-	-	(*)
Share-based compensation	-	1,234	-	-	1,234
Balance as of December 31, 2019	**75**	**140,871**	**(17)**	**(125,760)**	**15,169**

* Represents an amount lower than $1.

The accompanying notes are an integral part of the consolidated financial statements.

Consolidated Statements of Cash Flows

U.S. dollars in thousands

	Year ended December 31,		
	2021	**2020**	**2019**
Cash flows from operating activities:			
Profit (loss) for the year	**(13,551)**	(9,196)	4,955
Adjustments to reconcile net profit (loss) to net cash provided by (used in) continuing operating activities:			
Adjustments to profit and loss items:			
Profit from discontinued operation	**-**	(80)	(2,889)
Depreciation and amortization	**1,238**	1,090	1,149
Share-based compensation	**1,673**	1,322	1,234
Revaluation of liabilities in respect of IIA grants	919	828	(392)
Revaluation of liabilities in respect of purchase of shares	**590**	(433)	1,690
Revaluation of lease liabilities	**188**	305	340
Increase (decrease) in severance pay liability, net	**13**	33	(105)
Net financing income	**(11)**	(297)	(434)
Un-realized foreign currency gain	**(137)**	(211)	(152)
	4,473	2,557	441
Changes in asset and liability items:			
Decrease (increase) in trade receivables	**929**	1,386	(3,553)
Decrease in inventories	**257**	141	67
Decrease (increase) in other receivables	**(763)**	(13)	6,376
Increase (decrease) in trade payables and accrued expenses	**1,723**	(1,096)	1,355
Increase (decrease) in other payables and deferred revenues	**(1,984)**	(479)	247
	162	(61)	4,492
Net cash provided by (used in) continuing operating activities	**(8,916)**	(6,700)	9,888
Net cash used in discontinued operating activities	**-**	(195)	(1,599)
Net cash provided by (used in) operating activities	**(8,916)**	(6,895)	8,289

The accompanying notes are an integral part of the consolidated financial statements.

Consolidated Statements of Cash Flows

U.S. dollars in thousands

	Year ended December 31,		
	2021	**2020**	**2019**
Cash flows from investing activities:			
Purchase of property and equipment	**(489)**	(923)	(792)
Interest received	**35**	274	184
Proceeds from (investments in) short term bank deposits, net	**4,002**	18,034	(5,050)
Net cash provided by (used in) continuing investing activities	**3,548**	17,385	(5,658)
Net cash used in discontinued investing activities	**-**	-	(1,239)
Net cash provided by (used in) investing activities	**3,548**	17,385	(6,897)
Cash flows from financing activities:			
Repayment of leases liabilities	**(693)**	(508)	(630)
Proceeds from exercise of options	**3**	(*)	(*)
Repayment of IIA grants, net	**(360)**	(121)	(376)
Net cash used in continuing financing activities	**(1,050)**	(629)	(1,006)
Exchange rate differences on cash and cash equivalent balances	**88**	273	140
Increase (decrease) in cash and cash equivalents from continuing activities	**(6,330)**	10,329	3,364
Decrease in cash and cash equivalents from discontinued activities	-	(195)	(2,838)
Balance of cash and cash equivalents at the beginning of the year	**17,376**	7,242	6,716
Balance of cash and cash equivalents at the end of the year	**11,046**	17,376	7,242
Supplement disclosure of Non-cash transactions:			
ROU asset, net recognized with corresponding lease liability	**155**	261	209
Exercise of RSU's	**147**	147	97

* Represents an amount lower than $1.

The accompanying notes are an integral part of the consolidated financial statements.

Note 1: General

a. Description of the Company and its operations:

MediWound Ltd. Was incorporated in Israel. The Company which is located in Yavne, Israel (The "Company" or "MediWound"), is biopharmaceutical company that develops, manufactures and commercializes novel, cost effective, bio-therapeutic solutions for tissue repair and regeneration. The Company's strategy leverages its breakthrough enzymatic technology platform into diversified portfolio of biotherapeutics across multiple indications to pioneer solutions for unmet medical needs. The Company's current portfolio is focused on next-generation bio-active therapies for burn and wound care and tissue repair.

The Company's first innovative biopharmaceutical product, NexoBrid, has received marketing authorization from the European Medicines Agency ("EMA") as well as the Israeli, Argentinean, South-Korean, Russian, Taiwanese, Ukrainian, United Arab Emirates, Chilean and Peruvian Ministries of Health, for removal of dead or damaged tissue, known as eschar, in adults with deep partial and full thickness thermal burns.

The Company sells NexoBrid in the European Union, United Kingdom, Norway, Switzerland and Israel through its commercial organizations while establishing additional local distribution channels to extend its outreach in the European Union. In other international markets the Company sells NexoBrid through local distributors which are also responsible for obtaining the local marketing authorization within the relevant territory. In the United States, the Company entered into exclusive license and supply agreements with Vericel Corporation ("Vericel") to commercialize NexoBrid in North America upon FDA's approval.

The Company's second investigational innovative product, EscharEx, a topical biological drug being developed for debridement of chronic and other hard-to-heal wounds, is currently under a U.S. phase 2 study and in January 2022, a positive topline results were announced from this study. Patient follow-up is ongoing and additional data, including secondary and exploratory endpoints as well as additional safety measurements, will allow further evaluation of clinical benefits, in the second quarter of 2022.

The third clinical-stage innovative product candidate, MW005, is a topical biological drug candidate for the treatment of non-melanoma skin cancers. A U.S. phase 1/2 study of MW005 for the treatment of low-risk basal cell carcinoma (BCC) was initiated in July 2021, and an investigator-initiated phase II trial of MW005 in non-melanoma skin cancer is being conducted in parallel in Israel.

b. The Company's securities are listed for trading on NASDAQ since March 2014. In March, 2022, the Company completed a follow-on public offering. A total of 5,208,333 new ordinary shares were issued at a public offering price of $1.92 per share . The gross proceeds before deducting underwriting discounts and commissions and offering expenses, were approximately $10 million. (see also Note 26).

c. The Company has three wholly owned subsidiaries: MediWound Germany GmbH, acting as Europe ("EU") marketing authorization holder and EU sales and marketing arm, MediWound UK Limited and MediWound US, Inc. are currently inactive companies.

Note 1: General (Cont.)

The Company awarded two contracts with the U.S. Biomedical Advanced Research and Development Authority ("BARDA") valued at up to $168,000 for the advancement of the development, manufacturing and emergency readiness for NexoBrid deployment as well as the procurement of NexoBrid as a medical countermeasure as part of BARDA preparedness for mass casualty events. In February 2022 BARDA has expanded its awarded contract providing supplemental funding of approxemently $9,000 to support the NexoBrid BLA resubmission to the FDA and the continuous expanded access program.

d. On June 29, 2021, the Company received a Complete Response Letter (CRL) from the U.S. Food and Drug Administration (FDA) regarding its Biologics License Application (BLA) seeking approval of NexoBrid for eschar removal (debridement) in adults with deep partial-thickness and/or full-thickness thermal burns.

The FDA communicated that it had completed its review of the BLA, as amended, and has determined that the application cannot be approved in its present form. The FDA identified issues related to the Chemistry, Manufacturing and Controls (“CMC”) section of the BLA and requested additional CMC information. The FDA acknowledged receipt of several CMC amendments, submitted by the Company in response to the CMC information requests, which were not reviewed yet by the FDA.

The FDA also stated that an inspection of NexoBrid's manufacturing facilities in Israel and Taiwan, are required before the FDA can approve the BLA, but it was unable to conduct the required inspections during the current review cycle due to COVID-19 related travel restrictions. The FDA stated that it will continue to monitor the public health situation as well as travel restrictions and is actively working to define an approach for scheduling outstanding inspections. In addition, the CRL cited certain observations identified during good clinical practice (GCP) inspections related to the U.S. Phase 3 study (DETECT), and requested the Company to provide its perspective on the potential impact, if any, of these observations on the efficacy findings in the study. The FDA also requested to provide a safety update as part of its BLA resubmission, although there were no safety issues raised in the CRL.

Following a productive Type A meeting with the FDA, the Company gained clarity on a path forward for resubmission of its NexoBrid BLA, which is anticipated in mid-2022. In addition, the FDA’s facility inspection schedule which has been affected by COVID-19-related travel restrictions, is required before the FDA can approve the NexoBrid BLA.

Consequently, the Company expects the timing of the potential approval of NexoBrid to be impacted.

e. The Company addressed the challenges associated with the ongoing COVID-19 pandemic during the year ended 2020 and 2021, while prioritizing the health and safety of its workforce and maintaining operational efficiency and flexibility.

Note 2: Basis of Preparation of the Consolidated Financial Statements

a. Statement of compliance with International Financial Reporting Standards

These financial statements have been prepared in accordance with International Financial Reporting Standards ("IFRS") as issued by the International Accounting Standards Board ("IASB").

These consolidated financial statements were approved by the board of directors on March 17, 2022.

b. Functional currency, reporting currency and foreign currency:

1. Functional currency and reporting currency:

The reporting currency of the financial statements is the U.S. dollar.

The Company determines the functional currency based on the currency in which it primarily generates and expends cash. The Company determined that its functional currency is the U.S. dollar since most of the Company's expenses are in U.S. dollars and the economic environment in which the Company operates in and performs its transactions is mostly affected by the U.S dollar. A certain portion of the Company's costs are denominated in NIS mainly due to payroll and related benefit costs incurred in Israel. To further support the Company's determination, the Company has analyzed the currency in which funds from financing activities are generated or held and the currency in which receipts from operating activities are usually retained. In this respect, funds from financing activities were principally derived from significant funds raising in U.S. dollars and U.S governmental funds.

The Company operates and plans its activities in U.S. dollars and accordingly its periodic budgets and internal management reports are prepared and monitored using the U.S. dollar as the primary currency and provides the basis for the determination of share-based compensation.

The functional currency of the Company's subsidiary in Germany has been determined to be its local currency - the EURO. Assets and liabilities of this subsidiary are translated at year end exchange rates and its statement of operations items are translated using the averegae exchange rates at the quarter of which those items are recognized. Such translation adjustments are recorded as a separate component of accumulated other comprehensive income (loss) in shareholders' equity (deficit).

2. Transactions, assets and liabilities in foreign currency:

Transactions denominated in foreign currency are recorded upon initial recognition at the exchange rate on the date of the transaction. After initial recognition, monetary assets and liabilities denominated in foreign currency are translated at the end of each reporting period into the functional currency at the exchange rate at that date.

Exchange differences are recognized in profit or loss.

Note 2: Basis of Preparation of the Consolidated Financial Statements (Cont.)

c. Use of estimates and judgments

The preparation of the financial statements requires management to make estimates and assumptions that have an effect on the application of the accounting policies and on the reported amounts of assets, liabilities and expenses.

Discussed below are the key assumptions made in the financial statements concerning uncertainties at the end of the reporting period and the critical estimates computed by the Company that may result in a material adjustment to the carrying amounts of assets and liabilities within the next financial year.

- Determining the fair value of share based compensation to employees and directors:

  The fair value of share based compensation to employees and directors is determined using the binomial option pricing models.The assumptions used in the models include the expected volatility, early exercise factor, expected dividend and risk-free interest rate.

- Liabilities in respect to IIA grants:

  Government grants received from the IIA are recognized as a liability if future economic benefits are expected from the research and development activity that will result in royalty-bearing sales. As the contingent liability is calculated based on future royalty-bearing sales, there is uncertainty regarding the estimated future cash flows and the estimated discount rate used to measure the amortized cost of the liability.

Note 3: Significant Accounting Policies

The accounting policies set out below have been consistently applied for all periods presented in these consolidated financial statements:

a. Basis of consolidation:

Consolidated financial statements include the financial statements of companies that the Company controls (subsidiaries). Control is achieved when the Company is exposed, or has rights, to variable returns from its investment with the investee and has the ability to affect those returns through its power over the investee.

The financial statements of the Company and its subsidiaries are prepared as of the same dates and periods. The consolidated financial statements are prepared using uniform accounting policies by all entities in the Group. Significant intercompany balances and transactions and gains or losses resulting from intercompany transactions are eliminated in full in the consolidated financial statements.

b. Cash equivalents:

Cash equivalents are considered as highly liquid investments, including unrestricted short-term bank deposits with an original maturity of three months or less from the date of deposit.

Note 3: Significant Accounting Policies (Cont.)

c. Short-term bank deposits:

Short-term bank deposits have a maturity of more than three months, but less than one year, from the deposit date.

d. Inventories:

Inventories are measured at the lower of cost and net realizable value. Net realizable value is the estimated selling price in the ordinary course of business less the estimated costs of completion and the estimated selling costs. The Company periodically evaluates the condition and age of inventories and makes provisions for slow moving inventories accordingly.

Cost of inventories is determined as follows:

Raw materials	-	At cost of purchase using the first-in, first-out method.
Finished goods	-	On the basis of average standard costs (which approximates actual cost on a weighted average basis) including materials, labor and other direct and indirect manufacturing costs based on practical capacity.

e. Liability in respect of Israeli Innovation Authority ("IIA"):

Grants from the IIA in respect of research and development projects are accounted for as forgivable loans according to IAS 20. Grants received from the IIA are recognized as a liability according to their fair value on the date of their receipt, unless on that date it is reasonably certain that the amount received will not be refunded. If future economic benefits are expected from the project that will result in royalty-bearing revenues from sale of products it will be treated as a contingent liability.

At the end of each reporting period, the Company evaluates whether there is reasonable assurance that the liability recognized, in whole or in part, will not be repaid based on its best estimate of future sales and any changes in the present value of the cash flows discounted at the original interest rate of the grant are recognized in profit or loss. The difference between the amount received and the fair value on the date of receiving the grant is recognized as a deduction of research and development expenses.

Note 3: Significant Accounting Policies (Cont.)

f. Leases:

The Company accounts for a contract as a lease when the contract terms convey the right to control the use of an identified asset for a period of time in exchange for consideration.

For leases in which the Company is the lessee, the Company recognizes on the commencement date of the lease a right-of-use ("ROU") asset and a lease liability, excluding leases whose term is up to 12 months and leases for which the underlying asset is of low value. For these excluded leases, the Company has elected to recognize the lease payments as an expense in profit or loss on a straight-line basis over the lease term. In measuring the lease liability, the Company has elected to apply the practical expedient in the Standard and does not separate the lease components from the non-lease components (such as management and maintenance services, etc.) included in a single contract.

Following are the amortization periods of the ROU assets by class of underlying asset:

	Years
Motor vehicles	3
Buildings and equipment	5-8

The Company tests for impairment of the ROU asset whenever there are indications of impairment pursuant to the provisions of IAS 36.

- Variable lease payments that depend on an index:

  On the commencement date, the Company uses the index rate prevailing on the commencement date to calculate the future lease payments.

  For leases in which the Company is the lessee, the aggregate changes in future lease payments resulting from a change in the index are discounted (without a change in the discount rate applicable to the lease liability) and recorded as an adjustment of the lease liability and the ROU assets, only when there is a change in the cash flows resulting from the change in the index (that is, when the adjustment to the lease payments takes effect).

- Lease extension and termination options:

  A non-cancelable lease term includes both the periods covered by an option to extend the lease when it is reasonably certain that the extension option will be exercised and the periods covered by a lease termination option when it is reasonably certain that the termination option will not be exercised.

  In the event of any change in the expected exercise of the lease extension option or in the expected non-exercise of the lease termination option, the Company remeasures the lease liability based on the revised lease term using a revised discount rate as of the date of the change in expectations. The total change is recognized in the carrying amount of the ROU asset until it is reduced to zero, and any further reductions are recognized in profit or loss.

Note 3: Significant Accounting Policies (Cont.)

- Lease modifications:

  If a lease modification does not reduce the scope of the lease and does not result in a separate lease, the Company remeasures the lease liability based on the modified lease terms using a revised discount rate as of the modification date and records the change in the lease liability as an adjustment to the ROU asset.

  If a lease modification reduces the scope of the lease, the Company recognizes a gain or loss arising from the partial or full reduction of the carrying amount of the ROU asset and the lease liability. The Company subsequently remeasures the carrying amount of the lease liability according to the revised lease terms, at the revised discount rate as of the modification date and records the change in the lease liability as an adjustment to the ROU asset.

Operating leases:

Leases in which substantially all the risks and rewards of ownership of the leased asset are not transferred to the Group are classified as operating leases. Lease payments are recognized as an expense in profit or loss on a straight-line basis over the lease term.

g. Property, plant and equipment, net:

Property, plant and equipment are measured at cost, including directly attributable costs, less accumulated depreciation, accumulated impairment losses and excluding day-to-day servicing expenses. Cost includes spare parts and auxiliary equipment that are used in connection with the plant and equipment.

Depreciation is calculated on a straight-line basis over the useful life of the assets at annual rates as follows:

	%
Office furniture	6-15
Manufacturing machinery and lab equipment	15-33
Computers	33
Leasehold improvements	See below

Leasehold improvements are depreciated on a straight-line basis over the shorter of the lease term (including the renewal option held by the Company which is expected to be exercised) and the expected life of the improvement.

The useful life, depreciation method and residual value of an asset are reviewed at least each year-end and any changes are accounted for prospectively as a change in accounting estimate.

h. Intangible assets, net:

Separately acquired intangible assets with finite useful life are measured on initial recognition at cost.

Note 3: Significant Accounting Policies (Cont.)

Intangible assets are amortized over their useful life using the straight-line method beginning in the period in which the intangible assets generates net cash inflows to the Company. The useful life is over the length of the patent or knowledge life. The intangible assets are reviewed for impairment at each reporting date until they begin generating net cash inflows and subsequently whenever there is an indication that the asset may be impaired.

i. Revenues recognition:

The Company recognizes revenue when the customer obtains control over the promised goods or services. The revenue is measured according to the amount of the consideration to which the Company expects to be entitled in exchange for the goods or services promised to the customer, other than amounts collected for third parties.

To determine revenue recognition for arrangements the Company evaluates the following criteria's, which are within the scope of IFRS 15, it performs the following five steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations within the contract and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when it determines that it is probable it will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer.

Performance obligations are promises commitments in a contract to transfer a distinct good or service to the customer that (i) the customer can benefit from on its own or together with other readily available resources, and (ii) is separately identifiable from other promises commitments in the contract. Goods or services that are not individually distinct performance obligations are combined with other promised commitment goods or services until such combined group of promises commitments meet the requirements of a performance obligation.

The Company determines transaction price based on the amount of consideration the Company expects to receive for transferring the promised goods or services in the contract.

Consideration may be fixed, variable, or a combination of both. At contract inception for arrangements that include variable consideration, the Company estimates the probability and extent of consideration it expects to receive under the contract utilizing either the most likely amount method or expected amount method, whichever best estimates the amount expected to be received. The Company then considers any constraints on the variable consideration and includes in the transaction price variable consideration to the extent it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. The Company then allocates the transaction price to each performance obligation based on the relative standalone selling price and recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) control is transferred to the customer and the performance obligation is satisfied.

Note 3: Significant Accounting Policies (Cont.)

The Company records amounts as accounts receivable when the right to consideration is deemed unconditional. Amounts received, or that are unconditionally due, from a customer prior to transferring goods or services to the customer under the terms of a contract are recognized as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as the current portion of deferred revenue. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

The Company's revenue generating arrangements typically include licensing arrangements, which comprise of upfront license fees, milestone payments and/or royalties and products sale arrangements.

The promised goods or services in the Company's licensing arrangements typically consist of a license to the Company's intellectual property and/or research and development services. The Company may provide customers with options to additional items in such arrangements, which are accounted for separately when the customer elects to exercise such options, unless the option provides a material right to the customer.

If a license is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from nonrefundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For performance obligations which consist of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, where the license is deemed to be the predominant item to which the royalties relate, the Company will recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

In 2019, the Company entered into exclusive license and supply agreements with Vericel to commercialize NexoBrid in North America (the "Collaboration Agreements") (see Note 19b). The Collaboration Agreements have multiple performance obligations, due to the contract covering multiple phases of the product lifecycle. Under the Vericel license and supply agreements, the Company identified three distinct performance obligations: (1) license rights (2) development services for BLA approval and (3) manufacturing and supply of NexoBrid.

Note 3: Significant Accounting Policies (Cont.)

The Company allocated the Collaboration Agreements transaction price to each performance obligation using the best estimate of the standalone selling price of each distinct good or service in the contract.

The Company determined the license to the Intellectual Property ("IP") to be a right to use the IP, which has significant standalone functionality. Since Vericel has sublicensing rights, effective control over the development strategy in the Territory and is also entitled to generate revenues from BARDA procurement prior to BLA approval, the license is a distinct performance obligation and as such revenues are recognized at the point in time that control of the license is transferred to the customer. Since the manufacturing and development services are at market value, then the upfront payment was fully attributed to the license performance obligation. Future milestone payments are considered variable consideration and are subject to the variable consideration constraint (i.e. will be recognized once concluded that it is “probable” that a significant reversal of the cumulative revenues recognized under the contract will not occur in future periods when the uncertainty related to the variable considerations are resolved). Therefore, as the milestone payments are not probable, revenues were not recognized in respect to such milestone payments.

As royalties under this agreement are payable based on future commercial sales, which did not occur as of the financial statements date, the Company did not recognize any revenues from royalties.

Revenues from the sale of products to Vericel will be recognized when all the significant risks and rewards of ownership of the products have passed to the buyer and the seller no longer retains continuing managerial involvement. The delivery date of the products is usually the date of which ownership passes.

Revenues from distribution licensing arrangements:

The Company accounts for the bundled license provided to the distributers and related high specialized services as a single performance obligation and consequently recognize revenue using the cost-to-cost method, where the extent of progress towards completion is measured based on the ratio of actual costs incurred to the total estimated costs expected to be incurred upon satisfying such single performance obligation. The revenues from such bundled performance obligation are included within “Revenues from license agreements”. Significant finance components related to such arrangements are recognized as finance expense.

