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

FORM 20-F

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

OR

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

For the fiscal year ended December 31, 2018

OR

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

OR

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

Commission file number 001-36349

MEDIWOUND LTD.
(Exact name of Registrant as specified in its charter)

ISRAEL
(Jurisdiction of incorporation or organization)

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

Yaron Meyer, Adv.
General Counsel and Corporate Secretary
Telephone: +972 (77) 971-4100
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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	Name of each exchange on which registered
Ordinary shares, par value NIS 0.01 per share	**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, 2018, the registrant had outstanding 27,178,839 ordinary shares, par value NIS 0.01 per share.**

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 (§229.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post 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 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

Innovative solutions for wound & burn care

MEDIWOUND LTD.

FORM 20-F
ANNUAL REPORT FOR THE FISCAL YEAR ENDED DECEMBER 31, 2018

TABLE OF CONTENTS

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 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 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;
- 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;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act; 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. There are important factors that could cause our actual results, level of activity, performance or achievements to differ materially from the results, level of activity, performance or achievements expressed or implied by the forward-looking statements. 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: Wounds," 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. Selected Financial Data

The following tables set forth our selected consolidated financial data. You should read the following selected consolidated financial data in conjunction with "ITEM 5. Operating and Financial Review and Prospects" and our consolidated financial statements and related notes included elsewhere in this annual report.

The selected consolidated statements of operations data for each of the years in the three-year period ended December 31, 2018 and the consolidated balance sheet data as of December 31, 2018 and 2017 are derived from our audited consolidated financial statements appearing elsewhere in this annual report. The consolidated statements of operations data for the years ended December 31, 2014 and 2015 and the consolidated balance sheet data as of December 31, 2014, 2015 and 2016 are derived from our audited consolidated financial statements that are not included in this annual report. The historical results set forth below are not necessarily indicative of the results to be expected in future periods. Our financial statements have been prepared in accordance with International Financial Reporting Standards ("IFRS") as issued by the International Accounting Standards Board ("IASB").

	Year Ended December 31,				
	2014	2015	2016	2017	2018
	(in thousands, except per share data)				
Consolidated statements of operations data:					
Revenues	$ 259	$ 601	$ 1,558	$ 2,496	$ 3,401
Cost of revenues[1]	2,785	2,519	2,158	1,578	2,088
Gross (loss) profit	(2,526)	(1,918)	(600)	918	1,313
Operating expenses:					
Research and development, gross	6,054	8,139	14,779	14,625	17,915
Participation by BARDA and the Israeli Innovation Authority	(705)	(2,118)	(7,711)	(9,163)	(13,843)
Research and development, net of participations[1][2]	5,349	6,021	7,068	5,462	4,072
Selling and marketing[1]	8,829	9,284	8,403	5,362	4,188
General and administrative[1]	4,723	4,004	4,084	3,781	3,799
Other income, net	-	-	-	-	6,786
Operating loss	(21,427)	(21,227)	(20,155)	(13,687)	(3,960)
Financial income (expense), net	2,552	(444)	1,270	(846)	(1,705)
Loss from continuing operations	(18,875)	(21,671)	(18,885)	(14,533)	(5,665)
Profit (loss) from discontinued operation[1][3]	-	(417)	-	(7,616)	4,608
Net loss	$ (18,875)	$ (22,088)	$ (18,885)	$ (22,149)	$ (1,057)
Foreign currency translation adjustments	14	2	7	(29)	13
Total comprehensive loss	$ (18,861)	$ (22,086)	$ (18,878)	$ (22,178)	$ (1,044)
Basic loss per share[4]	$ (0.95)	$ (1.02)	$ (0.86)	$ (0.95)	$ (0.04)
Diluted loss per share[4]	$ (0.95)	$ (1.02)	$ (0.86)	$ (0.95)	$ (0.04)
Weighted average number of ordinary shares used in computing loss per ordinary share (in thousands):					
Basic:	19,940	21,718	21,862	23,341	27,114
Diluted:	19,940	21,718	21,862	23,341	27,114

	As of December 31,				
	2014	2015	2016	2017	2018
			(in thousands)		
Consolidated balance sheet data:					
Cash and cash equivalents and short-term bank deposits	$ 64,853	$ 45,768	$ 30,029	$ 36,069	$ 23,633
Working capital, net[5]	64,600	45,189	28,232	36,087	27,816
Total assets	71,121	52,523	35,764	44,135	35,276
Total non-current liabilities	24,353	23,847	22,614	29,082	21,407
Total shareholders' equity	42,871	23,470	7,770	9,620	8,972

(1) Includes share-based compensation expense as follows:

	Year Ended December 31,				
	2014	2015	2016	2017	2018
			(in thousands)		
Cost of revenues	$ 763	$ 372	$ 504	$ 188	$ 71
Research and development	657	511	752	488	181
Selling and marketing	1,430	669	765	204	63
General and administrative	1,977	1,107	1,150	483	330
Total share-based compensation expenses	$ 4,827	$ 2,659	$ 3,171	$ 1,363	$ 645

(2) Research and development expenses, net is presented net of participation by the U.S. Biomedical Advanced Research and Development Authority ("BARDA") and others and net of the change in the fair value of the liability associated with government grants from the Israeli Innovation Authority (IIA). The effect of the participation by IIA totaled $0.7 million, $1.3 million, $2.1 million, $0.6 million and $0.6 million for the years ended December 31, 2014, 2015, 2016, 2017 and 2018, respectively. The effect of the participation by BARDA totaled $0.8 million, $5.6 million, $8.6 million and 13.2 million for the years ended December 31, 2015, 2016, 2017, and 2018 respectively. See "ITEM 5.B. Liquidity and Capital Resources" for more information.

(3) Discontinued operation consists of revenues and expenses related to our exclusive, worldwide license for the development, production and commercialization of the PolyHeal Product, which expired following the termination of our collaboration with Teva. We account for our discontinued operation in accordance with IFRS accounting standard 5, "Non-current Assets Held for Sale and Discontinued Operations." See "ITEM 5.A. Operating Results—Discontinued operation" for more information.

(4) Basic and diluted net income (loss) per ordinary share is computed based on the basic and diluted weighted average number of ordinary shares outstanding during each period. For additional information, see Note 21 to our consolidated annual financial statements included elsewhere in this report.

(5) Working capital, net is defined as total current assets minus total current liabilities.

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 Our Business and Our Industry

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 proteolytic enzyme technology for marketing authorization of NexoBrid in the U.S. and for new indications, such as for debridement of chronic and other hard-to-heal wounds and treatment of connective tissue 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. For example, on August 3, 2004, the U.S. Food and Drug Administration (the "FDA") put one of our Phase 2 studies of NexoBrid on a clinical hold due to safety concerns in the study group, including four deaths and a higher incidence of pain and pyrexia compared to the standard of care ("SOC") group. Although the Data Safety Monitoring Board unanimously concluded that no causal relationship between these deaths and the NexoBrid treatment was established and provided a reasoning for the higher incidence of such adverse events, the FDA delayed the continuation of the development plan until we proposed to initiate an additional smaller Phase 2 study to demonstrate the effectiveness of our proposed corrective measures. We successfully completed this smaller Phase 2 study, allowing us to continue the development plan, but experienced a significant delay and higher costs as a result. 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.

Similar or other 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 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 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; and
- delays may occur in obtaining our clinical materials.

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 rely on sales of NexoBrid in Europe for the treatment of severe burns for a significant portion of our total revenues. 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 FDA. We recently announced top-line results from the Phase 3 pivotal study to support a Biologics License Application ("BLA") submission to the FDA, according to which the study has met its primary and all secondary endpoints, and we plan to submit the Biologics License Application ("BLA") in the second half of 2019 based on the above available acute primary, secondary, and safety data with the long term twelve-month safety follow-up data submitted during the BLA review, subject to FDA concurrence at a pre BLA meeting planned for first half of 2019. FDA may decide not to grant us the meeting or not to accept a BLA submission without the long term twelve-month safety follow-up data, in which case we will not be able to submit a BLA until the study is completed or until such time that the FDA accepts our BLA submission. We cannot predict whether the study will be successful and, even if it is successful in every aspect the FDA will accept a BLA submission following this study, how long the FDA may not take to review and approve NexoBrid following our BLA submission or whether any such approval in the United States will ultimately be granted. Similarly, we cannot predict how long regulatory authorities outside of the United States and Europe will 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 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 materially adverse impact on our business prospects.