Revenues from development services:

Revenues from development services are recognized over time, during the period the customer receives and consumes the benefits provided by the Company's performance (see Note 3k).

Note 3: Significant Accounting Policies (Cont.)

Revenues from the sale of products:

The Company generates revenues from sales of its innovative biopharmaceutical product, NexoBrid, to burn centers and hospital burn units in Europe, U.S Israel and local distributors in international markets.

Revenues from sale of goods is recognized in profit or loss at the point in time when the control of the goods is transferred to the customer, generally upon delivery of the goods to the customer. The transaction price is the amount of the consideration that is expected to be received based on the contract terms, excluding amounts collected on behalf of third parties (such as taxes).

j. Research and development expenses:

Research and development expenses are recognized in profit or loss when incurred. An intangible asset arising from a development project or from the development phase of an internal project is recognized if the Company can demonstrate the technical feasibility of completing the intangible asset so that it will be available for use or sale; the Company's intention to complete the intangible asset and use or sell it; the Company's ability to use or sell the intangible asset; how the intangible asset will generate future economic benefits; the availability of adequate technical, financial and other resources to complete the intangible asset; and the Company's ability to measure reliably the expenditure attributable to the intangible asset during its development. Since the Company's research and development projects are often subject to regulatory approval procedures and other uncertainties, the conditions for the capitalization of costs incurred before receipt of approvals are not normally satisfied and, therefore, research and development expenses are recognized in profit or loss when incurred.

k. Funding by BARDA:

Non-royalty bearing funds from BARDA for funding research and development projects were recognized at the time the Company was entitled to such grants on the basis of the related costs incurred.

The participation by BARDA was classified as reimbursement (deduction) of research and development expenses. Starting May 2019, following entrance into the Vericel license and supply agreements, in which Vericel has assumed the effective control over the BARDA contracts, funding by BARDA was classified as Revenues from development services.

l. Impairment of non-financial assets:

The Company evaluates the need to record an impairment of the carrying amount of non-financial assets whenever events or changes in circumstances indicate that the carrying amount is not recoverable. If the carrying amount of non-financial assets exceeds their recoverable amount, the assets are reduced to their recoverable amount. The recoverable amount of an asset that does not generate independent cash flows is determined for the cash-generating unit to which the asset belongs, and is calculated based on the projected cash flows that will be generated by the cash generating unit.

Note 3: Significant Accounting Policies (Cont.)

An impairment loss of an asset, is reversed only if there have been changes in the estimates used to determine the asset's recoverable amount since the last impairment loss was recognized. Reversal of an impairment loss, as above, may not increase the value above the lower of (i) the carrying amount that would have been determined (net of depreciation or amortization) had no impairment loss been recognized for the asset in prior years, and (ii) its recoverable amount.

m. Financial instruments:

The accounting policy for financial instruments in accordance with IFRS 9, "Financial Instruments" ("the Standard") is as follows:

1. Financial assets:

Financial assets are measured upon initial recognition at fair value plus transaction costs that are directly attributable to the acquisition of the financial assets, except for financial assets measured at fair value through profit or loss in respect of which transaction costs are recorded in profit or loss.

The Company classifies and measures debt instruments in the financial statements based on the following criteria:

- The Company's business model for managing financial assets; and
- The contractual cash flow terms of the financial asset.

Impairment of financial assets:

The Company evaluates at the end of each reporting period the loss allowance for financial debt instruments which are not measured at fair value through profit or loss.

The Company has short-term financial assets such as trade receivables in respect of which the Company applies a simplified approach and measures the loss allowance in an amount equal to the lifetime expected credit losses.

An impairment loss on debt instruments measured at amortized cost is recognized in profit or loss with a corresponding loss allowance that is offset from the carrying amount of the financial asset.

2. Financial liabilities:

a) Financial liabilities measured at amortized cost:

Financial liabilities are initially recognized at fair value less transaction costs that are directly attributable to the issue of the financial liability.

Note 3: Significant Accounting Policies (Cont.)

After initial recognition, the accounting treatment of financial liabilities is based on their classification as follows:

After initial recognition, the Company measures all financial liabilities at amortized cost using the effective interest rate method, except for Financial liabilities at fair value through profit or loss such as derivatives;

b) Financial liabilities measured at fair value through profit or loss:

At initial recognition, the Company measures financial liabilities that are not measured at amortized cost at fair value. Transaction costs are recognized in profit or loss.

After initial recognition, changes in fair value are recognized in profit or loss.

3. Fair value:

Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date.

Fair value measurement is based on the assumption that the transaction will take place in the asset's or the liability's principal market, or in the absence of a principal market, in the most advantageous market.

The fair value of an asset or a liability is measured using the assumptions that market participants would use when pricing the asset or liability, assuming that market participants act in their economic best interest.

A fair value measurement of a non-financial asset takes into account a market participant's ability to generate economic benefits by using the asset in its highest and best use or by selling it to another market participant that would use the asset in its highest and best use.

The Company uses valuation techniques that are appropriate in the circumstances and for which sufficient data are available to measure fair value, maximizing the use of relevant observable inputs and minimizing the use of unobservable inputs.

Note 3: Significant Accounting Policies (Cont.)

4. Classification of financial instruments by fair value hierarchy:

All assets and liabilities for which fair value is measured or disclosed in the financial statements are categorized within the fair value hierarchy, described as follows, based on the lowest level input that is significant to the fair value measurement as a whole:

Level 1	-	quoted prices (unadjusted) in active markets for identical assets or liabilities.
Level 2	-	inputs other than quoted prices included within level 1 that are observable either directly or indirectly.
Level 3	-	inputs that are not based on observable market data (valuation techniques which use inputs that are not based on observable market data).

5. Offsetting financial instruments:

Financial assets and financial liabilities are offset and the net amount is reported in the consolidated statement of financial position if there is a currently enforceable legal right to offset the recognised amounts and there is an intention to settle on a net basis, to realise the assets and settle the liabilities simultaneously.

n. Provisions:

A provision in accordance with IAS 37 is recognized when the Company has a present (legal or constructive) obligation as a result of a past event, it is expected to require the use of economic resources to clear the obligation and a reliable estimate has been made.

o. Short-term employee benefits and severance pay liability, net:

The Company has several employee benefit plans:

1. Short-term employee benefits:

Short-term employee benefits include salaries, paid annual leave, paid sick leave, recreation and social security contributions and are recognized as expenses as the services are rendered. A liability in respect of a cash bonus is recognized when the Company has a legal or constructive obligation to make such payment as a result of past service rendered by an employee and a reliable estimate of the amount can be made.

2. Post-employment benefits:

The Company has liabilities for severance pay for its employees in several of jurisdictions and in Israel.

Post-employment benefit plans in Israel are normally financed by contributions to insurance companies and classified as defined contribution plans or as defined benefit plans. The Company has defined contribution plans for Israeli employees pursuant to the Severance Pay Law into which the Company pays fixed contributions and has no legal or constructive obligation to pay further contributions on account of severance pay if the fund does not hold sufficient amounts to pay all employee benefits relating to employee service in current and prior periods.

Note 3: Significant Accounting Policies (Cont.)

The Company recognizes liability for severance pay due to its employees in EU in accordancewith local laws.

p. Share-based compensation:

Certain Company employees and directors are entitled to remuneration in the form of equity-settled share-based compensation.

Equity-settled transactions

The cost of equity-settled transactions with employees is measured at the fair value of their equity instruments granted at grant date. The fair value is determined using the binomial option pricing model.

The cost of equity-settled transactions is recognized in profit or loss, together with a corresponding increase in equity, during the period which the performance or service conditions are to be satisfied, ending on the date on which the relevant employees become fully entitled to the award.

q. Discontinued operation:

A discontinued operation is a component of the Company that either has been disposed of or is classified as held for sale. Disposal group to be abandoned meets the criteria for being a discontinued operation at the date of which it ceases to be used. The operating results relating to the discontinued operation are separately presented in the consolidated statements of comprehensive income or loss.

r. Profit / Loss per share:

Profit/loss per share is calculated by dividing the profit/loss attributable to Company shareholders by the weighted average number of outstanding ordinary shares during the period. Potential ordinary shares are only included when their conversion decreases income per share or increases loss per share from continuing operation.

Furthermore, potential ordinary shares converted during the period are included in diluted loss per share only until the conversion date and from that date in basic loss per share.

s. Reclassification

Certain amounts previously reported in the consolidated financial statements have been reclassified to conform to current year presentation. Such reclassifications did not affect net loss, Changes in Stockholders' Equity or cash flows.

U.S. dollars in thousands (except of share and per share data)

Note 4: Cash and Cash Equivalents

	December 31	
	2021	**2020**
Balance in USD	**7,735**	13,067
Balance in other currencies	**3,311**	4,309
	11,046	17,376

Note 5: Short-Term Bank Deposits

	December 31,	
	2021	**2020**
USD bank deposits (1)	**-**	4,024
Restricted bank deposits (2)	**-**	184
	-	4,208

(1) The USD deposits bear annual interest of 1.12% for the period of 282 days for 2020.

(2) Restricted bank deposits which are primarily used as security for the Company's office leases.

Note 6: Trade Receivables

	December 31	
	2021	**2020**
BARDA (see also Note 18a)	**1,085**	2,189
Other trade receivables	**696**	578
Less provision for impairment	**(2)**	-
	694	578
	1,779	2,767

Note 7: Inventories

	December 31,	
	2021	**2020**
Raw materials	**694**	631
Finished goods	**506**	749
	1,200	1,380

Note 8: Other Receivables- Short Term

	December 31,	
	2021	**2020**
Government authorities	**141**	73
Contract asset related to BARDA	**347**	-
Prepaid expenses and other	**439**	389
	927	462

U.S. dollars in thousands (except of share and per share data)

Note 9: Other Receivables- Long Term

	December 31,	
	2021	2020
Income receivables	280	-
Restricted bank deposits (1)	189	-
	469	-

(1) Restricted bank deposits which are primarily used as security for the Company's office leases.

Note 10: Property, Plant And Equipment, Net

	Office furniture	Manufacturing machinery and lab equipment	Computers	Leasehold improvements	Total
Cost					
Balance as of January 1, 2021	**332**	**4,775**	**169**	**2,904**	**8,180**
Additions	**18**	**193**	**45**	**233**	**489**
Disposals	**(89)**	**(205)**	**(36)**	**-**	**(330)**
Foreign currency translation	**(4)**	**1**	**(2)**	**-**	**(5)**
Balance as of December 31, 2021	**257**	**4,764**	**176**	**3,137**	**8,334**
Balance as of January 1, 2020	301	4,534	124	2,315	7,274
Additions	20	241	73	445	779
Disposals	-	-	(29)	-	(29)
Re-classified from RSU assets	-	-	-	144	144
Foreign currency translation	11	-	1	-	12
Balance as of December 31, 2020	332	4,775	169	2,904	8,180
Accumulated Depreciation					
Balance as of January 1, 2021	**204**	**3,092**	**76**	**2,178**	**5,550**
Additions	**22**	**483**	**55**	**81**	**641**
Disposals	**(89)**	**(204)**	**(35)**	**-**	**(328)**
Foreign currency translation	**(4)**	**(1)**	**(2)**	**-**	**(7)**
Balance as of December 31, 2021	**133**	**3,370**	**94**	**2,259**	**5,856**
Balance as of January 1, 2020	175	2,606	60	2,129	4,970
Additions	18	486	44	49	597
Disposals	-	-	(29)	-	(29)
Foreign currency translation	11	-	1	-	12
Balance as of December 31, 2020	204	3,092	76	2,178	5,550
Carrying amounts of all fixed asset items					
December 31, 2021	**124**	**1,394**	**82**	**878**	**2,478**
December 31, 2020	128	1,683	93	726	2,630

U.S. dollars in thousands (except of share and per share data)

Note 11: Leases

a. Lease Agreements:

The Company's offices and its production facility in Israel are located in a building that the Company leases from its Parent Company (see Note 25a), in accordance with a sub-lease agreement. The Company subleases approximately 3,000 square meters of laboratory, office and clean room space at a monthly rent fee of NIS 119 (approximately $38) and NIS 125 starting November 2022 (approximately $40). This sub-lease agreement was amended on October 2021, to extand the priod up to October 2025 which was included in the calculation of the lease liability and RoU asset.

In addition the Company and its subsidiary have lease agreements for 13 vehicles for a period of three years.

b. Amounts recognized in profit or loss and in the statement of cash flows

	Year ended December 31,	
	2021	**2020**
Interest expense on lease liabilities	**120**	144
Depreciation expenses relating to short-term leases	**531**	427
Cash outflow for leases (1)	**693**	652

(1) For the year ended December 31,2020 the cash flow for leases includes $144 which were capitalized to Leasehold improvements.

The Company was assisted by external third party valuation expert in determining the appropriate interest rate for discounting its leases based on: credit risk, the weighted average term of the leases and other economic variables. A weighted average incremental borrowing in a range of 1% to 6.7% was used to discount future lease payments in the calculation of the lease liability on the date of initial application of the standard (IFRS 16).

U.S. dollars in thousands (except of share and per share data)

Note 11: Leases (Cont.)

c. Disclosures in respect of Right- of- Use assets:

	Buildings	Motor vehicles	Total
Cost			
Balance as of January 1, 2021	**2,225**	**512**	**2,737**
New leases	**-**	**162**	**162**
Adjustments for indexation	**42**	**7**	**49**
Disposals	**-**	**(27)**	**(27)**
Balance as of December 31, 2021	**2,267**	**654**	**2,921**
Accumulated depreciation			
Balance as of January 1, 2021	**698**	**155**	**853**
Depreciation and amortization	**330**	**201**	**531**
Disposals	**-**	**(11)**	**(11)**
Balance as of December 31, 2021	**1,028**	**345**	**1,373**
Depreciated cost			
Balance as of December 31, 2021	**1,239**	**309**	**1,548**

	Buildings	Motor vehicles	Total
Cost			
Balance as of January 1, 2020	2,362	442	2,804
New leases	-	305	305
Adjustments for indexation	(17)	(18)	(35)
Disposals	(76)	(217)	(293)
Termination of leases	(44)	-	(44)
Balance as of December 31, 2020	2,225	512	2,737
Accumulated depreciation			
Balance as of January 1, 2020	381	194	575
Depreciation and amortization	249	178	427
Capitalized to Leasehold improvements (1)	144	-	144
Disposals	(76)	(217)	(293)
Balance as of December 31, 2020	698	155	853
Depreciated cost			
Balance as of December 31, 2020	1,527	357	1,884

(1) As of the year ended December 31,2020 the cash flow for leases includes $144 which were capitalized to Leasehold improvements.

U.S. dollars in thousands (except of share and per share data)

Note 11: Leases (Cont.)

d. Disclosures of the Company's lease liabilities :

	Buildings	Motor vehicles	Total
Balance as of January 1, 2021	**1,953**	**354**	**2,307**
Repayment of leases liabilities	**(477)**	**(216)**	**(693)**
Effect of changes in exchange rates	**55**	**13**	**68**
New finance lease obligation recognized	-	**155**	**155**
Adjustments for indexation	**42**	**7**	**49**
Interest	**118**	**2**	**120**
Disposals-Termination of leases	-	**(16)**	**(16)**
Balance as of December 31, 2021	**1,691**	**299**	**1,990**
Current maturities of long-term leases	**(403)**	**(196)**	**(599)**
Lease liability Balance as of December 31, 2021	**1,288**	**103**	**1,391**

	Buildings	Motor vehicles	Total
Balance as of January 1, 2020	2,225	225	2,450
Repayment of leases liabilities	(479)	(173)	(652)
Effect of changes in exchange rates	134	28	162
New finance lease obligation recognized	-	283	283
Adjustments for indexation	(17)	(18)	(35)
Interest	134	10	144
Disposals-Termination of leases	(44)	(1)	(45)
Balance as of December 31, 2020	1,953	354	2,307
Current maturities of long-term leases	(396)	(170)	(566)
Lease liability Balance as of December 31, 2020	1,557	184	1,741

U.S. dollars in thousands (except of share and per share data)

Note 12: Intangible Assets, Net

	License and Knowhow	
	2021	2020
Cost		
Balance as of January 1,	**1,538**	1,538
Additions	**-**	-
Balance as of December 31,	**1,538**	1,538
Accumulated Amortization		
Balance as of January 1,	**1,175**	1,109
Additions	**66**	66
Balance as of December 31,	**1,241**	1,175
Amortized cost		
Balance as of December 31,	**297**	363

Intangible assets include exclusive licenses to use patents, know-how and intellectual property for the development, manufacturing and marketing of products related to burn treatments and other products in the field of wound care. These licenses were purchased from third parties and from one of the Company's shareholders.

Note 13: Other Payables

	December 31	
	2021	2020
Employees and payroll accruals	**1,639**	1,910
Liability in respect of purchase of shares (see Note 17c)*	**417**	-
Related parties	**241**	225
Deferred revenues	**543**	462
Other	**780**	260
	3,620	2,857

- An amount of $667 was classified from Liability in respect of purchase of shares to current maturities for the year ended 31, December 2020.

Note 14: Liabilities in Respect of IIA Grants

	December 31	
	2021	2020
Balance as of January 1,	**7,528**	6,935
Royalties	**(342)**	(235)
Amounts carried to Profit or Loss	**919**	828
Balance as of December 31,	**8,105**	7,528
Current maturities	**(220)**	(261)
Long term liabilities in respect of IIA grants	**7,885**	7,267

The Company is committed to pay royalties to the IIA up to the total grants received plus the applicable accrued interest. The total amount of grants received from IIA including accrued LIBOR interest, net of royalties as of December 31, 2021 is approximately $13,681, while the amortized cost of this liability as of that date is $ 8,105, using the interest method.

Note 15: Financial Instruments

a. Risk management:

The Board of Directors has overall responsibility for the establishment and oversight of the Company's risk management framework.

The Company's risk management practice was formulated to identify and analyze the risks that the Company faces, to set appropriate limits for the risks and controls, and to monitor the risks and their compliance within the limits. The risk policy and risk management methods are reviewed regularly to reflect changes in market conditions and in the Company's operations.

The Company Audit Committee oversees how management monitors compliance with the Company's risk management policies and procedures, and reviews the adequacy of the risk management framework in relation to the risks faced by the Company. The Company Audit Committee is assisted in its oversight role by Internal Audit. Internal Audit undertakes both regular and ad hoc reviews of risk management controls and procedures, the results of which are reported to the Audit Committee.

The Company's activities expose it to various financial market risks mainly foreign currency risk, interest rate risk and liquidity risk.

1. Foreign currency risk

The Company operates primarily in an international environment and is exposed to foreign exchange risk resulting from the fact that a certain portion of the Company's costs are denominated in NIS and EURO, mainly due to payroll and related benefit costs incurred in Israel and additionally due to marketing expenses incurred in Europe.

2. Sensitivity tests relating to changes in market factors:

The Company operates in an international environment and is exposed to foreign exchange risk resulting from the exposure to different currencies, mainly NIS and EURO. Foreign exchange risks arise from recognized assets and liabilities denominated in a foreign currency other than the functional currency.

	December 31	
	2021	**2020**
Gain (loss) from change:		
5% increase in NIS and EURO exchange rate	**$ 3**	$ 76
5% decrease in NIS and EURO exchange rate	**$ (3)**	$ (76)

The Company has performed sensitivity tests of principal market risk factors that may affect its reported operating results or financial position.

The sensitivity tests present the profit or loss for the relevant risk variables chosen as of each reporting date.

U.S. dollars in thousands (except of share and per share data)

Note 15: Financial Instruments (Cont.)

3. Liquidity risk

Liquidity risk is the risk that the Company will not be able to meet its financial obligations as they fall due. The Company's approach to managing liquidity is to ensure, as far as possible, that it will always have sufficient liquidity to timely meet its liabilities, under both normal and stressed conditions, without incurring unwanted losses.

The Company manages the liquidity risk by holding cash balances, short-term deposits and secured bank credit facilities.

	December 31, 2021			
	Carrying amount	**12 months or less**	**1-2 years**	**2-8 years**
Non-derivative financial liabilities				
Current liabilities				
Current maturities of long-term liabilities	**3,024**	3,024		
Trade payables and accrued expenses	**4,693**	4,693		
Other payables	**3,620**	3,620		
Non-current liabilities				
Liabilities in respect of IIA grants	**15,286**		369	14,917
Liabilities in respect of purchase of shares	**5,867**		1,667	4,200
Lease liabilities	**1,522**		589	933

Note 15: Financial Instruments (Cont.)

b. Fair value:

The carrying amount of cash and cash equivalents, short-term bank deposits, trade and other receivables and trade and other payables approximates their fair value due to the short-term maturities of such instruments.

The fair value of liabilities in respect to IIA grants with fixed interest is based on a calculation of the present value of the cash flows at the interest rate for a loan with similar terms. The Company used a discount rate of 12% based in part of the Company's estimation at the time of the Company's recognition of the IIA grants which approximates the fair value at the respective balance sheet date.

The fair value of the contingent consideration for purchase of shares as presented in balance sheet is based on a calculation of the present value of future payments. The expected cash flows already reflect assumptions about the uncertainty in future defaults, and therefore the Company used a discount rate of 14% that is commensurate with the risk inherent in the expected cash flows.

Note 16: Severance Pay Liabilty, Net

The Company has liabilities for severance pay for its employees in Israel and in several EU jurisdictions. The Company's liability for employee benefits is based on local laws, valid labor agreements, the employee's salary and the applicable terms of employment, which together generate a right to severance compensation. Post-employment employee benefits are partially financed by deposits with defined contribution plans, as detailed below.

The Israeli Severance Pay Law, 1963 ("Severance Pay Law"), specifies that Israeli employees are entitled to severance payment, following the termination of their employment. Under the Severance Pay Law, the severance payment is calculated as one month salary for each year of employment, or a portion thereof. Under Section 14 of the Severance Pay Law ("Section 14"), employees are entitled to have monthly deposits, at a rate of 8.33% of their monthly salary, made on their behalf to their insurance funds.