Development and commercialization of NexoBrid 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 and Europe, 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, Israel, Argentina South Korea and Russia. 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"), as well as potential audits of the non-clinical and clinical trial sites that generated the data cited in the marketing authorization application.

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 example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law in the United States. The Cures Act, among other things, is intended to modernize the regulation of drugs and biologics and spur innovation. 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. For example, certain policies of the current U.S. presidential administration may impact our business and industry. Namely, this administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, 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 the EMA does not accept such study or 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 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 for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency 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 the FDA and other agencies may also slow the time necessary for new drugs and biologics to be reviewed and/or approved by necessary government agencies, 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 the FDA, have had to furlough critical FDA employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We are dependent on our contract with the U.S. Biomedical Advanced Research and Development Authority to fund our Phase 3 pivotal studies and other development activities of NexoBrid in the United States, and if we do not continue to receive funding under this contract, we may need to obtain alternative sources of funding.

We have a contract with BARDA valued at up to $132 million for the advancement of the development and manufacturing, as well as the procurement, of NexoBrid in the United States. Under the contract, BARDA has agreed to fund up to $56 million of the development costs of NexoBrid required to obtain marketing approval in the United States, including our ongoing pediatric phase 3 study and its expansion to include U.S. pediatric burn care sites, and has an option to further fund $10 million in development activities for other potential NexoBrid indications. BARDA has also made a $16.5 million commitment for procurement of NexoBrid, which is contingent upon the U.S. FDA Emergency Use Authorization (EUA) and/or FDA marketing authorization for NexoBrid, and has a $50 million option for additional procurement of NexoBrid. In addition, we were recently awarded a new contract to develop NexoBrid for the treatment of Sulfur Mustard injuries as part of BARDA preparedness for mass casualty events. The 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 Efficacy Rule and contains options for 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. However, both contracts provides that 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. 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 occur nor when or whether BARDA's option to fund additional development activities for NexoBrid will be exercised.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

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, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, a sweeping law 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 Affordable Care Act of importance to our potential product candidates are the following:

- an annual, nondeductible 2.3% 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. Through a series of legislative amendments, the tax was suspended for 2016 through 2019, but is scheduled to return beginning in 2020, absent further Congressional action;
- 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.

There have been judicial and congressional challenges to certain aspects of the Affordable Care Act, and we expect the current U.S. presidential administration to continue to seek amendments to or repeal of the Affordable Care Act. While Congress has not passed repeal legislation, the Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the Affordable Care Act are invalid as well. While the Trump Administration and CMS have both stated that the ruling will have no immediate effect, it is unclear how this decision, subsequent appeals, if any, and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act and our business. Congress may consider other legislation to repeal or replace elements of the Affordable Care Act in the future. We cannot predict what legislation, if any, to repeal or replace the Affordable Care Act will become law, or what impact any such legislation may have on our product candidate

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 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, 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.

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 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.

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 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 and South Korea, 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, Israel, Argentina, south Korea and Russia, if we receive marketing approval, in other countries 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 their acceptance 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.

Our success will depend initially on our ability to commercialize NexoBrid in Europe.

We are currently marketing a single product, NexoBrid, based on our patented proteolytic enzyme technology, which has already been approved by the EMA and the Israeli, Argentinean, Russian and South Korean Ministries of Health for marketing in the European Union, Israel, Argentina, Russia and South Korea respectively, for the treatment of adults with deep partial- and full-thickness burns, which we refer to as severe burns. NexoBrid is not currently approved for marketing in any other jurisdiction, including the United States, and has not been approved for any other indication or for use in children. We launched NexoBrid in Europe in 2014, in Israel in 2015, and in Argentina in 2016, South Korea and Russia in 2019, through our local distributors. In November 2017, the European Commission re-granted a five-year renewal of our NexoBrid marketing authorization. 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.

We are marketing, selling and distributing NexoBrid in Europe and in Israel through our own sales force. We have established a commercial organization for the marketing, sales and distribution of NexoBrid, including our European headquarters in Germany and sales and marketing teams throughout Europe. In order to successfully commercialize NexoBrid, we must successfully manage and operate our marketing, sales, distribution, managerial and other non-technical capabilities, which includes many challenges, such retaining talented personnel; training employees; having the appropriate system of incentives; managing headcount in Europe; and managing business units in Europe. The continued operation of our own sales infrastructure is expensive and time-consuming. Moreover, we do not have substantial experience as a company in operating a significant sales infrastructure and we cannot be certain that we will be able to do so successfully. We will have to compete with other pharmaceutical, biotechnology and wound care companies to recruit, hire, train and retain personnel for medical affairs, marketing and sales.

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 are not profitable and have incurred significant net losses, including net losses of $22.2 million and $1.0 million for the years ended December 31, 2017 and 2018, respectively. As of December 31, 2018, we had an accumulated deficit of $130.7 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 shareholders equity and working capital.

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.

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 product candidate for the treatment of connective tissue disorders or other indications;
- continue to operate our sales, marketing and distribution infrastructure in Europe and thereafter in the United States to commercialize NexoBrid and any pipeline product candidates for which we obtain marketing approval;
- 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;
- 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. For example, on March 7, 2016, the SEC declared our shelf registration statement on Form F-3 effective. Under this shelf registration statement, we could 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 September 2017, we used the shelf registration statement to complete an underwritten public offering of 5,037,664 of our ordinary shares, for net proceeds of $22.7 million, after deducting the underwriting discount and offering expenses payable by us.

Our September 2017 offering diluted then-existing shareholders and to the extent that we raise additional capital through, for example, the sale of equity or convertible debt securities, 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 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 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 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.

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, an intermediate drug substance 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.

If our manufacturing facility in Yavne, Israel were to suffer a serious accident, or if a force majeure event materially affected 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 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 products. 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, even if we obtain a new facility, that 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 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.

Although we have not experienced 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 may result in 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 more costly manufacturing alternatives.

Our ability to continue manufacturing and distributing our products depends on our continued adherence to current good manufacturing practices regulations.

The manufacturing processes for our products are governed by detailed regulations that are set forth in the current cGMP. Failure by our manufacturing and quality operations unit to adhere to established regulations or to meet a specification or procedure set forth in cGMP requirements could require that a product or material be rejected and destroyed. Our adherence to cGMP 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 reflects ever-evolving standards, we need to regularly update our manufacturing processes and procedures to comply with cGMP. 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 discontinuation of the availability of the disposables 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 have liabilities under our former agreements with PolyHeal Ltd.

In 2010 we entered into a series of agreements with Teva Pharmaceutical Industries Ltd. (“Teva”), and PolyHeal Ltd. (“PolyHeal”), to collaborate in the development, manufacturing and commercialization of PolyHeal’s wound product (the “PolyHeal Product”). Under the 2010 series of agreements between PolyHeal and the company (collectively, the “2010 PolyHeal Agreements”), PolyHeal granted us an exclusive global license to develop, manufacture and commercialize the PolyHeal Product, and we granted an exclusive sub-license to Teva to commercialize the PolyHeal Product worldwide. In addition, in accordance with the 2010 PolyHeal Agreements, Teva made investments in our ordinary shares and agreed to fund our research and development expenses and certain manufacturing costs and perform all marketing activities for the PolyHeal Product, under the 2010 PolyHeal Agreement. On November 15, 2012, we informed Teva of the first administration of the next generation of the PolyHeal Product in humans, which constituted a milestone under the 2010 PolyHeal Agreements. Upon achievement of this milestone, Teva was required to invest an additional $6.75 million in exchange for our ordinary shares, and following and pending such investment, we were required to purchase, for an identical amount, ordinary shares of PolyHeal from its existing shareholders. In addition, we believe that Teva was obligated to us for certain payments pursuant to a 2007 collaboration agreement between Teva ("2007 Teva Agreement")and the Company and the 2010 PolyHeal Agreement. On March 24, 2019 we entered into a settlement agreement and mutual general release (the “Teva Settlement Agreement”) with Teva, which settles any and all debts, obligations or liabilities that each party or any of its controlled affiliates had or has to the other party or any of its controlled affiliates under, in connection with or arising out of 2007 Teva agreement and 201 PolyHeal Agreement, which have terminated effective as of December 31, 2012 and September 2, 2013, as applicable, and which related to the Company's Product, NexoBrid, and to PolyHeal.