Payments in accordance with Section 14 release the Company from the liability for any future severance payments in respect of those employees.

The majority of the Company's liability for severance pay is covered by Section 14. Acordingly, the Company does not recognize any liability for severance pay due to these employees and the deposits under Section 14 are not recorded as an asset in the Company's balance sheet. These contributions for compensation represent defined contribution plans. The Company recognizes liability for severance pay due to its employees in EU in accordance with local laws and its Israeli employees which are not under Section 14.

Note 17: Contingent Liabilities and Commitments

a. In 2000, the Company signed an exclusive license agreement (as amended in 2007) with a third party with regard to its patents and intellectual property. Pursuant to the agreement, the Company received an exclusive license to use the third party's patents and intellectual property, for the purpose of developing, manufacturing, marketing, and commercializing products for treatment of burns and other wounds.

In consideration for this exclusive license, the Company paid an aggregate amount of $ 950 following the achievement of certain development milestones as set forth in the agreement. In addition, the Company undertook to pay royalties of 1.5% to 2.5% from future revenues from sales of products which are based on this patent for a period ranging between 10 to 15 years from the first commercial delivery in a major country, and thereafter the Company will have a fully paid-up royalty-free license for these patents. In addition, royalties will be paid at the rate of 10% - 20% from sub-licensing of such patents and for lump sum amounts paid to the Company by a third party, the Company will pay 2% of the proceeds up to $1,000 and 4% of the proceeds above this amount. Moreover, the Company agreed to pay a one-time lump-sum amount of $ 1,500 when the aggregate revenues based on these patents reach $ 100,000. The amount of royalty payments for the years 2020 and 2021 amounted to $42 and $149 respectively.

b. Under the Research and Development Law, (the "R&D Law") the Company undertook to pay royalties of 3% on the revenues derived from sales of products or services developed in whole or in part using IIA grants. The maximum aggregate royalties paid cannot exceed 100% of the grants received by the Company, plus annual interest equal to the 12-month LIBOR applicable to dollar deposits, as published on the first business day of each calendar year. (see also Note 14).The total royalties amount paid as of December 31, 2021 is $1,303.

c. Beginning in 2007, the Company entered into a number of agreements with Teva Pharmaceutical Industries Limited (“Teva”) related to collaboration in the development, manufacturing and commercialization of solutions for the burn and chronic wound care markets. In consideration for these agreements, Teva made investments in the Company's ordinary shares and agreed to fund certain research and development expenses and manufacturing costs and perform all marketing activities for both NexoBrid, under the 2007 Teva Agreement, and the PolyHeal Product, under the 2010 PolyHeal Agreements (see also Note 22). As of December 31, 2012, all of these agreements were terminated.

On September 2, 2013, in accordance with the terms of the Teva Shareholders’ Rights Agreement, the Company exercised its rights to repurchase all of its shares held by Teva, and purchased 755,492 ordinary shares, in consideration for an obligation to pay Teva future royalty payments.

Pursuant to a Settlement Agreement signed on March 2019, Teva agreed to reduce the contingent consideration that is payable to Teva pursuant to the Company's repurchase of its shares from Teva in 2013 and to paid the Company $4,000 in cash. As a result, the Company is obligated to pay Teva annual payments at a reduced rate of 15% of its recognized revenues from the sale or license of NexoBrid after January 1, 2019, up to a reduced aggregate amount of $10,200.

Note 17: Contingent Liabilities and Commitments (Cont.)

In addition, the Company also agreed to indemnify, defend and hold harmless Teva and its directors, officers, agents and employees from and against claims relating to a certain milestone related to PolyHeal under an agreement associated with the Collaboration Agreements, up to an amount of $10,200, if a notice of such claim has been received by the Company prior to December 31, 2023.

In December 2020, Teva has agreed to revise the Settlement Agreement from March 2019. Under the new settlement the Company paid $1,000 in cash and became obligated to pay an amount of $2,000 over three years, in addition to a modified contingent consideration up to the amount of $7,200 in quarterly fixed payments starting 2021 subject to revenues generated from sales of NexoBrid. Total liabilities recorded as of December 31, 2021 and 2020 were approximately$ 5,928 and $6,587, respectively, and financial expenses (income) of $590 and ($433), respectively, were recorded in profit or loss within financial income of financial expenses.

Note 18: Materials Agreements

a. BARDA Contracts

In September 2015, the Company was awarded the First BARDA Contract for treatment of thermal burn injuries, which was valued at up to $112,000. In July 2017 and in May 2019, BARDA expanded its commitment by an aggregate supplemental amount of $41,000. In March 2020, BARDA further expanded its commitment by additional $5,500 to support emergency readiness for NexoBrid deployment upon request of use of NexoBrid in mass casualty situations and in February 2022 BARDA has expanded its awarded contract providing supplemental funding of $9,000 to support the NexoBrid BLA resubmission to the FDA and the continuous expanded access program (collectively the "First BARDA Contract").

Under the First BARDA Contract, BARDA provided technical assistance and a total of up to $91,000 in funding for NexoBrid development activities needed to request U.S. marketing approval from the FDA. In January 2020, BARDA committed an additional $16,500 to procure NexoBrid as part of the HHS mission to build national preparedness for public health medical emergencies. The contract further includes a $10,000 option to fund development of other potential NexoBrid indications and an option to procure additional NexoBrid valued at up to $50,000.

In September 2018, the Company were awarded the second BARDA contract (the "Second BARDA Contract"), which is an additional, separate contract to develop NexoBrid for the treatment of Sulfur Mustard injuries as part of BARDA’s preparedness for mass casualty events. The Second BARDA Contract provides approximately $12,000 of funding to support research and development activities up to pivotal studies in animals under the U.S. FDA Animal Rule and contains options for BARDA to provide additional funding of up to $31,000 for additional development activities, animal pivotal studies, and the BLA submission for licensure of NexoBrid for the treatment of Sulfur Mustard injuries.

Note 18: Materials Agreements (Cont.)

The total aggregate value awarded by BARDA Contracts is up to $211,000 comprised of $144,500 to support research and development activities and $66,500 to procure NexoBrid for U.S. emergency preparedness (which will be splited between the Company and Vericel following Vericel agreement (see Note 18b)).

As of December 31, 2021, the Company has received approximately $69,400 in funding in the aggregate, from BARDA under the two contracts, and an additional of approximately $14,600 for procurement of NexoBrid for U.S. emergency preparedness which were recorded at the net amount of approximately $9,300 following the split of gross profit agreement with Vericel for the initial BARDA procurement.

b. Vericel Agreement:

On May 6, 2019, the Company entered into exclusive license and supply agreements with Vericel to commercialize NexoBrid in North America (the "Collaboration Agreements"). Pursuant to the Collaboration Agreements, Vericel will obtain the authority over and control of the development, regulatory approval and commercialization of licensed products in the North America territory. MediWound will be responsible for the development of the product through BLA approval, supported and funded by BARDA, as well as the manufacture and supply of NexoBrid. In addition, MediWound retains the commercial rights to NexoBrid in non-North American territory.

Under the terms of the license agreement, Vericel has made an upfront payment to MediWound of $17,500 which was recorded as revenues from license agreements in 2019 and agreed to make an additional $7,500 payment contingent upon BLA approval and up to $125,000 in payments contingent upon meeting certain annual sales milestones. Vericel has also agreed to pay MediWound tiered royalties on net sales ranging from high single-digit to teen-digit percentages, a split of gross profit on committed BARDA procurement orders and a teen-digits royalty on any additional future BARDA purchases of NexoBrid. Under the terms of the supply agreement, Vericel will procure NexoBrid from MediWound at a transfer price of cost plus a fixed margin percentage.

As of the financial statements date, the Company did not recognize any revenues from royalties.

U.S. dollars in thousands (except of share and per share data)

Note 19: Equity

a. Share capital:

	December 31	
	2021	**2020**
Authorized number of shares	**50,000,000**	50,000,000
Issued and outstanding number of shares	**27,272,818**	27,236,752

b. Rights attached to shares:

An ordinary share confers upon its holder(s) a right to vote at the general meeting, a right to participate in distribution of dividends, and a right to participate in the distribution of surplus assets upon liquidation of the Company.

c. Movement in share capital:

- During 2019, the authorized number of shares was increased by 12,755,492 shares which has a nominal value of $40.
- On December 31, 2019, the Company issued additional 23,956 ordinary shares upon vesting of outstanding RSU's.
- During 2020 and 2021 the Company issued additional 33,958 ordinary shares for each year upon vesting of outstanding RSU's.

Note 20: Share-Based Compensation

a. Expense recognized in the financial statements:

The expenses recognized for services received from employees and directors is as follows:

	Year ended December 31		
	2021	**2020**	**2019**
Cost of revenues	**153**	115	226
Research and development	**333**	179	375
Selling and marketing	**-**	3	40
General and administrative	**1,187**	1,025	593
Total share-based compensation	**1,673**	1,322	1,234

b. Share-based payment plan for employees and directors:

The Company has granted options and restricted stock units ("RSUs") for total of 3,863,089 ordinary shares.

U.S. dollars in thousands (except of share and per share data)

Note 20: Share-Based Compensation (Cont.)

As of December 31, 2021, 490,927 ordinary shares of the Company were still available for future grant.

Any options or RSUs, which are forfeited or not exercised before expiration, become available for future grants.

Options granted under the Company's 2003 Israeli Share Option Plan ("Plan") are exercisable in accordance with the terms of the Plan, within 5-10 years from the date of grant, against payment of an exercise price or cashless exercise. The options generally vest over a period of 3-4 years.

In March 2014, the Company adopted and obtained shareholder approval for its 2014 Equity Incentive Plan (the "2014 Plan").

Options and RSU's granted under the Company's 2014 Plan are exercisable in accordance with the terms of the Plan. Options are exercisable within 5-10 years from the date of grant, against payment of an exercise price or cashless exercise and share units are granted immediately upon vesting of the RSU's. The options and the RSU's generally vest over a period of 1-4 years.

c. Share options activity:

The following table lists the number of share options, the weighted average exercise prices of share options and changes that were made in the option plan to employees and directors

	2021		2020		2019	
	Number of options	**Weighted Average Exercise price**	**Number of options**	**Weighted Average Exercise price**	**Number of options**	**Weighted Average Exercise price**
Outstanding Options at beginning of year	**3,597,811**	**6.55**	2,334,432	9.18	2,313,249	9.31
Options Granted	**377,790**	**5.36**	1,274,379	1.43	95,000	4.45
Options Exercised	**(3,750)**	**2.88**	-	-	-	-
Options Forfeited and/or expired	**(210,833)**	**8.13**	(11,000)	7.19	(73,817)	5.17
Outstanding options and at end of year	**3,761,018**	**6.35**	3,597,811	6.55	2,334,432	9.18
Option's Exercisable at end of year	**2,335,325**	**8.34**	1,952,014	9.98	1,753,803	4.76

U.S. dollars in thousands (except of share and per share data)

Note 20: Share-Based Compensation (Cont.)

The following table summarizes information about share options outstanding as of December 31, 2021:

	Options outstanding as of December 31, 2021		
Range of exercise prices ($)	**Number of options**	**Weighted Average Remaining contractual life**	**Weighted average exercise price**
1.75-5.36	**2,307,469**	**6.19**	**3.29**
6.02- 9.58	**642,249**	**3.68**	**9.01**
12.89 - 13.76	**811,300**	**1.92**	**12.93**
Total	**3,761,018**	**4.84**	**6.35**

The following table summarizes information about RSU's outstanding:

	RSU's 2021	**RSU's 2020**	**RSU's 2019**
Outstanding at beginning of year	**74,587**	108,544	95,833
Granted	**62,947**	-	36,667
Forfeited	**(1,505)**	-	-
Vested	**(33,958)**	(33,958)	(23,956)
Outstanding at the end of the period	**102,071**	74,587	108,544

The fair value of the options and RSU's granted to employees and directors at the grant date for the years ended December 31, 2019, 2020 and 2021 was $441 ,$1,819 and $1,392 respectively.

The options and RSU’s of the Company are managed by a trustee.

1. On March 24, 2019, the Company granted to its incoming CEO and chairman of the board 60,000 options (40,000 and 20,000 respectively) to purchase ordinary shares, for an exercise price of $ 4.92 per share, and 30,000 RSU's (20,000 and 10,000 respectively), under the "2014 Share Incentive Plan". The options are exercisable in accordance with the terms of the plan and will vest over three-four years. The fair value of the options and RSU's granted, as of the grant date, was estimated at approximately $164 and $158, respectively. On May 2, 2019, the general meeting of the Company approved the abovementioned grants.

2. On June 6, 2019, the Company granted to its incoming CFO 40,000 options to purchase ordinary shares, for an exercise price of $ 3.84 per share, and 6,667 RSU's, under the "2014 Share Incentive Plan". The options are exercisable in accordance with the terms of the plan and will vest over four years. The fair value of the options and RSU's granted, as of the grant date, was estimated at approximately $93 and $26, respectively.

U.S. dollars in thousands (except of share and per share data)

Note 20: Share-Based Compensation (Cont.)

3. On April 23, 2020, the Company's Board of Directors approved the grant of 1,274,379 options to purchase ordinary shares under the "2014 Share Incentive Plan", for an exercise price of $ 1.75 per share to its employees, managments and board members of the Company. The fair value of the options granted, as of the grant date, was estimated at approximately $1,819.

4. On March 4, 2021, the Company's Board of Directors approved the grant of: (a) 238,090 options to purchase ordinary shares and 39,682 RSU's under the "2014 Share Incentive Plan" to its CEO, officers and board members of the Company at a fair value of $663 and $196, respectively, and (b) 139,700 options to purchase ordinary shares and 23,265 RSU's under the "2014 Share Incentive Plan" to its employees at a fair value of $417 and $116, respectively. The options are exercisable for an exercise price of $ 5.36 per share.

d. The fair value of the Company's share options granted to employees and directors for the years ended December 31, 2019, 2020 and 2021 was estimated using the binomial option pricing models using the following assumptions:

	December 31		
	2021	**2020**	**2019**
Dividend yield (%)	**0**	0	0
Expected volatility of the share prices (%)	**55-78**	51-71	41-53
Risk-free interest rate (%)	**0.1-1.5**	0.2-0.9	1.85-2.45
Early exercise factor (%)	**100-150**	100-150	150
Weighted average share prices (Dollar)	**2.88**	2.43	4.83

Measurement inputs include the share price on the measurement date, the exercise price of the instrument, expected volatility (based on the weighted average volatility of the Company's shares, over the expected term of the options), expected term of the options (based on general option holder behavior and expected share price), expected dividends, and the risk-free interest rate (based on government debentures).

Note 21: Income Tax

a. The Company operates in two main tax jurisdictions: Israel and Germany. As such, the Company is subject to the applicable tax rates in the jurisdictions in which it conducts its business..

b. Corporate tax rate in Israel:

The tax rates relevant to the Company in the years 2019-2021 is 23%.

c. Benefits under the Law for the Encouragement of Capital Investments:

Tax benefits under the Israel Law for the Encouragement of Capital Investments, 1959 (the "Investment Law"):

Note 21: Income Tax (Cont.)

Under the Investment Law, the Company has been granted "Beneficiary Enterprise" status which provides certain benefits, including tax exemptions and reduced tax rates. Income not eligible for Beneficiary Enterprise benefits is taxed at a regular rate.

During the benefit period, the Company will be tax exempt in the first two years of the benefit period and subject to tax at the reduced rate of 10%- 25% for an additional period of five to eight years (depending on the percentage of foreign investments in the Company) of the benefit period. The benefit entitlement period starts from the first year that the Beneficiary Enterprise first earned taxable income, and is limited to 12 years from the year in which the Company requested to have tax benefits apply. In the event of distribution of dividends from the said tax exempt income, the amount distributed will be subject to corporate tax at the reduced rate ordinarily applicable to the Beneficiary Enterprise's income.

Tax exempt income generated under the Company's "Beneficiary Enterprise" program will be subject to taxes upon dividend distribution or complete liquidation. The entitlement to the above benefits is conditional upon the Company's fulfilling the conditions stipulated by the Investment Law and regulations published thereunder. Should the Company fail to meet such requirements in the future, income attributable to its Beneficiary Enterprise programs could be subject to the statutory Israeli corporate tax rate and the Company could be required to refund a portion of the tax benefits already received, with respect to such programs.

d. The principal tax rates applicable to the subsidiary whose place of incorporation is outside of Israel is:

The statutory corporate tax rate in Germany was 29.79% in 2021, 2020 and 2019.

e. Final tax assessments:

The Company has finalized its tax assessments through the 2015 tax year.

The Company's subsidiary has not received a final tax assessment since its incorporation.

f. Net operating carryforward losses for tax purposes and other temporary differences:

As of December 31, 2021, the Company had carryforward losses and other temporary differences mainly from R&D expenses together amounting to approximately $148,000.

g. Deferred taxes:

The Company did not recognize deferred tax assets for temporary differences at the amount of approximately $9,500 because their utilization in the foreseeable future is not probable.

h. Current taxes on income:

The Company did not record any current taxes for the years ended December 31, 2019, 2020 and 2021 as a result of its carryforward losses.

Note 21: Income Tax (Cont.)

i. Theoretical tax:

The reconciliation between the tax expense, assuming that all the income and expenses, gains and losses in the statement of income were taxed at the statutory tax rate and the taxes on income recorded in profit or loss, does not provide significant information and therefore was not presented (the main reconciliation item is due to operating losses and other temporary differences for which deferred tax assets were not recognized).

Note 22: Discontinued Operation

On September 15, 2014, a Statement of Claim was filed against the Company by some shareholders of Polyheal (the "Plaintiffs") related to '2010 PolyHeal Agreement' in which PolyHeal granted the Company an exclusive global license to manufacture, develop and commercialize all the Polyheal Products in consideration for royalty payments.

During December 2017, following the Tel- Aviv District Court Ruling, the Company paid the Plaintiffs approximately $1,497 in consideration for PolyHeal's shares and recorded a full provision of $6,003 which represents the purchase price for the residual number of shares that the 2010 PolyHeal Agreements contemplate would be acquired by the Company from the shareholders of PolyHeal (the “Provision”).

On March 24, 2019, the Company entered into a settlement agreement and mutual general release with the Plaintiffs (the "Polyheal Settlement Agreement"). Pursuant to the terms of Polyheal Settlement Agreement, the Plaintiffs repaid to MediWound a portion of the amount that was ruled in their favor under the Tel Aviv District Court Ruling, and it resulted the cancellation of the 2017 Ruling that was issued by the District Court against MediWound.

In September 2019, the Company entered a new series of settlement agreements (the "New PolyHeal Settlement Agreements") with the majority of the shareholders of Polyheal, including Clal Biotechnology Industries Ltd., its controlling shareholder. Pursuant to the terms of New PolyHeal Settlement Agreements, the Company paid an aggregate amount of approximately $2,800 and received 14,473 shares of PolyHeal, which was classified as royalty rights arising from the Company’s ownership of shares of Polyheal.

As a result of the New PolyHeal Settlement Agreements, the Company recognized one-time profit from discontinued operation of $2,889, following the decrease of the provision which was offset by an impairment of the royalty rights and settlement fees.

In 2020 the Company finalized PolyHeal Settlement Agreements and paid $195 for 1,558 shares of PolyHeal. As of December 31, 2020, the provision for liability in respect of discontinued operation, was fully offset.

U.S. dollars in thousands (except of share and per share data)

Note 23: Supplementary Information to the Statements of Comprehensive Profit or Loss

a. Additional information on Revenues:

Major customers:

BARDA contributed 76% of the Company's total revenues in 2021, 83% in 2020, and 34% in 2019. Verical contributed 55% in 2019. (see also Note 18b).

No other customer contributed 10% or more of the Company's revenues in 2021, 2020 and 2019.

Revenue Re-classification:

Revenues in the amount of $383 from distributions agreements were classified from revenues from sale of products for the year ended 31, December 2020.

Geographic information:,

The revenues reported in the financial statements are based on the location of the customers, as follows:

	Year ended December 31		
	2021	**2020**	**2019**
USA (see also Note 18a, 18b)	**18,102**	18,030	28,504
EU and other international markets	**5,661**	3,733	3,285
	23,763	21,763	31,789

b. Cost of Revenues:

1. *Cost of Revenues from sale of products*

	Year ended December 31		
	2021	**2020**	**2019**
Salary and benefits (including share-based compensation)	**2,201**	2,139	1,916
Subcontractors	**204**	153	89
Depreciation and amortization	**603**	554	512
Cost of materials	**1,091**	704	456
Other manufacturing expenses	**953**	840	657
Decrease in inventory of finished products	**242**	155	344
Allotment of manufacturing costs to R&D	**(311)**	(1,394)	(1,621)
	4,983	3,151	2,353

2. *Cost of Revenues from development services*

	Year ended December 31		
	2021	**2020**	**2019**
Salary and benefits	**2,003**	2,320	1,404
Subcontractors	**7,904**	8,747	7,412
	9,907	11,067	8,816

U.S. dollars in thousands (except of share and per share data)

Note 23: Supplementary Information to the Statements of Comprehensive Profit or Loss (Cont.)

3. *Cost of Revenues from license agreements*

	Year ended December 31		
	2021	**2020**	**2019**
Salary and benefits	**102**	-	-
Royalties payments	-	-	680
	102	-	680
Total Cost of Revenues	**14,992**	14,218	11,849

c. Research and development expenses, net of participations:

	Year ended December 31		
	2021	**2020**	**2019**
Salary and benefits (including share-based compensation)	**2,811**	2,094	2,965
Subcontractors	**6,309**	3,173	4,694
Depreciation and amortization	**352**	346	342
Cost of materials	**295**	517	311
Allotment of manufacturing costs	**209**	1,394	1,621
Other research and development expenses	**280**	174	137
Research and development, gross	**10,256**	7,698	10,070
Participations:			
BARDA funds	**-**	-	(3,785)
Revaluation of liabilities in respect of IIA grants	-	-	(1,316)
	10,256	7,698	4,969

d. Selling and marketing expenses:

	Year ended December 31		
	2021	**2020**	**2019**
Salary and benefits (including share based compensation) (1)	**1,643**	1,700	2,028
Marketing and medical support	**627**	740	1,298
Depreciation and amortization	**44**	82	49
Shipping and delivery	**490**	282	200
Registration and marketing license fees	**584**	424	489
	3,388	3,228	4,064

(1) The salary costs for the year ended December 31,2020 includes one time payment of $243 derived from restructuring astrategy at the EU Subsidiary.

U.S. dollars in thousands (except of share and per share data)

Note 23: Supplementary Information to the Statements of Comprehensive Profit or Loss (Cont.)

e. General and administrative expenses:

	Year ended December 31		
	2021	**2020**	**2019**
Salary and benefits (including share-based compensation)	**2,905**	2,784	2,621
Professional fees	**2,480**	2,267	1,628
Depreciation and amortization	**239**	108	247
Other	**724**	300	746
	6,348	5,459	5,242

f. Other expenses:

The other one-time expenses amounted $1,172 for the year ended December 31, 2019, are associated with the review and assessment of the strategic deal with Vericel (see Note 18b).

g. Financial income and expense:

	Year ended December 31		
	2021	**2020**	**2019**
Financial income:			
Interest income	**11**	297	434
Revaluation of liabilities in respect of the purchase of shares	**-**	433	-
Exchange differences, net	**-**	113	122
	11	843	556
Financial expense:			
Interest in respect of IIA grants	**903**	832	925
Revaluation of liabilities in respect of IFRS16	**120**	144	140
Finance expenses in respect of deferred revenues	**143**	247	161
Revaluation of liabilities in respect of the purchase of shares	**590**	-	1,690
Exchange differences, net	**511**	-	-
Other	**47**	56	67
	2,314	1,279	2,983
Financial expenses, net	**(2,303)**	(436)	(2,427)

U.S. dollars in thousands (except of share and per share data)

Note 24: Net Profit (Loss) Per Share

a. Details of the number of shares and loss used in the computation of loss per share from continuing operations:

Year ended December 31					
2021		2020		2019	
Weighted average number of shares	Loss	Weighted average number of shares	Loss	Weighted average number of shares	Profit
27,244,475	**(13,551)**	27,209,878	(9,276)	27,178,839	2,066

b. Details of the number of shares and profit (loss) used in the computation of profit or (loss) per share from discontinued operation:

Year ended December 31					
2021		2020		2019	
Weighted average number of shares	Profit	Weighted average number of shares	Profit	Weighted average number of shares	Profit
-	-	27,209,878	80	27,178,839	2,889

c. Net profit (loss) per share from continuing and discontinued operations:

	Year ended December 31		
	2021	2020	2019
Basic and Diluted loss per share:			
Profit (loss) from from continuing operations	**(0.50)**	(0.34)	0.08
Profit from discontinued operation	-	-	0.10
Profit (loss) per share	**(0.50)**	(0.34)	0.18

Note 25: Balances and Transactions With Related Parties and Key Officer

a. Related parties consist of:

- Clal Biotechnologies Industries Ltd.- Parent Company.
- Directors of the Company.
- CureTech Ltd.-Sister Company.

U.S. dollars in thousands (except of share and per share data)

Note 25: Balances and Transactions With Related Parties and Key Officers (Cont.)

1. Balances of related parties:

	Other Payables
Parent Company (1):	
As of December 31, 2020	138
As of December 31, 2021	**144**
Directors:	
As of December 31, 2020	86
As of December 31, 2021	**96**

2. Transactions with related parties:

Rental fee:

	Year ended December 31		
	2021	**2020**	**2019**
Parent Company	**469**	446	415
Sister Company	-	-	(59)

Professional fee:

	Year ended December 31		
	2021	**2020**	**2019**
Directors	**375**	272	249
Parent Company	**85**	54	52
	460	326	301
Number of Directors	8	8	6

- Not included share based compensation detailed in Note 20.

U.S. dollars in thousands (except of share and per share data)

Note 25: Balances and Transactions With Related Parties and Key Officers (Cont.)

b. Key Officers:

1. Balances of Key Officers of the Company

	Other Payables
Key Officers of the Company	
As of December 31, 2021	**353**

- Represents the officer's gross salary, bonuses and vacation provisions.

2. Compensation of Key Officers of the Company:

The following amounts disclosed in the table are recognized as an expense during the reporting period related to officers:

	Year ended December 31		
	2021	**2020**	**2019**
Short-term employee benefits (*)	1,788	1,993	2,533
Share-based compensation	518	467	565
	2,306	2,460	3,098
Number of officers	5	5	7

(*) The amount for 2019 includes one-time payments for previous-CEO on the amount of $196.

In December 2007, the Company's board of directors approved one-time bonus payments to the Chief Medical Officer in the amounts of $ 120, to be paid upon achieving marketing approval in the United States.

Note 26: Subsiquents events:

On March 7, 2022, the Company completed a follow-on public offering. A total of 5,208,333 new ordinary shares were issued in consideration to offering price of $1.92 per share. The net proceeds, were $8,662, after deducting commissions and other offering expenses. MediWound also granted the underwriters a 30-day option to purchase up to an additional 781,249 ordinary shares at the public offering price, less underwriting discounts and commissions at an additional net proceeds of $1,388.

In addition, certain entities affiliated with CBI purchased 1,458,333 of ordinary shares in the obove-mentioned offering at the public offering price.

Exhibit 1.1

AMENDED AND RESTATED
ARTICLES OF ASSOCIATION
OF
MEDIWOUND LTD.

A COMPANY LIMITED BY SHARES
UNDER THE COMPANIES LAW, 5759 – 1999

INTERPRETATION

1.

1.1. In these Articles, unless the context requires another meaning the words in the first column of the following table shall have the meanings set opposite them in the second column:

"**Alternate Nominee**"	as defined in Article 77.1;
"**Articles**"	these Articles of Association, as amended from time to time by a Resolution (as defined below);
"**Auditors**"	the auditors of the Company;
"**Board of Directors**"	all of the directors of the Company holding office pursuant to these Articles, including alternates, substitutes or proxies;
"**Chief Executive Officer**"	chief executive officer of the Company;
"**Chairman of the Board of Directors**"	as defined in Article 81;
"**Companies Law**"	the Israeli Companies Law, 5759-1999, as amended from time to time, including the regulations promulgated thereunder, or any other law which may come in its stead, including all amendments made thereto;
"**Company**"	MediWound Ltd. or מדיוונד בע"מ;
"**Committee of Directors**"	as defined in Article 93;
"**Compensation Committee**"	as defined in the Companies Law;
"**Deed of Transfer**"	as defined in Article 44;
"**Derivative Transaction**"	as defined in Article 56;
"**Effective Time**"	the closing of the initial underwritten public offering of the Company's Ordinary Shares, at which time these Articles shall first become effective;

"**Director(s)**"	a member or members of the Board of Directors elected to hold office as director(s);
"**External Directors**"	as defined in the Companies Law;
"**General Meetings**"	all annual and extraordinary meetings of the Shareholders;
"**Incapacitated Person**"	as defined under the Israeli Legal Capacity and Guardianship Law, 5722-1962, as amended from time to time, including a minor who has not yet attained the age of 18 years, a person unsound of mind and a bankrupt in respect of whom no rehabilitation has been granted;
"**NIS**"	New Israeli Shekels;
"**Nominees**"	as defined in Article 77.1;
"**Ordinary Shares**"	as defined in Article 6;
"**Office**"	the registered office of the Company at that time;
"**Office Holder**"	as defined in the Companies Law;
"**Person**"	includes an individual, corporation, company, cooperative society, partnership, trust of any kind or any other body of persons, whether incorporated or otherwise;
"**Proposal Request**"	as defined in Article 56;
"**Proposing Shareholder**"	as defined in Article 56;
"**Register**"	the Register of Shareholders administered in accordance with the Companies Law;
"**Resolution**"	a resolution of Shareholders. Except as required under the Companies Law or these Articles, any Resolution shall be adopted by a majority of the voting power present and voting at the applicable General Meeting, in person or by proxy;
"**Rights**"	as defined in Article 113.1;
"**Shareholder(s)**"	shall mean the shareholder(s) of the Company, at any given time;
"**Special Fund**"	as defined in Article 113.1;
"**Transferor**"	as defined in Article 44;
"**Transferee**"	as defined in Article 44;
"**U.S. Rules**"	the applicable rules of the NASDAQ Stock Market and the U.S. securities rules and regulations, as amended from time to time; and
"**writing**"	handwriting, typewriting, photography, telex, email or any other legible form of writing.

1.2. Subject to the provisions of this Article 1, in these Articles, unless the context necessitates another meaning, terms and expressions which have been defined in the Companies Law shall have the meanings ascribed to them therein.

1.3. Words in the singular shall also include the plural, and vice versa. Words in the masculine shall include the feminine and vice versa, and words which refer to persons shall also include corporations, and vice versa.

1.4. The captions to articles in these Articles are intended for the convenience of the reader only, and no use shall be made thereof in the interpretation of these Articles.

LIMITED LIABILITY

2. The Company is a limited liability company and therefore each shareholder's obligations for the Company's obligations shall be limited to the payment of the nominal value of the shares held by such shareholder, subject to the provisions of the Companies Law.

THE COMPANY'S OBJECTIVES

3. The Company's objectives are to conduct all types of business as are permitted by law. The Company may donate a reasonable amount of money for any purpose that the Board of Directors finds appropriate, even if the donation is not for business considerations or for the purpose of achieving profits for the Company.

THE BUSINESS

4. Any branch or type of business that the Company is authorized to engage in, either expressly or implied, may be commenced or engaged in by the Board of Directors at all or any time as it deems fit. The Board of Directors shall be entitled to cease the conduct of any such branch or type of business, whether or not the actual conduct thereof has commenced at its own discretion.

REGISTERED OFFICE

5. The registered office shall be at such place as is decided from time to time by the Board of Directors.

SHARE CAPITAL

6. The share capital of the Company shall consist of NIS 500,000 divided into 50,000,000 Ordinary Shares, of a nominal value of NIS 0.01 each (the "**Ordinary Shares**").

RIGHTS ATTACHING TO THE ORDINARY SHARES

7.

7.1. The Ordinary Shares in respect of which all calls have been fully paid shall confer on the holders thereof the right to attend and to vote at General Meetings of the Company, both ordinary as well as extraordinary meetings.

7.2. The Ordinary Shares shall confer on a holder thereof the right to receive a dividend, to participate in a distribution of bonus shares and to participate in the distribution of the assets of the Company upon its winding-up, pro rata to the nominal amount paid up on the shares or credited as paid up in respect thereof, and without reference to any premium which may have been paid in respect thereof.

MODIFICATION OF CLASS RIGHTS

8.

8.1. Subject to applicable law, if at any time the share capital of the Company is divided into different classes of shares and unless the terms of issue of such class of shares otherwise stipulate, the rights attaching to any class of shares (including rights prescribed in the terms of issue of the shares) may be altered, modified or canceled, by a Resolution passed at a separate General Meeting of the Shareholders of that class.

8.2. The provisions contained in these Articles with regard to General Meetings shall apply, *mutatis mutandis* as the case may be, to every General Meeting of the holders of each such class of the Company's shares.

8.3. Unless otherwise provided by these Articles, the increase of an authorized class of shares, or the issuance of additional shares thereof out of the authorized and unissued share capital, shall not be deemed, for purposes of this Article 8.30, to modify or abrogate the rights attached to previously issued shares of such class or of any other class.

UNISSUED SHARE CAPITAL

9. The unissued shares in the capital of the Company shall be under the control of the Board of Directors, which shall be entitled to allot or otherwise grant the same to such Persons under such restrictions and conditions as it shall deem fit, whether for consideration or otherwise, and whether for consideration in cash or for consideration which is not in cash, above their nominal value or at a discount, all on such conditions, in such manner and at such times as the Board of Directors shall deem fit, subject to the provisions of the Companies Law. The Board of Directors shall be entitled, *inter alia*, to differentiate between Shareholders with regard to the amounts of calls in respect of the allotment of shares (to the extent that there are calls) and with regard to the time for payment thereof. The Board of Directors may also issue options or warrants for the purchase of shares of the Company and prescribe the manner of the exercise of such options or warrants, including the time and price for such exercise and any other provision which is relevant to the method for distributing the issued shares of the Company amongst the purchasers thereof.

10. The Board of Directors shall be entitled to prescribe the times for the issue of shares of the Company and the conditions therefore and any other matter which may arise in connection with the issue thereof.

11. In every case of a rights offering the Board of Directors shall be entitled, in its discretion, to resolve any problems and difficulties arising or that are likely to arise in regard to fractions of rights, and without prejudice to the generality of the foregoing, the Board of Directors shall be entitled to specify that no shares shall be allotted in respect of fractions of rights, or that fractions of rights shall be sold and the (net) proceeds shall be paid to the persons entitled to the fractions of rights, or, in accordance with a decision by the Board of Directors, to the benefit of the Company.

11A. The Company may, subject to applicable law, issue redeemable shares and redeem the same. Shares issued by the Company may be redeemable upon terms and conditions to be set forth in a written agreement between the Company and the holder of such shares.

INCREASE OF AND ALTERATIONS TO CAPITAL

12. The Company may, from time to time, by a Resolution, increase its share capital by way of the creation of new shares, whether or not all the existing shares have been issued up to the date of the resolution, whether or not it has been decided to issue same, and whether or not calls have been made on all the issued shares.

13. The increase of share capital shall be in such amount and divided into shares of such nominal value, and with such restrictions and conditions and with such rights and privileges as the Resolution dealing with the creation of the shares prescribes, and if no provisions are contained in the Resolution, then as the Board of Directors shall prescribe.

14. Unless otherwise stated in the Resolution approving the increase of the share capital, the new shares shall be subject to those provisions in regard to issue, allotment, alteration of rights, payment of calls, liens, forfeiture, transfer, transmission and other provisions which apply to the shares of the Company.

15. By Resolution, the Company may, subject to any applicable provisions of the Companies Law:

    15.1. consolidate its existing share capital, or any part thereof, into shares of a larger denomination than the existing shares;

    15.2. sub-divide its share capital, in whole or in part, into shares of a smaller denomination than the nominal value of the existing shares and without prejudice to the foregoing, one or more of the shares so created may be granted any preferred or deferred rights or any special rights with regard to dividends, participation in assets upon winding-up, voting and so forth, subject to the provisions of these Articles;

    15.3. reduce its share capital; or

    15.4. cancel any shares which on the date of passing of the Resolution have not been issued and to reduce its share capital by the amount of such shares.

16. In the event that the Company shall adopt any of the Resolutions described in Article 15 above, the Board of Directors shall be entitled to prescribe arrangements necessary in order to resolve any difficulty arising or that are likely to arise in connection with such Resolutions, including, in the event of a consolidation, it shall be entitled to (i) allot, in contemplation of or subsequent to such consolidation or other action, shares or fractional shares sufficient to preclude or remove fractional share holdings; (ii) redeem, in the case of redeemable shares, and subject to applicable law, such shares or fractional shares sufficient to preclude or remove fractional share holdings; (iii) round up, round down or round to the nearest whole number, any fractional shares resulting from the consolidation or from any other action which may result in fractional shares; or (iv) cause the transfer of fractional shares by certain Shareholders to other Shareholders thereof so as to most expediently preclude or remove any fractional shareholdings, and, cause the transferees of such fractional shares to pay the transferors thereof the fair value thereof, and the Board of Directors is hereby authorized to act in connection with such transfer, as agent for the transferors and transferees of any such fractional shares, with full power of substitution, for the purposes of implementing the provisions of this Article 16

SHARE CERTIFICATES

17. To the extent shares are certificated, share certificates evidencing title to the shares of the Company shall be issued under the seal or rubber stamp of the Company, and together with the signatures of two members of the Board of Directors, or one Director together with the Chief Executive Officer, the Chief Financial Officer, the Secretary of the Company or any other person designated by the Board of Directors. The Board of Directors shall be entitled to decide that the signatures be effected in any mechanical or electronic form, provided that the signature shall be effected under the supervision of the Board of Directors in such manner as it prescribes.

18. Every Shareholder shall be entitled, free of charge, to one certificate in respect of all the shares of a single class registered in his name in the Register.

19. The Board of Directors shall not refuse a request by a Shareholder to obtain several certificates in place of one certificate, unless such request is, in the opinion of the Board of Directors, unreasonable. Where a Shareholder has sold or transferred some of his shares, he shall be entitled, free of charge, to receive a certificate in respect of his remaining shares, provided that the previous certificate is delivered to the Company before the issuance of a new certificate.

20. Every share certificate shall specify the number of the shares in respect of which such certificate is issued and also the amounts which have been paid up in respect of each share.

21. No Person shall be recognized by the Company as having any right to a share unless such Person is the registered owner of the shares in the Register. The Company shall not be bound by and shall not recognize any right or privilege pursuant to the laws of equity, or a fiduciary relationship or a chose in action, future or partial, in any share, or a right or privilege to a fraction of a share, or (unless these Articles otherwise direct) any other right in respect of a share, except the absolute right to the share as a whole, where same is vested in the owner registered in the Register.

22. A share certificate registered in the names of two or more persons shall be delivered to one of the joint holders, and the Company shall not be obliged to issue more than one certificate to all the joint holders of shares and the delivery of such certificate to one of the joint holders shall be deemed to be delivery to all of them.

23. If a share certificate should be lost, destroyed or defaced, the Board of Directors shall be entitled to issue a new certificate in its place, provided that the certificate is delivered to it and destroyed by it, or it is proved to the satisfaction of the Board of Directors that the certificate was lost or destroyed and security has been received to its satisfaction in respect of any possible damages and after payment of such amount as the Board of Directors shall prescribe.

CALLS ON SHARES

24. The Board of Directors may from time to time, in its discretion, make calls on Shareholders in respect of amounts which are still unpaid in respect of the shares held by each of the Shareholders (including premiums), and the terms of issue which do not prescribe that same be paid at fixed times, and every Shareholder shall be obliged to pay the amount of the call made on him, at such time and at such place as stipulated by the Board of Directors.

25. In respect of any such call, prior notice of at least fourteen (14) business days shall be given, stating to whom the amount called is to be paid, the time for payment and the place thereof, provided that prior to the due date for payment of such call, the Board of Directors may, by written notice to the Shareholders to which the call was made, cancel the call or extend the date of payment thereof.

26. If according to the terms of issue of any share, or otherwise, any amount is required to be paid at a fixed time or in installments at fixed times, whether the payment is made on account of the share capital in respect of the share or in form of a premium, every such payment or every such installment shall be paid as if it was a call duly made by the Board of Directors, in respect of which notice was duly given, and all the provisions contained in these Articles in regard to calls shall apply to such amount or to such installment.

27. Joint holders of a share shall be jointly and severally liable for the payment of all installments and calls due in respect of such share.

28. In the event that a call or installment due on account of a share is not paid on or before the date fixed for payment thereof, the holder of the share, or the Person to whom the share has been allotted, shall be obliged to pay linkage differentials and interest on the amount of the call or the installment, at such rate as shall be determined by the Board of Directors, commencing from the date fixed for the payment thereof and until the date of actual payment. The Board of Directors may, however, waive the payment of the linkage differentials or the interest or part thereof.

29. A Shareholder shall not be entitled (i) to receive a dividend and (ii) to exercise any right as a Shareholder, including but not limited to, the right to attend and vote at a General Meeting of any type and to transfer the shares to another; unless he has paid all the calls payable from time to time and which apply to any of his shares, whether he holds same alone or jointly with another, plus linkage differentials, interest and expenses, if any.

30. The Board of Directors may, if it deems fit, accept payment from a Shareholder wishing to advance the payment of all moneys which remain unpaid on account of his shares, or part thereof which are over and above the amounts which have actually been called, and the Board of Directors shall be entitled to pay such Shareholder linkage differentials and interest in respect of the amounts paid in advance, or that portion thereof which exceeds the amount called for the time being on account of the shares in respect of which the advance payment is made, at such rate as is agreed upon between the Board of Directors and the Shareholder, with this being in addition to dividends payable (if any) on the paid-up portion of the share in respect of which the advance payment is made.

The Board of Directors may, at any time, repay the amount paid in advance as aforesaid, in whole or in part, in its sole discretion, without premium or penalty. Nothing in this Article 30 shall derogate from the right of the Board of Directors to make any call for payment before or after receipt by the Company of any such advance.

FORFEITURE AND LIEN

31. If a Shareholder fails to make payment of any call or other installment on or before the date fixed for the payment thereof, the Board of Directors may, at any time thereafter and for as long as the part of the call or installment remains unpaid, serve on such Shareholder a notice demanding that he make payment thereof, together with the linkage differentials and interest at such rate as is specified by the Board of Directors and all the expenses incurred by the Company in consequence of such non-payment.

32. The notice shall specify a further date, which shall be at least fourteen (14) business days after the date of the delivery of the notice, and a place or places at which such call or installment is to be paid, together with linkage differentials and interest and expenses as aforesaid. The notice shall further state that, if the amount is not paid on or before the date specified, and at the place mentioned in such notice, the shares in respect of which the call was made, or the installment is due, shall be liable to forfeiture.

33. If the demands contained in such notice are not complied with the Board of Directors may treat the shares in respect of which the notice referred to in Articles 31 and 32 was given as forfeited. Such forfeiture shall include all dividends, bonus shares and other benefits which have been declared in respect of the forfeited shares which have not actually been paid prior to the forfeiture.