On September 15, 2014, a statement of claim was filed against the company by certain shareholders of PolyHeal. The plaintiffs allege that the company is obligated to pay them a total amount of approximately $1.3 million plus applicable interest (totaled $1.5 million as of the date of the ruling) in exchange for their respective portion of PolyHeal's shares, following the milestone occurrence. On November 13, 2017, the Tel Aviv District Court issued a ruling in favor of the plaintiffs (the "2017 Ruling"). The Court ruled that we are obligated to purchase PolyHeal's shares for approximately $6.75 million plus applicable interest (totaled $7.5 million as of the date of the ruling), which represents the purchase price for the total number of shares that we were obligated to purchase from PolyHeal subject to the receipt of equivalent funds from Teva. On December 27, 2017, we filed an appeal to the Supreme Court over the said ruling (the "Appeal"), alleging, among other things, that the agreement according to which the ruling was granted was misinterpreted by the District Court. We further alleged that both the wording of the agreement and the conduct of the parties thereunder prove that our' obligation to purchase PolyHeal's shares was subject to the prior receipt of funds, which were never received, from Teva. On January 30, 2018, certain PolyHeal shareholders filed a cross appeal, alleging that they are entitled to receive from us a full repayment of their counsel's fees in a sum equal to 12.5% of the consideration to be paid for their shares (the "Cross Appeal"). In accordance with the 2017 Ruling, on February 7, 2018, we purchased PolyHeal's Shares in consideration for a total sum of approximately $1.5 million.

On March 24, 2019, we entered into a settlement agreement and mutual general release (the "PolyHeal Settlement Agreement") with the plaintiffs, which contingent upon the Supreme Court's approval of the PolyHeal Settlement Agreement, settles any and all debts, obligations or liabilities that we and the plaintiffs had, has or may have to the other party under, in connection with or arising out of the transactions described above. Pursuant to the terms of this PolyHeal Settlement Agreement, the plaintiffs will repay to the company a non-material portion of the amount that was ruled in their favor under the 2017 Ruling, and the Israeli Supreme Court will approve and accept the appeal that was filed by us on December, 2017, cancel the 2017 Ruling that was issued by the District Court against us, and reject the Cross-Appeal. However, if the Israeli Supreme Court does not approve of the PolyHeal Settlement Agreement or refuses to take the actions requested from the court in the PolyHeal Settlement Agreement, these matters may result in the continuation of the existing litigation which would increase our expenses and may disrupt our management's focus on our business.

In addition, we could be required to purchase an equivalent of $6 million of additional ordinary shares of PolyHeal from other shareholders, which could have a material adverse effect on our liquidity and financial condition. Accordingly, a full provision for the purchase price of the shares, plus the accrued interest, totaling $6 million, was recorded within the loss from discontinued operations in respect of the consideration for PolyHeal's shares.

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 proteolytic enzyme technology, although their specific formulations or mode of applications may vary. Like most pharmaceutical products, our approval labels in Europe, Israel, Argentina, South Korea and Russia for NexoBrid lists 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 occur:

- 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.

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.

We face competition from the existing standard of care and potential changes in medical practice and technology and the possibility that our competitors may develop products, treatments or procedures that are similar, more advanced, safer or more effective than ours.