34. Any share so forfeited or waived shall be deemed to be the property of the Company and the Board of Directors shall be entitled, subject to the provisions of these Articles and the Companies Law, to sell, re-allot or otherwise dispose thereof, as it deems fit, whether the amount paid previously in respect of that share is credited, in whole or in part.

35. The Board of Directors may, at any time before any share forfeited as aforesaid is sold or re-allotted or otherwise dispose of, cancel the forfeiture on such conditions as it deems fit.

36. Any Person whose shares have been forfeited shall cease to be a Shareholder in respect of the forfeited shares, but shall, nonetheless remain liable for the payment to the Company of all calls, installments, linkage differentials, interest and expenses due on account of or in respect of such shares on the date of forfeiture, in respect of the forfeited shares, together with interest on such amounts reckoned from the date of forfeiture until the date of payment, at such rate as the Board of Directors shall from time to time specify. However, such Person’s liability shall cease after the Company has received all the amounts called in respect of the shares as well as any expenses incurred by the Company relating to collecting the amounts called. The Board of Directors shall be entitled to collect the moneys which have been forfeited, or part thereof, as it shall deem fit, but it shall not be obliged to do so.

37. The provisions of these Articles in regard to forfeiture shall also apply to cases of non-payment of any amount, which, according to the terms of issue of the share, or which under the conditions of allotment the due date for payment of which fell on a fixed date, whether this be on account of the nominal value of the share or in the form of a premium, as if such amount was payable pursuant to a call duly made and notified.

38. The Company shall have a first and paramount lien over all the shares which have not been fully paid up and which are registered in the name of any Shareholder (whether individually or jointly with others) and also over the proceeds of the sale thereof, as security for the debts and obligations of such Shareholder to the Company and his contractual engagements with it, either individually or together with others. This right of lien shall apply whether or not the due date for payment of such debts or the fulfillment or performance of such obligations has arrived, and no rights in equity shall be created in respect of any share, over which there is a lien as aforesaid. The aforesaid lien shall apply to all dividends or benefits which may be declared, from time to time, on such shares, unless the Board of Directors shall decide otherwise.

39. In order to foreclose on such lien, the Board of Directors may sell the shares under lien at such time and in such manner as, it shall deem fit, but no share may be sold unless the period referred to below has elapsed and written notice has been given to the Shareholder, his trustee, liquidator, receiver, the executors of his estate, or anyone who acquires a right to shares in consequence of the bankruptcy of a Shareholder, as the case may be, stating that the Company intends to sell the shares, if he or they should fail to pay the aforesaid debts, or fail to discharge or fulfill the aforesaid obligations within fourteen (14) business days from the date of the delivery of the notice.

40. The net proceeds of any such sale of shares, as contemplated by Article 39 above, after deduction of the expenses of the sale, shall serve for the discharge of the debts of such shareholder or for performance of such Shareholder's obligations (including debts, undertakings and contractual engagements the due date for the payment or performance of which has arrived) and the surplus, if any, shall be paid to the Shareholder, his trustee, liquidator, receiver, guardians, the executors of his estate, or to his successors-in-title.

41. In every case of a sale following forfeiture or waiver, or for purposes of executing a lien by exercising all of the powers conferred above, the Board of Directors shall be entitled to appoint a person to sign an instrument of transfer of the shares sold, and to arrange for the registration of the name of the buyer in the Register in respect of the shares sold.

42. An affidavit signed by the Chairman of the Board of Directors that a particular share of the Company was forfeited, waived or sold by the Company by virtue of a lien, shall serve as conclusive evidence of the facts contained therein as against any person claiming a right in the share. The purchaser of a share who relies on such affidavit shall not be obliged to investigate whether the sale, re-allotment or transfer, or the amount of consideration and the manner of application of the proceeds of the sale, were lawfully effected, and after his name has been registered in the Register he shall have a full right of title to the share and such right shall not be adversely affected by a defect or invalidity which occurred in the forfeiture, waiver, sale, re-allotment or transfer of the share.

TRANSFER AND TRANSMISSION OF SHARES

43. No transfer of shares shall be registered unless a proper instrument of transfer is delivered to the Company or, in the case of shares registered with a transfer agent, delivered to such transfer agent or to such other place specified for this purpose by the Board of Directors. Subject to the provisions of these Articles, an instrument of transfer of a share in the Company shall be signed by the transferor and the transferee. The Board of Directors may approve other methods of recognizing the transfer of shares in order to facilitate the trading of the Company's shares on the Nasdaq Global Market or on any other stock exchange. The transferor shall be deemed to remain the holder of the share up until the time the name of the transferee is registered in the Register in respect of the transferred share.

44. Insofar as the circumstances permit, the instrument of transfer of a share shall be substantially in the form set out below, or in any other form that the Board of Directors may approve (the "**Deed of Transfer**").

I _____, I.D. _____ of _____ (the "**Transferor**"), in consideration for an amount of NIS _____ (in words) paid to me by _____ I.D. _____ of _____ (hereinafter: the "**Transferee**"), hereby transfer to the Transferee _____ _____ shares of nominal value NIS _____ each, marked with the numbers _____ to _____ (inclusive) of a company known as MediWound Ltd., to be held by the Transferee, the acquires of his rights and his successors-in title, under all the same conditions under which I held same prior to the signing of this instrument, and I, the Transferee, hereby agree to accept the aforementioned share in accordance with the above mentioned conditions.

In witness whereof we have hereunto signed this _____ day of _____ 20__.

Transferor _____ Transferee _____

Witnesses to Signature _____

45. The Company may close the transfer registers and the Register for such period of time as the Board of Directors shall deem fit.

46. Every instrument of transfer shall be submitted to the Office or to such other place as the Board of Directors shall prescribe, for purposes of registration, together with the share certificates to be transferred, or if no such certificate was issued, together with a letter of allotment of the shares to be transferred, and/or such other proof as the Board of Directors may demand in regard to the transferor's right of title or his right to transfer the shares. The Board of Directors shall have the right to refuse to recognize an assignment of shares until the appropriate securities under the circumstances have been provided, as shall be determined by the Board of Directors in a specific case or from time to time in general. Instruments of transfer which serve as the basis for transfers that are registered shall remain with the Company.

47. Every instrument of transfer shall relate to one class of shares only, unless the Board of Directors shall otherwise agree.

48. The executors of the will or administrator of a deceased Shareholder's estate (such Shareholder not being one of a joint owners of a share) or, in the absence of an administrator of the estate or executor of the will, the persons specified in Article 49 below, shall be entitled to demand that the Company recognize them as owners of rights in the share. The provisions of Article 46 above shall apply, *mutatis mutandis*, also in regard to this Article.

49. In the case of the death of one of the holders of a share registered in the names of two or more Persons, the Company shall recognize only the surviving owners as Persons having rights in the share. However, the aforementioned shall not be construed as releasing the estate of a deceased joint Shareholder from any and all undertakings in respect of the shares. Any Person who shall become an owner of shares following the death of a Shareholder shall be entitled to be registered as owner of such shares after having presented to an officer of the Company to be designated by the Chief Executive Officer an inheritance order or probation order or order of appointment of an administrator of estate and any other proof as required - if these are sufficient in the opinion of such officer - testifying to such Person's right to appear as shareholder in accordance with these Articles, and which shall testify to his title to such shares. The provisions of Article 46 above shall apply, *mutatis mutandis*, also in regard to this Article.

50. The receiver or liquidator of a Shareholder who is a company or the trustee in bankruptcy or the official receiver of a Shareholder who is bankrupt, upon presenting appropriate proof to the satisfaction of an officer of the Company to be designated by the Chief Executive Officer that such Shareholder has the right to appear in this capacity and which testifies to such Shareholder's title, may, with the consent of the Board of Directors (the Board of Directors shall not be obligated to give such consent) be registered as the owner of such shares. Furthermore, such Shareholder may assign such shares in accordance with the rules prescribed in these Articles. The provisions of Article 46 above shall apply, *mutatis mutandis*, also in regard to this Article.

51. A Person entitled to be registered as a Shareholder following assignment pursuant to these Articles shall be entitled, if approved by the Board of Directors and to the extent and under the conditions prescribed by the Board of Directors, to dividends and any other monies paid in respect of the shares, and shall be entitled to give the Company confirmation of the payments; however, he shall not be entitled to be present or to vote at any General Meeting of the Company or, subject to the provisions of these Articles, to make use of any rights of Shareholders, until he has been registered as owner of such shares in the Register.

GENERAL MEETING

52. A General Meeting shall be held at least once in every year, not later than 15 (fifteen) months after the last General Meeting, at such time and at such place as the Board of Directors shall determine. Such General Meeting shall be called an annual meeting, and all other meetings of the Shareholders shall be called extraordinary meetings.

53. The Board of Directors may call an extraordinary meeting whenever it sees fit to do so.

54. The Board of Directors shall be obliged to call an extraordinary meeting upon a requisition in writing in accordance with the Companies Law.

55. The Company shall provide prior notice in regard to the holding of an annual meeting or an extraordinary meeting in accordance with the requirements of these Articles, the Companies Law and the regulations promulgated thereunder. Subject to the provisions of the Companies Law and the regulations promulgated thereunder, in counting the number of days of prior notice given, the day of publication of notice shall not be counted, but the day of the meeting shall be counted. The notice shall specify those items and contain such information as shall be required by the Companies Law, the regulations promulgated thereunder and any other applicable law and regulations.

56. Any Shareholder (a "**Proposing Shareholder**")requesting to add an item to the agenda of a General Meeting may submit such a request (a "**Proposal Request**") in accordance with the Companies Law. Subject to any requirements under the Law, to be considered timely and thereby be added to such agenda, a Proposal Request must be delivered, either in person or by certified mail, postage prepaid, and received at the Office, (i) in the case of a General Meeting that is an annual meeting, no less than sixty (60) days nor more than one-hundred twenty (120) days prior to the date of the first anniversary of the preceding year's annual meeting, provided, however, that, in the event that the date of the annual meeting is advanced more than thirty (30) days prior to or delayed by more than thirty (30) days after the anniversary of the preceding year's annual meeting, notice by the Proposing Shareholder to be timely must be so received not earlier than the close of business one-hundred twenty (120) days prior to such annual meeting and not later than the close of business on the later of ninety (90) days prior to such annual meeting or the tenth (10^{th}) day following the day on which public announcement of the date of such meeting is first made, and (ii) in the case of a General Meeting that is an extraordinary meeting, no earlier than one-hundred twenty (120) days prior to such extraordinary meeting and no later than sixty (60) days prior to such extraordinary meeting or the tenth (10^{th}) day following the day on which public announcement of the date of such meeting is first made, subject to applicable law.

In no event shall the public announcement of an adjournment or postponement of a General Meeting commence a new time period (or extend any time period) for the giving of a Shareholder's notice as described above. Subject to any requirements under the Companies Law, nominations of persons for election to the Board of Directors may only be made at an extraordinary meeting if directors are to be elected at such meeting (a) by or at the direction of the Board of Directors, or (b) by any shareholder who is entitled to vote at the meeting and who complies with the notice procedures set forth in this Article. Such request shall also set forth: (i) the name and address of the Proposing Shareholder making the request; (ii) a representation that the Proposing Shareholder is a holder of record of shares of the Company entitled to vote at such meeting and intends to appear in person or by proxy at the meeting; (iii) a description of all arrangements or understandings between the Proposing Shareholder and any other Person or Persons (naming such Person or Persons) in connection with the subject which is requested to be included in the agenda; (iv) a description of all Derivative Transactions (as defined below) by the Proposing Shareholder during the previous twelve (12) month period, including the date of the transactions and the class, series and number of securities involved in, and the material economic terms of, such Derivative Transactions; and (v) a declaration that all the information that is required under the Companies Law and any other applicable law to be provided to the Company in connection with such subject, if any, has been provided. Furthermore, the Board of Directors, may, in its discretion, to the extent it deems necessary, request that the Proposing Shareholder(s) provide additional information necessary so as to include a subject in the agenda of a General Meeting, as the Board of Directors may reasonably require.

A "**Derivative Transaction**" means any agreement, arrangement, interest or understanding entered into by, or on behalf or for the benefit of, any Proposing Shareholder or any of its affiliates or associates, whether of record or beneficial: (a) the value of which is derived in whole or in part from the value of any class or series of shares or other securities of the Company, (b) which otherwise provides any direct or indirect opportunity to gain or share in any gain derived from a change in the value of securities of the Company, (c) the effect or intent of which is to mitigate loss, manage risk or benefit of security value or price changes, or (d) which provides the right to vote or increase or decrease the voting power of such Proposing Shareholder, or any of its affiliates or associates, with respect to any shares or other securities of the Company, which agreement, arrangement, interest or understanding may include, without limitation, any option, warrant, debt position, note, bond, convertible security, swap, stock appreciation right, short position, profit interest, hedge, right to dividends, voting agreement, performance-related fee or arrangement to borrow or lend shares (whether or not subject to payment, settlement, exercise or conversion in any such class or series), and any proportionate interest of such Proposing Shareholder in the shares or other securities of the Company held by any general or limited partnership, or any limited liability company, of which such Proposing Shareholder is, directly or indirectly, a general partner or managing member. The information required pursuant to this Article 56 shall be updated as of the record date of the General Meeting, five (5) business days before the General Meeting, and any adjournment or postponement thereof.

57. Subject to Article 65 below, in the event that the Company has established that an adjourned meeting shall be held on such date which is later than the date provided for in Section 78(b) of the Companies Law, such later date shall be included in the notice. The Company may add additional places for Shareholders to review the full text of the proposed resolutions, including an internet site. The notice shall be provided in the manner prescribed below under the heading "Notices" in Articles 128 to 131 below.

PROCEEDINGS AT GENERAL MEETING

58. No business shall be conducted at a General Meeting unless a quorum is present, and no resolution shall be passed unless a quorum is present at the time the resolution is voted on. Except in cases where it is otherwise stipulated, a quorum shall be constituted when there are personally present, or represented by proxy, at least two (2) Shareholders who hold, in the aggregate, at least 25% of the voting rights in the Company. A proxy may be deemed to be two (2) or more Shareholders pursuant to the number of Shareholders he represents.

59. If within half an hour from the time appointed for the meeting, a quorum is not present, without there being an obligation to notify the Shareholders to that effect, the meeting shall be adjourned to the same day, in the following week, at the same hour and at the same place or to a later time and date if so specified in the notice of the meeting, unless such day shall fall on a statutory holiday (either in Israel or in the United States), in which case the meeting will be adjourned to the first business day afterwards which is not a statutory holiday.

If the original meeting was convened upon requisition under Section 63 of the Companies Law, one or more Shareholders, present in person or by proxy, and holding the number of shares required for making such requisition, shall constitute a quorum at the adjourned meeting, but in any other case any two (2) Shareholders present in person or by proxy, shall constitute a quorum at the adjourned meeting.

60. The Chairman of the Board of Directors, or any other Person appointed for this purpose by the Board of Directors, shall preside at every General Meeting. If within fifteen (15) minutes from the time appointed for the meeting, the designated chairman for the meeting shall not be present, the Shareholders present at the meeting shall elect one of their number to serve as chairman of the meeting.

61. Resolutions at the General Meeting shall be passed in accordance with the definition of "Resolution" set forth in Article 1.1 above, unless otherwise required by Companies Law or these Articles. Every vote at a General Meeting shall be conducted according to the number of votes to which each Shareholder is entitled on the basis of the number of Ordinary Shares held by such Shareholder (in accordance with the provisions of Article 7.1 above).

62. Where a poll has been demanded, the chairman of the meeting shall be entitled - but not obliged - to accede to the demand. Where the chairman of the meeting has decided to hold a poll, such poll shall be held in such manner, at such time and at such place as the chairman of the meeting directs, either immediately or after an interval or postponement, or in any other way, and the results of the vote shall be deemed to be the Resolution at the meeting at which the poll was demanded. A person demanding a poll may withdraw his demand prior to the poll being held.

63. A demand for the holding of a poll shall not prevent the continued business of the meeting on all other questions apart of the question in respect of which a poll was demanded.

64. The announcement by the chairman of the meeting that a Resolution has been passed unanimously or by a particular majority, or has been rejected, and a note recorded to that effect in the Company's minute book, shall serve as *prima facie* proof of such fact, and there shall be no necessity for proving the number of votes or the proportion of votes given for or against the Resolution, unless otherwise required under applicable law and regulation.

65. The Chairman of a General Meeting at which a quorum is present may, with the consent of holders of a majority of the voting power represented in person and by proxy and voting on the question of adjournment, adjourn the meeting from time to time and from place to place, but no business shall be transacted at any adjourned meeting except business which might lawfully have been transacted at the meeting as originally called. Subject to these Articles, it shall not be necessary to give any notice of an adjournment unless the meeting is adjourned for more than twenty-one (21) days, in which case notice thereof shall be given in the manner required for the meeting as originally called. Where a General Meeting has been adjourned without changing its agenda, to a date which is not more than twenty-one (21) days, notices shall be given for the new date, as early as possible, and by no later than seventy-two (72) hours before the General Meeting.

VOTES OF SHAREHOLDERS

66. The voting rights of every shareholder entitled to vote at a General Meeting shall be as set forth in Article 7.1 of these Articles.

67. In the case of joint Shareholders, the vote of the senior joint holder, given personally or by proxy, shall be accepted, to the exclusion of the vote of the remaining joint Shareholders, and for these purposes the senior of the joint Shareholders shall be the Person amongst the joint holders whose name appears first in the Register.

68. A Shareholder who is an Incapacitated Person may vote solely through his guardian or other person who fulfills the function of such guardian and who was appointed by a court, and any guardian or other person as aforesaid shall be entitled to vote by way of a proxy, or in such manner as the court directs.

69. Any corporation which is a Shareholder of the Company shall be entitled, by way of resolution of its board of directors or another organ which manages said corporation, to appoint such person which it deems fit, whether or not such person is a Shareholder of the Company, to act as its representative at any General Meeting of the Company or at a meeting of a class of shares in the Company which such corporation is entitled to attend and to vote thereat, and the appointed as aforesaid shall be entitled, on behalf of the corporation whom he represents, to exercise all of the same powers and authorities which the corporation itself could have exercised had it been a natural person holding shares of the Company.

70. Every Shareholder who is entitled to attend and vote at a General Meeting of the Company, shall be entitled to appoint a proxy. A proxy can be appointed by more than one Shareholder, and vote in different ways on behalf of each principal.

The instrument appointing a proxy shall be in writing signed by the Person making the appointment or by his authorized representative, and if the Person making the appointment is a corporation, the power of attorney shall be signed in the manner in which the corporation signs on documents which bind it, and a certificate of an attorney with regard to the authority of the signatories to bind the corporation shall be attached thereto. The proxy need not be a shareholder of the Company.

71. The instrument appointing a proxy, or a copy thereof certified by an attorney, shall be lodged at the Office, or at such other place as the Board of Directors shall specify, not less than forty-eight (48) hours prior to the meeting at which the proxy intends to vote based on such instrument of proxy. Notwithstanding the above, the chairman of the meeting shall have the right to waive the time requirement provided above with respect to all instruments of proxies and to accept any and all instruments of proxy until the beginning of a General Meeting. A document appointing a proxy shall be valid for every adjourned meeting of the meeting to which the document relates.

72. Every instrument appointing a proxy, whether for a meeting specifically indicated, or otherwise, shall, as far as circumstances permit, be substantially in the following form, or in any other form approved by the Board of Directors:

I _____ of _____ being a shareholder holding voting shares in MediWound Ltd., hereby appoint Mr. _____ of _____ or failing him, Mr. _____ of _____, or failing him, Mr. _____ of _____, to vote in my name, place and stead at the (ordinary/extraordinary) General Meeting of the Company to be held on the ____ of _____ 20__, and at any adjourned meeting thereof.

In witness whereof I have hereto set my hand on the _____ day of _____.

73. No Shareholder shall be entitled to vote at a General Meeting unless he has paid all of the calls and all of the amounts due from him, for the time being, in respect of his shares.

74. A vote given in accordance with the instructions contained in an instrument appointing a proxy shall be valid notwithstanding the death or bankruptcy of the appointer, or the revocation of the proxy, or the transfer of the share in respect of which the vote was given as aforesaid, unless notice in writing of the death, revocation or transfer is received at the Office, or by the chairman of the meeting, prior to such vote.

75. Subject to the Companies Law, an instrument appointing a proxy shall be deemed revoked (i) upon receipt by the Company or the chairman of the meeting, subsequent to receipt by the Company of such instrument, of written notice signed by the person signing such instrument or by the Shareholder appointing such proxy canceling the appointment thereunder (or the authority pursuant to which such instrument was signed) or of an instrument appointing a different proxy, provided such notice of cancellation or instrument appointing a different proxy were so received at the place and within the time for delivery of the instrument revoked thereby as referred to in Article 71 hereof, or (ii) if the appointing shareholder is present in person at the meeting for which such instrument of proxy was delivered, upon receipt by the chairman of such meeting of written notice from such shareholder of the revocation of such appointment, or if and when such Shareholder votes at such meeting. A vote cast in accordance with an instrument appointing a proxy shall be valid notwithstanding the revocation or purported cancellation of the appointment, or the presence in person or vote of the appointing Shareholder at a meeting for which it was rendered, unless such instrument of appointment was deemed revoked in accordance with the foregoing provisions of this Article 75 at or prior to the time such vote was cast.

THE BOARD OF DIRECTORS

76. Unless otherwise resolved by a Resolution, the prescribed number of Directors of the Company shall be between five (5) and nine (9) (including the External Directors), as may be fixed, from time to time, by the Board of Directors. At any time the minimum number of Directors (other than the External Directors) shall not fall below three (3). Any Director shall be eligible for re-election upon termination of his term of office, subject to applicable law.

77.

77.1. Prior to every annual General Meeting of the Company, the Board of Directors of the Company (or a Committee of Directors) shall select, via a resolution adopted by a majority of the Board of Directors (or such committee), a number of persons to be proposed to the Shareholders for election as directors of the Company at such annual General Meeting for service until the annual General Meeting to be held in the next year following the year of their election (the "**Nominees**"). Any shareholder entitled under applicable law to nominate one or more persons for election as directors at a General Meeting (each such person, an "**Alternate Nominee**") may make such nomination only if a written notice of such shareholder's intent to make such nomination or nominations has been given to the Secretary of the Company (or, if there is no such Secretary, the Chief Executive Officer). Each such notice shall set forth: (a) the name and address of the shareholder who intends to make the nomination and of the Alternate Nominees; (b) a representation that the shareholder is a holder of record of shares of the Company entitled to vote at such meeting (including the number of shares held of record by the shareholder) and intends to appear in person or by proxy at the meeting to nominate the Alternate Nominees; (c) a description of all arrangements or understandings between the shareholder and each Alternate Nominee and any other person or persons (naming such person or persons) pursuant to which the nomination or nominations are to be made by the shareholder; and (d) the consent of each Alternate Nominee to serve as a director of the Company if so elected and a declaration signed by each Alternate Nominee declaring that there is no limitation under the Companies Law for the appointment of such a nominee and that all of the information that is required under the Companies Law to be provided to the Company in connection with such an appointment has been provided. The Board of Directors may refuse to acknowledge the nomination of any person not made in compliance with the foregoing procedure.

77.2. The Nominees or Alternate Nominees shall be elected by a Resolution at the annual General Meeting at which they are subject to election.

77.3. Every director shall hold office until the end of the next annual General Meeting following the annual General Meeting at which he was elected, unless his office is vacated in accordance with Article 79 or Article 82 below. If, at an annual General Meeting, no Nominees or Alternate Nominees are elected, the directors then in office shall continue to hold office until the convening of a General Meeting at which Nominees or Alternate Nominees shall be elected.

77.4. If the office(s) of members(s) of the Board of Directors shall be vacated, the remaining members of the Board of Directors shall be entitled to appoint additional director(s) in place of the director(s) whose office(s) have been vacated, for a term of office equal to the remaining period of the term of office of the director(s) whose office(s) have been vacated.

78. The Directors in their capacity as such shall be entitled to receive remuneration as shall be determined in compliance with the Companies Law and the regulations promulgated thereunder. The conditions (including remuneration) of the terms of office of members of the Board of Directors shall be decided by the Board of Directors and/or any committee thereof, but the same shall be valid only if ratified in the manner required under the Companies Law. The remuneration of Directors may be fixed as an overall payment or other consideration and/or as a payment or other consideration in respect of attendance at meetings of the Board of Directors. In addition to his remuneration, each Director shall be entitled to be reimbursed, retroactively or in advance, in respect of his reasonable expenses connected with performing his functions and services as a Director. Such entitlement shall be determined in accordance with, and shall be subject to, a specific resolution or policy adopted by the Board of Directors regarding such matter and in accordance with the requirements of applicable law.

79.

79.1. Subject to the provisions of the Companies Law with regard to External Directors and subject to Article 77 above and Article 82 below, the office of a member of the Board of Directors shall be vacated in any one of the following events:

79.1.1. if he resigns his office by way of a letter signed by him, lodged at the Office;

79.1.2. if he is declared bankrupt;

79.1.3. if he becomes insane or unsound of mind;

79.1.4. upon his death;

79.1.5. if he is prevented by applicable law from serving as a Director of the Company;

79.1.6. if the Board terminates his office according to Section 231 of the Companies Law;

79.1.7. if a court order is given in accordance with Section 233 of the Companies Law;

79.1.8. if he is removed from office by a Resolution at a General Meeting of the Company adopted by a majority of the voting power in the Company; or

79.1.9. if his period of office has terminated in accordance with the provisions of these Articles.

79.2. If the office of a member of the Board of Directors should be vacated, the remaining members of the Board of Directors shall be entitled to act for all purposes, for as long as their number does not fall below the minimum, for the time being, specified for the Directors, as prescribed in Article 76 above. Should their number fall below the aforesaid minimum, the Directors shall not be entitled to act, except for the appointment of additional directors, or for the purpose of calling a General Meeting for the appointment of additional directors, or for the purpose of calling a General Meeting for the appointment of a new Board of Directors.

79.3. The office of an External Director shall be vacated only in accordance with the provisions for the vacation of office and the removal of External Directors under the Companies Law.

OTHER PROVISIONS REGARDING DIRECTORS

80.

80.1. Subject to any mandatory provisions of applicable law, a Director shall not be disqualified by virtue of his office from holding another office in the Company or in any other company in which the Company is a shareholder or in which it has any other form of interest, or of entering into a contract with the Company, either as seller or buyer or otherwise. Likewise, no contract made by the Company or on its behalf in which a Director has any form of interest may be nullified and a Director shall not be obliged to account to the Company for any profit deriving from such office, or resulting from such contract, merely by virtue of the fact that he serves as a Director or by reason of the fiduciary relationship thereby created, but such Director shall be obliged to disclose to the Board of Directors the nature of any such interest at the first opportunity.

A general notice to the effect that a Director is a shareholder or has any other form of interest in a particular firm or a particular company and that he must be deemed to have an interest in any business with such firm or company shall be deemed to be adequate disclosure for purposes of this Article in relation to such Director, and after such general notice has been given, such Director shall not be obliged to give special notice in relation to any particular business with such firm or such company.

80.2. Subject to the provisions of the Companies Law and these Articles, the Company shall be entitled to enter into a transaction in which an Office Holder of the Company has a personal interest, directly or indirectly, and may enter into any contract or otherwise transact any business with any third party in which contract or business an Office Holder has a personal interest, directly or indirectly.

81. The Board of Directors shall elect one (1) or more of its members to serve as the Chairman of the Board of Directors (the "**Chairman of the Board of Directors**"), provided that, subject to the provisions of Section 121(c) of the Companies Law, the Chief Executive Officer of the Company shall not serve as Chairman of the Board of Directors. The office of Chairman of the Board of Directors shall be vacated in each of the cases mentioned in Articles 79.1 above and 82 below. The Board of Directors may also elect one or more members to serve as Vice Chairman, who shall have such duties and authorities as the Board of Directors may assign to him or her.

82. Subject to the relevant provisions of the Companies Law, the Company may, in a General Meeting, by a Resolution adopted by a majority of the voting power in the Company, dismiss any Director, prior to the end of his term of office and the Board of Directors shall be entitled, by regular majority, with the exception of the External Directors who shall be appointed and removed in accordance with the Companies Law, to appoint another individual in his place as a Director. The individual so appointed shall hold such office only for that period of time during which the director whom he replaces would have held office.

83. A Director shall not be obliged to hold any share in the Company.

CHIEF EXECUTIVE OFFICER

84.

84.1. The Board of Directors shall, from time to time, appoint a Chief Executive Officer and subject to the provisions of the Companies Law delineate his powers and authorities and his remuneration. Subject to any contract between the Chief Executive Officer and the Company, the Board of Directors may dismiss him or replace him at any time it deems fit.

84.2. A Chief Executive Officer need not be a Director or Shareholder.

Subject to the provisions of any contract between the Chief Executive Officer and the Company, if the Chief Executive Officer is also a Director, all of the same provisions with regard to appointment, resignation and removal from office shall apply to the Chief Executive Officer in his capacity as a Director, as apply to the Company's other Directors.

84.3. The Board of Directors shall be entitled from time to time to delegate to the Chief Executive Officer for the time being such of the powers it has pursuant to these Articles as they deem appropriate, and the Board of Directors shall be entitled to grant such powers for such period and for such purposes and on such conditions and with such restrictions as it deem appropriate, and it shall be entitled to grant such powers without renouncing the powers and authorities of the Board of Directors in such regard, and it may, from time to time, revoke, annul and alter such delegated powers and authorities, in whole or in part.

84.4. Subject to the provisions of any applicable law, the remuneration of the Chief Executive Officer shall be fixed from time to time by the Board of Directors (and, so long as required by the Companies Law, shall be approved by the Compensation Committee and by the Shareholders unless exempted from Shareholders approval) and such remuneration may be in the form of a fixed salary or commissions or a participation in profits, or in any other manner which may be decided by the Board of Directors (and approved according to this Article 84.4).

PROCEEDINGS OF THE BOARD OF DIRECTORS

85.

85.1. The Board of Directors shall convene for a meeting at least once every fiscal quarter.

85.2. The Board of Directors may meet in order to exercise its powers pursuant to Section 92 of the Companies Law, including without limitation to supervise the Company's affairs, and it may, subject to the provisions of the Companies Law, adjourn its meetings and regulate its proceedings and operations as it deems fit. It may also prescribe the quorum required for the conduct of business. Until otherwise decided a quorum shall be constituted if a majority of the Directors holding office for the time being are present.

85.3. Should a Director or Directors be barred from being present and voting at a meeting of the Board of Directors pursuant to Section 278 of the Companies Law, the quorum shall be a majority of the Directors entitled to be present and to vote at the meeting of the Board of Directors.

86. Any Director, the Chief Executive Officer or the auditor of the Company in the event stipulated in Section 169 of the Companies Law, may, at any time, demand the convening of a meeting of the Board of Directors. The Chairman of the Board shall be obliged, on such demand, to call such meeting on the date requested by the Director, the Chief Executive Officer or the auditor of the Company soliciting such a meeting, provided that proper notice pursuant to Article 87 is given.

87. Every Director shall be entitled to receive notice of meetings of the Board of Directors, and such notice may be in writing or by facsimile, or electronic mail, sent to the last address (whether physical or electronic) or facsimile number given by the Director for purposes of receiving notices, provided that the notice shall be given at least a reasonable amount of time prior to the meeting and in no event less than 48 (forty eight) hours prior notice, unless the urgency of the matter(s) to be discussed at the meeting reasonably require(s) a shorter notice period.

88. Every meeting of the Board of Directors at which a quorum is present shall have all the powers and authorities vested for the time being in the Board of Directors.

89. Questions which arise at meetings of the Board of Directors shall be decided by a simple majority of the members of the Board of Directors attending such meeting and voting on such matter. In the case of an equality of votes of the Board of Directors, the Chairman of the Board of Directors shall not have a second or casting vote, and the proposal shall be deemed to be defeated.

If the Chairman of the Board of Directors is not present within 30 (thirty) minutes after the time appointed for the meeting, the Directors present shall elect one of their members to preside at such meeting.

90. The Board of Directors may adopt resolutions, without actually convening a meeting of the Board of Directors, provided that all the Directors entitled to participate in the meeting and to vote on the subject brought for decision agree thereto. If resolutions are made as stated in this Article 90, the Chairman of the Board of Directors shall record minutes of the decisions stating the manner of voting of each Director on the subjects brought for decision, as well as the fact that all the Directors agreed to take the decision without actually convening.

91. The Board of Directors may hold meetings by use of any means of communication, on condition that all participating Directors can hear each other at the same time. In the case of a resolution passed by way of a telephone call or any such other means of communication, a copy of the text of the resolution shall be sent, as soon as possible thereafter, to the Directors.

GENERAL POWERS OF THE BOARD OF DIRECTORS

92. The supervision of the Company's affairs shall be in the hands of the Board of Directors, which shall be entitled to exercise all of the powers and authorities to perform any act and deed which the Company is entitled to exercise and to perform in accordance with these Articles or according to the Companies Law, and in respect of which there is no provision or requirement in these Articles, or in the Companies Law or/and in the U.S. Rules, that such powers and authorities may be exercised or done by the Shareholders in a General Meeting or by a Committee of Directors.

93. The Board of Directors may, as it deems fit and subject to any applicable law, delegate to a committee (a "**Committee of Directors**") certain of its powers and authorities, in whole or in part (as appropriate). The curtailment or revocation of the powers and authorities of a Committee of Directors by the Board of Directors shall not invalidate a prior act of such Committee of Directors or an act taken in accordance with its instructions, which would have been valid had the powers and authorities of the Committee of Directors not been altered or revoked by the Board of Directors. Subject to applicable law, a Committee of Directors may be comprised of one (1) Director or of several Directors, and in the case of a Committee of Directors that is appointed to advise the Board of Directors only, persons who are not Directors may be appointed to it.

94. The meetings and proceedings of every such Committee of Directors which is comprised of 2 (two) or more members shall be conducted in accordance with the provisions contained in these Articles in regard to the conduct of meetings and proceedings of the Board of Directors to the extent that the same are suitable for such committee, and so long as no provisions have been adopted in replacement thereof by the Board of Directors.

RATIFICATION OF ACTIONS

95. Subject to the Companies Law, all acts taken in good faith by the Board of Directors and/or a Committee of Directors or by an individual acting as a member thereof shall be valid even if it is subsequently discovered that there was a defect in the appointment of the Board of Directors, the Committee of Directors or the member, as the case may be, or that the members, or one of them, was/were disqualified from being appointed as a Director/s or to a Committee of Directors.

96.

96.1. The Board of Directors or any Committee of Directors may ratify any act the performance of which at the time of the ratification was within the scope of the authority of the Board of Directors or the relevant Committee of Directors.

96.2. The General Meeting shall be entitled to ratify any act taken by the Board of Directors and/or any Committee of Directors without authority or which was tainted by some other defect.

96.3. From the time of the ratification, every act ratified as aforesaid, shall be treated as though lawfully performed from the outset.

97. The Board of Directors may, from time to time, in its absolute discretion, borrow or secure any amounts of money required by the Company for the conduct of its business.

98. The Board of Directors shall be entitled to raise or secure the repayment of an amount obtained by them, in such way and on such conditions and times as they deem fit. The Board of Directors shall be entitled to issue documents of undertaking, such as options, debentures or debenture stock, whether linked or redeemable, convertible debentures or debentures convertible into other securities, or debentures which carry a right to purchase shares or to purchase other securities, or any mortgage, pledge, collateral or other charge over the property of the Company and its undertaking, in whole or in part, whether present or future, including the uncalled share capital or the share capital which has been called but not yet paid.

The deeds of undertaking, debentures of various types or other forms of collateral security may be issued at a discount, at a premium or otherwise and with such preferential or deferred or other rights, as the Board of Directors shall, from time to time, decide.

SIGNING POWERS

99. Subject to any other resolution on the subject passed by the Board of Directors, the Company shall be bound only pursuant to a document in writing bearing its seal or its rubber stamp or its printed name, and the signature of whomever may be authorized by the Board of Directors, which shall be entitled to empower any person, either alone or jointly with another, even if he is not a Shareholder or a Director, to sign and act in the name and on behalf of the Company.

100. The Board of Directors shall be entitled to prescribe separate signing power in regard to different businesses of the Company and in respect of the limit of the amounts in respect of which various persons shall be authorized to sign.

SECRETARY, OFFICE-HOLDERS, CLERKS AND REPRESENTATIVES

101. The Board of Directors shall be entitled, from time to time, to appoint, or to delegate to the Chief Executive Officer, either alone or together with other persons designated by the Board of Directors, the ability to appoint Office Holders (other than Directors), a Secretary for the Company, employees and agents to such permanent, temporary or special positions, and to specify and change their titles, authorities and duties, and may set, or delegate to the Chief Executive Officer, either alone or together with other persons designated by the Board of Directors, the ability to set salaries, bonuses and other compensation of any employee or agent who is not an Office Holder. Salaries, bonuses and compensation of Office Holders who are not Directors shall be determined and approved by the Chief Executive Officer, and/or in such other manner as may be required from time to time under the Companies Law. The Board of Directors, or the Chief Executive Officer, either alone or together with other persons designated by the Board of Directors, (in the case of any Office Holder, employee or agent appointed thereby), shall be entitled at any time, in its, his or their (as applicable) sole and absolute discretion, to terminate the services of one of more of the foregoing persons (in the case of a Director, however, subject to compliance with Article 79 above), subject to any other requirements under applicable law.

102. The Board of Directors and the Chief Executive Officer may from time to time and at any time, subject to their powers under these Articles and the Companies Law, empower any person to serve as representative of the Company for such purposes and with such powers and authorities, instructions and discretions for such period and subject to such conditions as the Board of Directors (or the Chief Executive Officer, as the case may be) shall deem appropriate. Consistent with the preceding sentence, the Board of Directors (or the Chief Executive Officer, as the case may be) may grant such person, *inter alia*, the power to transfer the authority, powers and discretions vested in him, in whole or in part. The Board of Directors may (or the Chief Executive Officer, as the case may be), from time to time, revoke, annul, vary or change any such power or authority, or all such powers or authorities collectively.

DIVIDENDS, BONUS SHARES, FUNDS AND CAPITALIZATION OF FUNDS AND PROFITS

103. Unless otherwise permitted by the Companies Law, no dividends shall be paid other than out of the Company's profits available for distribution as set forth in the Companies Law.

104. The Board of Directors may decide on the payment of a dividend or on the distribution of bonus shares.

105. A dividend in cash or bonus shares shall be paid or distributed, as the case may be, equally to the holders of the Ordinary Shares registered in the Register, pro rata to the nominal amount of capital paid up or credited as paid up on par value of the shares, without reference to any premium which may have been paid thereon. However, whenever the rights attached to any shares or the terms of issue of the shares do not provide otherwise, an amount paid on account of a share prior to the payment thereof having been called, or prior to the due date for payment thereof, and on which the Company is paying interest, shall not be taken into account for purposes of this Article as an amount paid-up on account of the share.

106. Unless other instructions are given, it shall be permissible to pay any dividend by way of a check or payment order to be sent by post to the registered address of the Shareholder or the Person entitled thereto, or in the case of joint Shareholders being registered, to the Shareholder whose name appears first in the Register in relation to the joint shareholding. Every such check shall be made in favor of the Person to whom it is sent. A receipt by the Person whose name, on the date of declaration of the dividend, was registered in the Register as the owner of the shares, or in the case of joint holders, by one of the joint holders, shall serve as a discharge with regard to all the payments made in connection with such share.

The Board of Directors shall be entitled to invest any dividend which has not been claimed for a period of one (1) year after having been declared, or to make use thereof in any other way for the benefit of the Company until such time as it is claimed. The Company shall not be obliged to pay interest or linkage in respect of an unclaimed dividend. The payment by the Board of Directors of any unclaimed dividend into a separate account shall not constitute the Company a trustee in respect thereof, and any dividend unclaimed after a period of seven (7) years from the date of declaration of such dividend, shall be forfeited and shall revert to the Company, provided, however, that the Board of Directors may, at its discretion, cause the Company to pay any such dividend, or any part thereof, to a person who would have been entitled thereto had the same not reverted to the Company.

107. Unless otherwise specified in the terms of issue of shares or securities convertible into, or which grant a right to purchase, shares, any shares that are fully paid-up or credited as paid-up shall at any time confer on their holders the right to participate in the full dividends and in any other distribution for which the determining date for the right to receive the same is the date at which the aforesaid shares were fully paid-up or credited as fully paid-up, as the case may be, or subsequent to such date.

108. A dividend or other beneficial rights in respect of shares shall not bear interest.

109. The Board of Directors shall be entitled to deduct from any dividend or other beneficial rights, all amounts of money which the holder of the share in respect of which the dividend is payable or in respect of which the other beneficial rights were given, may owe to the Company in respect of such share, whether or not the due date for payment thereof has arrived.

110. The Board of Directors shall be entitled to retain any dividend or bonus shares or other beneficial rights in respect of a share in relation to which the Company has a lien, and to utilize any such amount or the proceeds received from the sale of any bonus shares or other beneficial rights, for the discharge of the debts or liabilities in respect of which the Company has a lien.

111. The Board of Directors may decide that a dividend is to be paid, in whole or in part, by way of a distribution of assets of the Company in kind, including by way of debentures or debenture stock of the Company, or shares or debentures or debenture stock of any other company, or in any other way.

112.

112.1. The Board of Directors may, at any time and from time to time, decide that any portion of the amounts standing for the time being to the credit of any capital fund (including a fund created as a result of a revaluation of the assets of the Company), or which are held by the Company as profits available for distribution, shall be capitalized for distribution subject to and in accordance with the provisions of the Companies Law and of these Articles, amongst those Shareholders who are entitled thereto and pro rata to their entitlement under these Articles, provided that the same shall not be paid in cash but shall serve for the payment up in full either at par or with a premium as prescribed by the Company, of shares which have not yet been issued or of debentures of the Company which shall be allotted and distributed amongst the Shareholders in the aforesaid ratio as fully paid-up shares or debentures.

112.2. The Board of Directors shall be entitled to distribute bonus shares and to decide that the bonus shares shall be of the same class which confers on the Shareholders or the Persons entitled thereto the right to participate in the distribution of bonus shares, or may decide that the bonus shares shall be of a uniform class to be distributed to each of the Shareholders or Persons entitled to shares as aforesaid, without reference to the class of shares conferring the right to participate in the distribution on the holders of the shares or the Persons entitled thereto as aforesaid.

113.

113.1. In every case that the Company issues bonus shares by way of a capitalization of profits or funds at a time at which securities issued by the Company are in circulation and confer on the holders thereof rights to convert the same into shares in the share capital of the Company, or options to purchase shares in the share capital of the Company (such rights of conversion or options shall henceforth be referred to as the "**Rights**"), the Board of Directors shall be entitled (in a case that the Rights or part thereof shall not be otherwise adjusted in accordance with the terms of their issue) to transfer to a special fund designated for the distribution of bonus shares in the future (to be called by any name that the Board of Directors may decide on and which shall henceforth be referred to as the "**Special Fund**") an amount equivalent to the nominal amount of the share capital to which some or all of the Rights holders would have been entitled as a result of the issue of bonus shares, had they exercised their Rights prior to the determining date for the right to receive bonus shares, including rights to fractions of bonus shares, and in the case of a second or additional distribution of bonus shares in respect of which the Company acts pursuant to this Article, including entitlement stemming from a previous distribution of bonus shares.

113.2. In the case of the allotment of shares by the Company as a consequence of the exercise of entitlement by the owners of shares in those cases in which the Board of Directors has made a transfer to the Special Fund in respect of the Rights pursuant to Article 113.1 above, the Board of Directors shall allot to each such shareholder, in addition to the shares to which he is entitled by virtue of having exercised his rights, such number of fully paid-up shares the nominal value of which is equivalent to the amount transferred to the Special Fund in respect of his rights, by way of a capitalization to be effected by the Board of Directors of an appropriate amount out of the Special Fund. The Board of Directors shall be entitled to decide on the manner of dealing with rights to fractions of shares in its sole discretion.

113.3. If after any transfer to the Special Fund has been made the Rights should lapse, or the period should end for the exercise of Rights in respect of which the transfer was effected without such Rights being exercised, then any amount which was transferred to the Special Fund in respect of the aforesaid unexercised Rights shall be released from the Special Fund, and the Company may deal with the amount so released in any manner it would have been entitled to deal therewith had such amount not been transferred to the Special Fund.

114. For the implementation of any resolution regarding a distribution of shares or debentures by way of a capitalization of profits as aforesaid, the Board of Directors may:

114.1. Resolve any difficulty which arises or may arise in regard to the distribution in such manner as it deems fit and may take all of the steps that it deems appropriate in order to overcome such difficulty.

114.2. Issue certificates in respect of fractions of shares, or decide that fractions of less than an amount to be decided by the Board of Directors shall not be taken into account for purposes of adjusting the rights of the Shareholders or may sell the fractions of shares and pay the proceeds (net) to the Persons entitled thereto.

114.3. Sign, or appoint a Person to sign, on behalf of the Shareholders on any contract or other document which may be required for purposes of giving effect to the distribution, and, in particular, shall be entitled to sign or appoint a Person who shall be entitled to appoint and submit a contract as referred to in Section 291 of the Companies Law.

114.4. Make any arrangement or other scheme which is required in the opinion of the Board of Directors in order to facilitate the distribution.

115. The Board of Directors shall be entitled, as it deems appropriate and expedient, to appoint trustees or nominees for those registered Shareholders who have failed to notify the Company of a change of their address and who have not applied to the Company in order to receive dividends, shares or debentures out of capital, or other benefits during the aforesaid period. Such trustees or nominees shall be appointed for the use, collection or receipt of dividends, shares or debentures out of capital and rights to subscribe for shares which have not yet been issued and which are offered to the Shareholders but they shall not be entitled to transfer the shares in respect of which they were appointed, or to vote on the basis of holding such shares. In all of the terms and conditions governing such trusts and the appointment of such nominees it shall be stipulated by the Company that upon the first demand by a beneficial holder of a share being held by the trustee or nominee, such trustee or nominee shall be obliged to return to such shareholder the share in question and/or all of those rights held by it on the Shareholder's behalf (all as the case may be). Any act or arrangement effected by any such nominees or trustee and any agreement between the Board of Directors and a nominee or trustee shall be valid and binding in all respects.

116. The Board of Directors may from time to time prescribe the manner for payment of dividends or the distribution of bonus shares and the arrangement connected therewith. Without derogating from the generality of the foregoing, the Board of Directors shall be entitled to pay any dividends or moneys in respect of shares by sending a check via the mails to the address of the holder of registered shares according to the address registered in the register of Shareholders. Any dispatch of a check as aforesaid shall be done at the risk of the shareholder.

In those cases in which the Board of Directors specifies the payment of a dividend, distribution of shares or debentures out of capital, or the grant of a right to subscribe for shares which have not yet been issued and which are offered to the Shareholders against the delivery of an appropriate coupon attached to any share certificate, such payment, distribution or grant of right to subscribe against a suitable coupon to the holder of such coupon, shall constitute a discharge of the Company's debt in respect of such operation as against any person claiming a right to such payment, distribution or grant of right to subscribe, as the case may be.

117. If two (2) or more Persons are registered as joint holders of a share, each of them shall be entitled to give a valid receipt in respect of any dividend, share or debenture out of capital, or other moneys, or benefits, paid or granted in respect of such share.

BOOKS OF THE COMPANY

118. The Board of Directors shall comply with all the provisions of the Companies Law in regard to the recording of charges and the keeping and maintaining of a register of directors, register of Shareholders and register of charges.

119. Any book, register and record that the Company is obliged to keep in accordance with the Companies Law or pursuant to these Articles shall be recorded in a regular book, or by digital, electronic or other means, as the Board of Directors shall decide.

120. Subject to and in accordance with the provisions of Sections 138 and 139 of the Companies Law, the Company may cause supplementary registers to be kept in any place outside Israel as the Board of Directors may deem fit, and, subject to all applicable requirements of the Companies Law, the Board of Directors may from time to time adopt such rules and procedures as it may deem fit in connection with the keeping of such supplementary registers.

BOOKS OF ACCOUNT

121. The Board of Directors shall keep proper books of account in accordance with the provisions of the Companies Law. The books of account shall be kept at the Office, or at such other place or places as the Board of Directors shall deem appropriate, and shall at all times be open to the inspection of members of the Board of Directors. A Shareholder of the Company who is not a member of the Board of Directors shall not have the right to inspect any books or accounts or documents of the Company, unless such right has been expressly granted to him by the Companies Law, or if he has been permitted to do so by the Board of Directors or by the Shareholders based on a Resolution adopted at a General Meeting.

122. [RESERVED]

123. At least once each year the accounts of the Company and the correctness of the statement of income and the balance sheet shall be audited and confirmed by an independent auditor or auditors.

124. The Company shall, in an annual General Meeting, appoint an independent auditor or auditors who shall hold such position until the next annual General Meeting, and their appointment, remuneration and rights and duties shall be subject to the provisions of the Companies Law, provided, however, that in exercising its authority to fix the remuneration of the auditor(s), the Shareholders in an annual General Meeting may, by a Resolution, act (and in the absence of any action in connection therewith shall be deemed to have so acted) to authorize the Board of Directors to fix such remuneration subject to such criteria or standards, if any, as may be provided in such Resolution, and if no such criteria or standards are so provided, such remuneration shall be fixed in an amount commensurate with both the volume and nature of the services rendered by the auditor(s). By an act appointing such auditors, the Company may appoint the auditor(s) to serve for a period of up to the end of completion of the audit of the yearly financial statements for the three (3) year period then ended.

125. The auditors shall be entitled to receive notices of every General Meeting of the Company and to attend such meetings and to express their opinions on all matters pertaining to their function as the auditors of the Company.

126. Subject to the provisions of the Companies Law and the U.S. Rules, any act carried out by the auditors of the Company shall be valid as against any person doing business in good faith with the Company, notwithstanding any defect in the appointment or qualification of the auditors.

127. For as long as the Company is a Public Company, as defined in the Companies Law, it shall appoint an internal auditor possessing the authorities set forth in the Companies Law. The internal auditor of the Company shall present all of its proposed work plans to the Audit Committee of the Board of Directors, which shall have the authority to approve them, subject to any modifications in its discretion.

NOTICES

128.

128.1. The Company may serve any written notice or other document on a Shareholder by way of delivery by hand, by facsimile transmission or by dispatch by prepaid registered mail to his address as recorded in the Register, or if there is no such recorded address, to the address given by him to the Company for the sending of notices to him. Notwithstanding the foregoing or any other provision to the contrary contained herein, notices or any other information or documents required to be delivered to a Shareholder shall be deemed to have been duly delivered if submitted, published, filed or lodged in any manner prescribed by applicable law. With respect to the manner of providing such notices or other disclosures, the Company may distinguish between the Shareholders listed on its regular Registry and those listed in any "additional registry", as defined in Section 138(a) of the Companies Law, administered by a transfer agent or stock exchange registration company.

128.2. Any Shareholder may serve any written notice or other document on the Company by way of delivery by hand at the Office, by facsimile or email transmission to the Company or by dispatch by prepaid registered mail to the Company at the Office.

128.3. Any notice or document which is delivered or sent to a Shareholder in accordance with these Articles shall be deemed to have been duly delivered and sent in respect of the shares held by him (whether in respect of shares held by him alone or jointly with others), notwithstanding the fact that such Shareholder has died or been declared bankrupt at such time (whether or not the Company knew of his death or bankruptcy), and shall be deemed to be sufficient delivery or dispatch to heirs, trustees, administrators or transferees and any other persons (if any) who have a right in the shares.

128.4. Any such notice or other document shall be deemed to have been served:

128.4.1. in the case of mailing, 48 hours after it has been posted, or when actually received by the addressee if sooner than 48 hours after it has been posted;

128.4.2. in the case of overnight air courier, on the next day following the day sent, with receipt confirmed by the courier, or when actually received by the addressee if sooner;

128.4.3. in the case of personal delivery, when actually tendered in person to such Shareholder;

128.4.4. in the case of facsimile or other electronic transmission (including email), the next day following the date on which the sender receives automatic electronic confirmation by the recipient's facsimile machine or computer or other device that such notice was received by the addressee; or

128.4.5. in the case a notice is, in fact, received by the addressee, when received, notwithstanding that it was defectively addressed or failed, in some other respect, to comply with the provisions of this Article 128.

129. Any Shareholder whose address is not described in the Register, and who shall not have designated in writing an address for the receipt of notices, shall not be entitled to receive any notice from the Company. In the case of joint holders of a share, the Company shall be entitled to deliver a notice by dispatch to the joint holder whose name stands first in the Register in respect of such share.

130. Whenever it is necessary to give notice of a particular number of days or a notice for another period, the day of delivery shall be counted in the number of calendar days or the period, unless otherwise specified.

131. Notwithstanding anything to the contrary contained herein, notice by the Company of a General Meeting, containing the information required to be set forth in such notice under these Articles, which is published, within the time otherwise required for giving notice of such meeting, in:

131.1. at least two daily newspapers in the State of Israel shall be deemed to be notice of such meeting duly given, for the purposes of these Articles, to any Shareholder whose address as registered in the Register (or as designated in writing for the receipt of notices and other documents) is located in the State of Israel; and

131.2. one daily newspaper in New York, NY, United States, and in one international wire service shall be deemed to be notice of such meeting duly given, for the purposes of these Articles, to any shareholder whose address as registered in the Register (or as designated in writing for the receipt of notices and other documents) is located outside the State of Israel.

INSURANCE, INDEMNITY AND EXCULPATION

132. Subject to the provisions of the Companies Law, the Company shall be entitled to enter into a contract to insure all or part of the liability of an Office Holder of the Company, imposed on him in consequence of an act which he has performed by virtue of being an Office Holder, in respect of any of the following:

132.1. The breach of a duty of care to the Company or to any other Person;

132.2. The breach of a fiduciary duty to the Company, provided that the Office Holder acted in good faith and had reasonable grounds for believing that the action would not adversely affect the best interests of the Company;

132.3. A pecuniary liability imposed on him in favor of any other person in respect of an act done in his capacity as an Office Holder.

132.4. Any other circumstances arising under the law with respect to which the Company may, or will be able to, insure an Office Holder.

133. Subject to the provisions of the Companies Law, the Company shall be entitled to indemnify an Office Holder of the Company, to the fullest extent permitted by applicable law. Subject to the provisions of the Companies Law, including the receipt of all approvals as required therein or under any applicable law, the Company may resolve retroactively to indemnify an Office Holder with respect to the following liabilities and expenses, provided, in each of the below cases, that such liabilities or expenses were incurred by such Office Holder in such Office Holder's capacity as an Office Holder of the Company:

133.1. a monetary liability imposed on him in favor of a third party in any judgment, including any settlement confirmed as judgment and an arbitrator's award which has been confirmed by the court, in respect of an act performed by the Office Holder by virtue of the Office Holder being an Office Holder of the Company; provided, however, that: (a) any indemnification undertaking with respect to the foregoing shall be limited (i) to events which, in the opinion of the Board of Directors, are foreseeable in light of the Company's actual operations at the time of the granting of the indemnification undertaking, and (ii) to an amount or by criteria determined by the Board of Directors to be reasonable in the given circumstances; and (b) the events that in the opinion of the Board of Directors are foreseeable in light of the Company's actual operations at the time of the granting of the indemnification undertaking are listed in the indemnification undertaking together with the amount or criteria determined by the Board of Directors to be reasonable in the given circumstances;

133.2. reasonable litigation expenses, including legal fees, paid for by the Office Holder, in an investigation or proceeding conducted against such Office Holder by an agency authorized to conduct such investigation or proceeding, and which investigation or proceeding: (i) concluded without the filing of an indictment (as defined in the Companies Law) against such Office Holder and without there having been a monetary liability imposed against such Office Holder in lieu of a criminal proceeding (as defined in the Companies Law); (ii) concluded without the filing of an indictment against such Office Holder but with there having been a monetary liability imposed against such Office Holder in lieu of a criminal proceeding for an offense that does not require proof of criminal intent; or (iii) involves financial sanction;

133.3. reasonable litigation expenses, including legal fees, paid for by the Office Holder, or which the Office Holder is obligated to pay under a court order, in a proceeding brought against the Office Holder by the Company, or on its behalf, or by a third party, or in a criminal proceeding in which the Office Holder is found innocent, or in a criminal proceeding in which the Office Holder was convicted of an offense that does not require proof of criminal intent; and

133.4. any other event, occurrence or circumstances in respect of which the Company may lawfully indemnify an Office Holder of the Company (including, without limitation, indemnification with respect to the matters referred to under Section 56h(b)(1) of the Israeli Securities Law 5728-1968, as amended.

133.5. The Company may undertake to indemnify an Office Holder as aforesaid: (i) prospectively, provided that the undertaking is limited to categories of events which in the opinion of the Board of Directors can be foreseen when the undertaking to indemnify is given, and to an amount set by the Board of Directors as reasonable under the circumstances, and (ii) retroactively.

134. Subject to the provisions of the Companies Law including the receipt of all approvals as required therein or under any applicable law, the Company may, to the maximum extent permitted by the Companies Law, exempt and release, in advance, any Office Holder from any liability for damages arising out of a breach of a duty of care towards the Company.

135.

135.1. Any amendment to the Companies Law adversely affecting the right of any Office Holder to be indemnified or insured pursuant to Articles 132, 133 and 134 and any amendments to Articles 132, 133 and 134 shall be prospective in effect, and shall not affect the Company's obligation or ability to indemnify or insure an Office Holder for any act or omission occurring prior to such amendment, unless otherwise provided by applicable law.

135.2. The provisions of Articles 132, 133 and 134 are not intended, and shall not be interpreted so as to restrict the Company, in any manner, in respect of the procurement of insurance and/or in respect of indemnification and/or exculpation, in favor of any person who is not an Office Holder, including, without limitation, any employee, agent, consultant or contractor of the Company who is not an Office Holder; and/or any Office Holder to the extent that such insurance and/or indemnification is not specifically prohibited under law.

WINDING-UP AND REORGANIZATION

136. Should the Company be wound up and the assets of the Company made available for distribution among Shareholders be insufficient to repay all of the Company's paid-up capital, such assets shall be divided in a manner whereby the losses shall, as far as possible, be borne by the Shareholders pro rata to the nominal value of the paid-up capital on the shares held by each of them, and, if at the time of the winding-up, the property of the Company available for distribution among the Shareholders should exceed the amount sufficient for the repayment of the full nominal value of the paid-up capital at the time of commencement of the winding-up, the surplus shall be distributed to the Shareholders pro rata to the paid-up capital held by each of them.

137. Upon the sale of the Company's assets, the Board of Directors may, or in the case of a liquidation, the liquidators may, if authorized to do so by a Resolution of the Company, accept fully or partly paid-up shares, or securities of another company, Israeli or non-Israeli, whether in existence at such time or about to be formed, in order to purchase the property of the Company, or part thereof, and to the extent permitted under the Companies Law, the Board of Directors may (or in the case of a liquidation, the liquidators may) distribute the aforesaid shares or securities or any other property of the Company among the Shareholders without realizing the same, or may deposit the same in the hands of trustees for the Shareholders, and the General Meeting by a Resolution may decide, subject to the provisions of the Companies Law, on the distribution or allotment of cash, shares or other securities, or the property of the Company and on the valuation of the aforesaid securities or property at such price and in such manner as the Shareholders at such General Meeting shall decide, and all of the Shareholders shall be obliged to accept any valuation or distribution determined as aforesaid and to waive their rights in this regard, except, in a case in which the Company is about to be wound-up and is in the process of liquidation, for those legal rights (if any) which, according to the provisions of the Companies Law, may not be changed or modified.

FORUM FOR ADJUDICATION OF DISPUTES

138. (a) Unless the Company consents in writing to the selection of an alternative forum, with respect to any causes of action arising under the Securities Act of 1933 as amended, the federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended, against any person or entity, including such claims brought against the Company, its directors, officers, employees, advisors, attorneys, accountants, or underwriters; and (b) unless the Company consents in writing to the selection of an alternative forum, the Tel Aviv District Court shall be the exclusive forum for (i) any derivative action or proceeding brought on behalf of the Company, (ii) any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the Company to the Company or the Company's shareholders, or (iii) any action asserting a claim arising pursuant to any provision of the Israeli Companies Law 5759-1999 or the Israeli Securities Law 5728-1968. Any person or entity purchasing or otherwise acquiring or holding any interest in shares of the Company shall be deemed to have notice of and consented to these provisions.

Exhibit 2.1

DESCRIPTION OF SECURITIES

Our authorized share capital consists of 50,000,000 ordinary shares, par value NIS 0.01 per share, of which 32,509,544 shares are issued and outstanding as of March 15, 2022.

All of our outstanding ordinary shares are validly issued, fully paid and non-assessable. Our ordinary shares are not redeemable and do not have any preemptive rights. All ordinary shares have identical voting and other rights in all respects.

Transfer of shares

Our fully paid ordinary shares are issued in registered form and may be freely transferred under our articles of association, unless the transfer is restricted or prohibited by another instrument, applicable law or the rules of a stock exchange on which the shares are listed for trade. The ownership or voting of our ordinary shares by non-residents of Israel is not restricted in any way by our articles of association or the laws of the State of Israel, except for ownership by nationals of some countries that are, or have been, in a state of war with Israel.

Dividend and liquidation rights

We may declare a dividend to be paid to the holders of our ordinary shares in proportion to their respective shareholdings. Under the Israeli Companies Law, dividend distributions are determined by the board of directors and do not require the approval of the shareholders of a company unless the company's articles of association provide otherwise. Our articles of association do not require shareholder approval of a dividend distribution and provide that dividend distributions may be determined by our board of directors.

Pursuant to the Israeli Companies Law, the distribution amount is limited to the greater of retained earnings or earnings generated over the previous two years, according to our then last reviewed or audited financial statements, provided that the end of the period to which the financial statements relate is not more than six months prior to the date of the distribution. If we do not meet such criteria, then we may distribute dividends only with court approval. In each case, we are only permitted to distribute a dividend if our board of directors and the court, if applicable, determines that there is no reasonable concern that payment of the dividend will prevent us from satisfying our existing and foreseeable obligations as they become due.

In the event of our liquidation, after satisfaction of liabilities to creditors, our assets will be distributed to the holders of our ordinary shares in proportion to their shareholdings. That right, as well as the right to receive dividends, may be affected by the grant of preferential dividend or distribution rights to the holders of a class of shares with preferential rights that may be authorized in the future.

Shareholder meetings

Under Israeli law, we are required to hold an annual general meeting of our shareholders once every calendar year that must be held no later than 15 months after the date of the previous annual general meeting. All meetings other than the annual general meeting of shareholders are referred to in our articles of association as extraordinary general meetings. Our board of directors may call extraordinary general meetings whenever it sees fit, at such time and place, within or outside of Israel, as it may determine. In addition, the Israeli Companies Law provides that our board of directors is required to convene an extraordinary general meeting upon the written request of (i) any two or more of our directors or one-quarter or more of the members of our board of directors or (ii) one or more shareholders holding, in the aggregate, either (a) 5% or more of our outstanding issued shares and 1% of our outstanding voting power or (b) 5% or more of our outstanding voting power.

Subject to the provisions of the Israeli Companies Law and the regulations promulgated thereunder, shareholders entitled to participate and vote at general meetings are the shareholders of record on a date to be decided by the board of directors, which may be for a company such as ours whose ordinary shares are traded publicly in the U.S., between four and 40 days prior to the date of the meeting. Furthermore, the Israeli Companies Law requires that resolutions regarding the following matters must be adopted at a general meeting of our shareholders:

- amendments to our articles of association;
- appointment or termination of our auditors;

- appointment of external directors;
- approval of certain related party transactions;
- increases or reductions of our authorized share capital;
- a merger; and
- the exercise of our board of directors' powers by a general meeting, if our board of directors is unable to exercise its powers and the exercise of any of its powers is required for our proper management.

The Israeli Companies Law requires that a notice of any annual general meeting or extraordinary general meeting be provided to shareholders at least 21 days prior to the meeting, and if the agenda of the meeting includes the appointment or removal of directors, the approval of transactions with office holders or interested or related parties, or an approval of a merger, notice must be provided at least 35 days prior to the meeting.

Under the Israeli Companies Law and our articles of association, shareholders are not permitted to take action by way of written consent in lieu of a meeting.

Voting Rights

Quorum requirements

Pursuant to our articles of association, holders of our ordinary shares are entitled to one vote for each ordinary share held on all matters submitted to a vote before the shareholders at a general meeting. As provided under our articles of association and as permitted under the NASDAQ Listing Rules due to our status as a foreign private issuer, the quorum required for our general meetings of shareholders consists of at least two shareholders present in person, by proxy or written ballot who hold or represent between them at least 25% of the total outstanding voting rights. A meeting adjourned for lack of a quorum is generally adjourned to the same day in the following week at the same time and place or to a later time or date if so specified in the notice of the meeting. At the reconvened meeting, any two or more shareholders present in person or by proxy (regardless of the number of ordinary shares held by them) shall constitute a lawful quorum.

Vote requirements

Our articles of association provide that all resolutions of our shareholders require a simple majority vote to be adopted, unless otherwise required by the Israeli Companies Law or by our articles of association. Under the Israeli Companies Law, each of (i) the approval of an extraordinary transaction with a controlling shareholder, (ii) the terms of employment or other engagement of the controlling shareholder of the company or such controlling shareholder's relative (even if such terms are not extraordinary), (iii) the terms of employment of the chief executive officer, (iv) the election of external directors and (v) the approval of the service by one individual as chairman of the board and chief executive officer simultaneously, for a maximum period of three years at a time, requires special majority approval under Israeli law. Under our articles of association, the alteration of the rights, privileges, preferences or obligations of any class of our shares requires a simple majority of the class so affected (or such other percentage of the relevant class that may be set forth in the governing documents relevant to such class), voting together at a shareholder meeting of that class.

Further exceptions to the simple majority vote requirement are a resolution for the voluntary winding up, or an approval of a scheme of arrangement or reorganization, of the company pursuant to Section 350 of the Israeli Companies Law, which requires the approval of holders of 75% of the voting rights represented at the meeting and voting on the resolution.

Access to corporate records

Under the Israeli Companies Law, shareholders are provided access to: minutes of our general meetings; our shareholders register and principal shareholders register, articles of association and annual audited financial statements; and any document that we are required by law to file publicly with the Israeli Companies Registrar or the Israel Securities Authority. In addition, shareholders may request any document related to an action or transaction requiring shareholder approval under the related party transaction provisions of the Israeli Companies Law. We may deny this request if we believe it has not been made in good faith or if such denial is necessary to protect our interest or protect a trade secret or patent.

Modification of class rights

Under the Israeli Companies Law and our articles of association, the rights attached to any class of share, such as voting, liquidation and dividend rights, may be amended by adoption of a resolution by the holders of a majority of the shares of that class present at a separate class meeting, or otherwise in accordance with the rights attached to such class of shares, as set forth in our articles of association.

Registration rights

We are party to an amended and restated registration rights agreement, dated April 6, 2021, with certain of our shareholders (the "Registration Rights Agreement"). The Registration Rights Agreement, which was approved by our shareholders at our 2021 annual general meeting of shareholders, replaced the registration rights agreement, dated March 3, 2014 (the "Original Registration Rights Agreement"), that we had entered into in connection with our initial public offering with certain of our pre-IPO shareholders, which expired by its own terms on its seven-year anniversary. The ordinary shares held by most of our pre-IPO shareholders who were party to the Original Registration Rights Agreement were no longer entitled to registration rights under that agreement as of the time that it expired, given their ability to freely sell their shares in the open market under Rule 144 of the Securities Act. However, each of CBI and Professor Lior Rosenberg, and their affiliated entities that hold ordinary shares (consisting of Clal Life Sciences LP and L.R. Research & Development Ltd., respectively) remained entitled to registration rights as of the time of the expiration of the Original Registration Rights Agreement, and we therefore entered into the Registration Rights Agreement with them as a means of extending those rights. . The Registration Rights Agreement provides to the holders of our ordinary shares that are party to the agreement the right to demand that we file a registration statement or request that their ordinary shares be covered by a registration statement that we are otherwise filing. In March 2019, we filed, and the SEC declared effective, on April 22, 2019, a shelf registration statement on Form F-3 that registered the resale of the 11,240,827 shares that were then entitled to registration rights under the Original Registration Rights Agreement. That registration statement remains in effect as of the date of this Annual Reports.

Demand registration rights

At any time, the holders of a majority of the registrable securities (as defined in the Registration Rights Agreement) then outstanding may request that we file a registration statement with respect to a majority of the registrable securities then outstanding (or a lesser percentage if the anticipated aggregate offering price, net of selling expenses, exceeds $5.0 million). Upon receipt of such registration request, we are obligated to file a registration statement. Currently, as we are eligible under applicable securities laws to file a registration statement on Form F-3, we may be required to effect up to two such registrations within any 12-month period.

We will not be obligated to file a registration statement at such time if in the good faith judgment of our board of directors, such registration would be materially detrimental to the company and its shareholders because such action would (i) materially interfere with a significant acquisition, corporate reorganization or other similar transaction involving us, (ii) require premature disclosure of material information that we have a bona fide business purpose for preserving as confidential or (iii) render us unable to comply with requirements under the Securities Act or Exchange Act. In addition, we have the right not to effect or take any action to effect a registration statement during the period that is 60 days (or 30 days in the case of a registration statement on Form F-3) before the date of filing our registration statement (as estimated by us in good faith), and ending on a date that is 180 days (or 90 days in the case of a registration statement on Form F-3) after the date of such filing.

Piggyback registration rights

In addition, if we register any of our ordinary shares in connection with the public offering of such securities solely for cash, the holders of all registrable securities are entitled to at least 10 days' notice of the registration and to include all or a portion of their ordinary shares in the registration. If the public offering that we are effecting is underwritten, the right of any shareholder to include shares in the registration related thereto is conditioned upon the shareholder accepting the terms of the underwriting as agreed between us and the underwriters and then only in such quantity as the underwriters in their sole discretion determine will not jeopardize the success of our offering.

Other provisions

We will pay all registration expenses (other than underwriting discounts and selling commissions) and the reasonable fees and expenses of a single counsel for the selling shareholders, related to any demand or piggyback registration. The demand and piggyback registration rights described above will expire on March 24, 2021, five years after our initial public offering.

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 a public Israeli 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 relevant class for the purchase of all of the issued and outstanding shares of that class. If 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, 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 also be accepted if 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 of 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 an 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 include 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 a tender offer is not accepted in accordance with the requirements set forth above, the acquirer may not acquire shares from shareholders who accepted the tender offer that will increase its holdings to more than 90% of the company's issued and outstanding share capital or of the applicable class.

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 25% or more of the voting rights in the company. This requirement 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 in 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, subject to certain exceptions. A special tender offer must be extended to all shareholders of a company but the offeror is not required to purchase shares representing more than 5% of the voting power attached to the company's outstanding shares, regardless of how many shares are tendered by shareholders. A special tender offer may be consummated only if (i) the offeror acquired shares representing at least 5% of the voting power in the company and (ii) the number of shares tendered by shareholders who accept the offer exceeds the number of shares held by shareholders who object to the offer (excluding the purchaser, controlling shareholders, holders of 25% or more of the voting rights in the company or any person having a personal interest in the acceptance of the tender offer). If a special tender offer is accepted, the purchaser or any person or entity controlling it or under common control with the purchaser or such controlling person or entity may not make a subsequent tender offer for the purchase of shares of the target company and may not enter into 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, by a majority vote of each party's shareholders. In the case of the target company, approval of the merger further requires a majority vote of each class of its shares.

For purposes of the shareholder vote, unless a court rules otherwise, the merger requires the approval by a majority of the votes of shares represented at the meeting of shareholders, after excluding shares held by the other party to the merger and any person (or group of persons acting in concert) who holds (or hold, as the case may be) 25% or more of the voting rights or the right to appoint 25% or more of the directors of the other party to the merger. If, however, the merger involves a merger with a company's own controlling shareholder or if the controlling shareholder has a personal interest in the merger, then the merger is instead subject to the same Special Majority approval that governs all extraordinary transactions with controlling shareholders.

If the transaction would have been approved by the shareholders of a merging company but for the separate approval of each class or the exclusion of the votes of certain shareholders as provided above, a court may still approve the merger upon the petition of holders of at least 25% of the voting rights of a company. For such petition to be granted, the court must find that the merger is fair and reasonable, taking into account the respective values assigned to each of the parties to the merger and the consideration offered to the shareholders of the target company. 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 merging entities, and may further give instructions to secure the rights of creditors.

A merger may not be consummated unless at least 50 days have passed from the date on which a proposal for approval of the merger is filed with the Israeli Registrar of Companies and at least 30 days have passed from the date on which the merger was approved by the shareholders of each party.

Anti-takeover measures under Israeli law

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 rights with respect to voting, distributions or other matters and shares having preemptive rights. As of February 15, 2019, no preferred shares are authorized under our articles of association. In the future, if we do authorize, create and issue a specific class of preferred shares, such class of shares, depending on the specific rights that may be attached to it, may have the ability to frustrate or prevent a takeover or otherwise prevent our shareholders from realizing a potential premium over the market value of their ordinary shares. The authorization and designation of a class of preferred shares will require an amendment to our articles of association, which requires the prior approval of the holders of a majority of the voting power attaching to our issued and outstanding shares at a general meeting. The convening of the meeting, the shareholders entitled to participate and the majority vote required to be obtained at such a meeting will be subject to the requirements set forth in the Israeli Companies Law as described above in "—Voting Rights."

Exhibit 4.11.7

AMENDMENT OF SOLICITATION/MODIFICATION OF CONTRACT	1. CONTRACT ID CODE	PAGE OF PAGES 1 5

2. AMENDMENT/MODIFICATION NO.	3. EFFECTIVE DATE	4. REQUISITION/PURCHASE REQ. NO.	5. PROJECT NO. *(If applicable)*
P00008	See Block 16C	OS289937	

6. ISSUED BY	CODE	ASPR-BARDA	7. ADMINISTERED BY *(If other than Item 6)*	CODE	ASPR-BARDA01
ASPR-BARDA 200 Independence Ave., S.W. Room 640-G Washington DC 20201			ASPR-BARDA 330 Independence Ave, SW, Rm G644 Washington DC 20201		

8. NAME AND ADDRESS OF CONTRACTOR *(No., street, county, State and ZIP Code)*		9A. AMENDMENT OF SOLICITATION NO.
MEDIWOUND LTD 1477616 MEDIWOUND LTD 42 HAYARKON 42 HAYARKON YAVNE 00812	(x)	9B. DATED *(SEE ITEM 11)*
	x	10A. MODIFICATION OF CONTRACT/ORDER NO. HHSO100201500035C
		10B. DATED *(SEE ITEM 13)* 09/29/2015
CODE 1477616 FACILITY CODE		

11. THIS ITEM ONLY APPLIES TO AMENDMENTS OF SOLICITATIONS

☐ The above numbered solicitation is amended as set forth in Item 14. The hour and date specified for receipt of Offers ☐ is extended. ☐ is not extended.
Offers must acknowledge receipt of this amendment prior to the hour and date specified in the solicitation or as amended , by one of the following methods: (a) By completing Items 8 and 15, and returning _____ copies of the amendment; (b) By acknowledging receipt of this amendment on each copy of the offer submitted ; or (c) By separate letter or telegram which includes a reference to the solicitation and amendment numbers. FAILURE OF YOUR ACKNOWLEDGEMENT TO BE RECEIVED AT THE PLACE DESIGNATED FOR THE RECEIPT OF OFFERS PRIOR TO THE HOUR AND DATE SPECIFIED MAY RESULT IN REJECTION OF YOUR OFFER. If by virtue of this amendment you desire to change an offer already submitted , such change may be made by telegram or letter, provided each telegram or letter makes reference to the solicitation and this amendment, and is received prior to the opening hour and date specified.

12. ACCOUNTING AND APPROPRIATION DATA *(If required)* Net Increase: $8,944,500.00

See Schedule

13. THIS ITEM ONLY APPLIES TO MODIFICATION OF CONTRACTS/ORDERS. IT MODIFIES THE CONTRACT/ORDER NO. AS DESCRIBED IN ITEM 14.

CHECK ONE	
	A. THIS CHANGE ORDER IS ISSUED PURSUANT TO: *(Specify authority)* THE CHANGES SET FORTH IN ITEM 14 ARE MADE IN THE CONTRACT ORDER NO. IN ITEM 10A.
	B. THE ABOVE NUMBERED CONTRACT/ORDER IS MODIFIED TO REFLECT THE ADMINISTRATIVE CHANGES *(such as changes in paying office, appropriation date, etc.)* SET FORTH IN ITEM 14, PURSUANT TO THE AUTHORITY OF FAR 43.103(b).
X	C. THIS SUPPLEMENTAL AGREEMENT IS ENTERED INTO PURSUANT TO AUTHORITY OF: FAR 52.243-2 Alt I - Changes - Cost Reimbursement and FAR 43.103(a) - By Mutual Agreements of the Parties
	D. OTHER *(Specify type of modification and authority)*

E. IMPORTANT: Contractor ☐ is not. ☒ is required to sign this document and return 1 copies to the issuing office.

14. DESCRIPTION OF AMENDMENT/MODIFICATION *(Organized by UCF section headings, including solicitation/contract subject matter where feasible.)*

Tax ID Number: C0-0000387
DUNS Number: 532040334
The purpose of this modification is to add funds to CLIN 0001 for increased costs as a result of FDA comments, and modify ARTICLE B.2. BASE PERIOD, ARTICLE C.1. STATEMENT OF WORK, ARTICLE G.1. CONTRACTING OFFICER, ARTICLE G.5. INDIRECT COST RATES, and SECTION J.

Funds Obligated Prior to this Modification: $ 98,418,394
Funds Obligated with Mod # 8: $ 8,944,500
Total Funds Obligated to Date: $ 107,362,894

Continued ...

Except as provided herein, all terms and conditions of the document referenced in Item 9 A or 10A, as heretofore changed, remains unchanged and in full force and effect.

15A. NAME AND TITLE OF SIGNER *(Type or print)*		16A. NAME AND TITLE OF CONTRACTING OFFICER *(Type or print)*	
Sharon Malka, CEO		KEVIN RESTREPO	
15B. CONTRACTOR/OFFEROR /s/ Sharon Malka *(Signature of person authorized to sign)*	15C. DATE SIGNED+ 02/08/2022	16B. UNITED STATES OF AMERICA /s/ KEVIN RESTREPO *(Signature of Contracting Officer)*	16C. DATE SIGNED 02/09/2022

ITEM NO. (A)	SUPPLIES/SERVICES (B)	QUANTITY (C)	UNIT (D)	UNIT PRICE (E)	AMOUNT (F)
	In consideration of the modification agreed to herein as complete equitable adjustments, the Contractor, hereby releases the Government from any and all liability under this contract for further equitable adjustments attributable to such fact or circumstance giving rise to this modification. Period of Performance: 09/29/2015 to 09/27/2024 Change Item 1 to read as follows(amount shown is the obligated amount):				
1	ASPR-15-08828 -- CLIN 0001 Advanced development studies for NexoBrid Accounting Info: 2015.1990002.26201 Appr. Yr.: 2015 CAN: 1990002 Object Class: 26201 Funded: $0.00 Accounting Info: 2017.1990007.25106 Appr. Yr.: 2017 CAN: 1990007 Object Class: 25106 Funded: $0.00 Accounting Info: 2019.1990051.25106 Appr. Yr.: 2019 CAN: 1990051 Object Class: 25106 Funded: $0.00 Accounting Info: 2022.1990178.25103 Appr. Yr.: 2022 CAN: 1990178 Object Class: 25103 Funded: $8,944,500.00				8,944,500.00

SUMMARY OF CHANGES

Beginning with the effective date of this modification, the Government and Contractor mutually agree as follows:

1. ARTICLE B.2. BASE PERIOD, is modified to add funding to CLIN 0001.
2. ARTICLE C.1. STATEMENT OF WORK, is modified to delete reference to the date of the Statement of Work.
3. ARTICLE G.1. CONTRACTING OFFICER, is modified to replace Matthew Rose with Jill Johnson.
4. ARTICLE G.5. INDIRECT COST RATES, is modified to reflect current mutual understanding of indirect rates.
5. SECTION J, Attachment 1, SOW, is replaced in its entirety.

ARTICLE B.2. BASE PERIOD is modified as follows:

CLIN	**Period of Performance**	**Supplies/ Services**	**Total Est. Cost**	**Fixed Fee (7%)**	**Total Cost Plus Fixed Fee**
		COST REIMBURSEMENT			
0001 (Base)	**09/28/2015 – 09/27/2024**	**Licensure, approval, and clearance of product through the FDA**	**~~$47,911,779~~ $55,986,743**	**~~$3,049,644~~ $3,919,180**	**~~$50,961,423~~ $59,905,923 (Funded)**
0004A (Base)- Activate optional Task in July, 2017	**08/01/2017- 07/31/2023**	**Pediatric Study**	**$23,989,225**	**$1,455,400**	**$25,444,625 (Funded)**
0006A,B,C (Base) New Task added in Feb 28,2020	**1/1/2020 - 6/31/2024**	**Emergency Readiness Tasks**	**$4,271,919**	**$299,034**	**$4,570,953 (Funded)**
0007A,B (Base) New Task added in Feb 28,2020	**TBD**	**Emergency Deployment Preparation**	**$903,350**	**$63,235**	**$966,585 (Funded)**
		FIRM FIXED PRICE			
CLIN	**Period of Performance**	**Supplies/ Services**	**Units (# of Product)**	**Unit Price ($)**	**Total ($)**
0002 (Base)	**09/28/2017 – 09/27/2019*(* see advanced understanding h.)**	**Initial Purchase, storage, and delivery of product**	**10,588**	**$1,052 (includes VMI)**	**$11,138,576 (Funded)**
0002 (Base)	**09/28/2019 – 3/31/2022**	**Initial Purchase, storage, and delivery of product**	**5412**	**$986 (includes VMI)**	**$5,336,232 (Funded)**
Total CLINS 001&002&004A&006&007	09/28/2015 – 09/27/2024	See Above Descriptions			~~$98,418,395~~ 107,362,894 (Funded)

ARTICLE C.1. STATEMENT OF WORK is modified as follows:

Independently and not as an agent of the Government, the Contractor shall furnish all the necessary services, qualified personnel, material, equipment, and facilities not otherwise provided by the Government as needed to perform the Statement of Work ~~dated September 28, 2015~~ set forth in SECTION J - List of Attachments, attached hereto and made a part of the contract.

ARTICLE G.1. CONTRACTING OFFICER is modified as follows:

The following Contracting Officer (CO) will represent the Government for the purpose of this contract:

Jill Johnson, Contracting Officer
202-690-7137
Jill.Johnson@hhs.gov

a. The Contracting Officer (CO) is the only individual who can legally commit the Government to the expenditure of public funds. No person other than the CO can make any changes to the terms, conditions, general provisions, specifications or other requirements of this contract.

b. The Contracting Officer (CO) is the only person with authority to act as agent of the Government under this contract. Only the CO has authority to: (1) direct or negotiate any changes in the statement of work; (2) modify or extend the period of performance; (3) change the delivery schedule; (4) authorize reimbursement to the Contractor for any costs incurred during the performance of this contract; or (5) otherwise change any terms and conditions of this contract.

c. No information, other than that which may be contained in an authorized modification to this contract duly issued by the CO, shall be considered grounds for deviation from this contract.

d. The Government may unilaterally change its CO designation

ARTICLE G.5. INDIRECT COST RATES is modified as follows:

1. The following interim provisional indirect rates will be utilized for billing purposes during the period of performance:

   Direct Labor Overhead - 80%.
   Direct Consultant Labor Overhead – 25%
   Final rate proposals must be sent to the Contracting Officer, within 6 months of the fiscal year end. See FAR Clause 52.216-7, Allowable Cost and Payment.

2. The interim provisional indirect rates used in this contract have been established after approval by the AMCG/BARDA Auditor.

SECTION J LIST OF ATTACHMENTS is modified as follows:

The following documents are attached and incorporated in this contract:

1. Statement of Work, dated January 26, 2022

2. Invoice/Financing Instructions for Cost-Reimbursement Type Contracts

3. Invoice Instructions for Fixed-Priced Type Contracts

4. Sample Invoice Form

5. Research Patient Care Costs

6. Report of Government Owned, Contractor Held Property

7. Form SF-LLL, Disclosure of Lobbying Activities

8. Inclusion Enrollment Report, 5/01 (Modified OAMP: 10/01)

END OF MODIFICATION P00008 to HHSO100201500035C

EXHIBIT 12.1

CERTIFICATIONS

I, Sharon Malka, certify that:

1. I have reviewed this annual report on Form 20-F of MediWound 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 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; and

5. The company's other certifying officer 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.

/s/Sharon Malka
Sharon Malka
Chief Executive Officer
Date: March 17, 2022

EXHIBIT 12.2

CERTIFICATIONS

I, Boaz Gur-Lavie, certify that:

1. I have reviewed this annual report on Form 20-F of MediWound 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 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; and

5. The company's other certifying officer 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.

/s/ Boaz Gur-Lavie
Boaz Gur-Lavie
Chief Financial Officer
Date: March 17, 2022

EXHIBIT 13.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO
18 U.S.C. SECTION 1350
AS ADOPTED PURSUANT TO SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of MediWound Ltd. (the "Company") on Form 20-F for the fiscal year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Sharon Malka, do certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my 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.

/s/Sharon Malka
Sharon Malka
Chief Executive Officer
Date: March 17, 2022

EXHIBIT 13.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO
18 U.S.C. SECTION 1350
AS ADOPTED PURSUANT TO SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of MediWound Ltd. (the "Company") on Form 20-F for the fiscal year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Boaz Gur-Lavie, do certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my 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.

/s/ Boaz Gur-Lavie
Boaz Gur-Lavie
Chief Financial Officer
Date: March 17, 2022

EXHIBIT 15.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the registration statement (No.'s 333-223767, 333-195517, 333-210375, 333-230487 and 333-236635) on Form S-8 and in the registration statement (No. 333-230490) on Form F-3 of our report dated March 17, 2022, with respect to the consolidated financial statements of MediWound Ltd. and its subsidiaries.

/s/ Somekh Chaikin
Somekh Chaikin
Member Firm of KPMG International

Haifa, Israel
March 17, 2022

EXHIBIT 15.2

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the registration statement (No.'s 333-223767, 333-195517, 333-210375, 333-230487 and 333-236635) on Form S-8 and in the registration statement (No. 333-230490) on Form F-3 of our report dated February 25, 2021, with respect to the consolidated financial statements of MediWound Ltd. and its subsidiaries.

/s/ KOST FORER GABBAY & KASIERER
KOST FORER GABBAY & KASIERER
Member Firm of Ernst & Young Global

Tel Aviv, Israel
March 17, 2022