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 is surgery, where debridement can occur by tangential excision, dermabrasion or hydro jet, or non-surgical alternatives, such as topical medications applied to the eschar to facilitate the natural healing process. We face competition in the removal of eschar in severe burns from surgery and topical medications such as gels. In chronic and other hard-to-heal wounds, we expect to face competition from Smith & Nephew Plc's Santyl, a collagenase-based product indicated for debriding chronic dermal ulcers and severely burned areas.

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.

We may lose orphan drug designation for NexoBrid in the United States and the European Union.

NexoBrid has been designated an orphan drug in the United States European Union and South Korea. One of the incentives provided by an orphan drug designation is market exclusivity for seven and ten years in the United States and the European Union, respectively. While the marketing exclusivity of an orphan drug prevents other sponsors from obtaining approval of a similar medicinal product for the same indication (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 indications. In addition, the FDA or the EMA may revisit any orphan drug designation and retains the ability to withdraw the designation at any time. The U.S. Congress has considered, and may consider in the future, legislation that would restrict the duration or scope of the market exclusivity of an orphan drug and, thus, we cannot be sure that the benefits to us of the existing statute will remain in effect.

Regulatory approval for NexoBrid, EscharEx and our 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, Israel, Argentina. South Korea and Russia 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 other regulatory authority and, like the EMA marketing approval for NexoBrid, would be subject to a renewal examination five years after the marketing approval was extended for an additional five years during 2017. Additionally, labeling restrictions limit the manner in which a product may be used. For example, NexoBrid's label provides that it 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 EMA, 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, these 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.

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 and expansion of our marketing and sales infrastructure. 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, which we estimate will be valid and qualified, subject to successful authorities' cGMP audit, during 2022 and which we believe will cost approximately $8-12 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.

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 dollar depreciated relative to the shekel by 9.8% and 1.5% in 2017 and 2016, respectively, while the dollar appreciated relative to the shekel by 8.1% in 2018. 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.

In addition, we expect that our revenues will continue to be denominated in currencies other than the dollar and the shekel, such as the Euro. Therefore, our operating results and cash flows are also subject to fluctuations due to changes in the relative values of the dollar and these foreign currencies. These fluctuations could negatively affect our operating results and could cause them to vary from quarter to quarter. Furthermore, 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.

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 are enforceable by criminal, civil and administrative penalties. 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 various 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, 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. 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. Violations of the federal Anti-Kickback Statute may result in civil monetary penalties up to $100,000 for each violation, plus up to three times the remuneration involved. 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 of up to 10 years. 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 of up to $22,363 for each false claim submitted for payment. Several 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. Other 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, the Affordable Care Act amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health ("HITECH") Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

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 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 civil monetary penalties of up to an aggregate of $150,000 per year, and up to an aggregate of $1 million per year for "knowing failures." Any failure to comply could result in significant fines and 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 federal government or otherwise restrict payments that may be made to healthcare providers; 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; 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.

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 contract. 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 existing BARDA contract 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 $10.0 million for claims in the European Union Israel Argentina, South Korea and Russia 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.

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 patent, 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, 2018, we had been granted a total of 96 patents and have 37 pending patent applications. The family of patents that covers NexoBrid specifically includes 35 granted patents worldwide and 1 pending national phase application. EscharEx is covered in 30 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 proteolytic enzyme 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 patent 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 if granted, the expiration date of these patents would be 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 be issued in a form that will 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 rights in related 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 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 or may fall within the scope of one or more claims in a published patent application that may be subsequently issued and 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.

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.

We are subject to foreign data privacy and security laws.

We are also subject to data privacy and security laws in the E.U. as well as the EEA, including Regulation (EU) 2016/679 (General Data Protection Regulation, or GDPR) in relation to our collection, control, processing, sharing, disclosure and other use of personal data (i.e. data relating to an identifiable living individual). The GDPR is directly applicable in each E.U. and EEA Member State, however, it provides that E.U. and EEA Member States may introduce further conditions, including limitations, which could limit our ability to collect, control, process, share, disclose and otherwise use personal data (including health and medical information), and/or could cause our compliance costs to increase, ultimately having an adverse impact on our business. The GDPR imposes a strict data protection compliance regime including with regard to engaging third party processors and cross-border transfers of personal data out of the E.U. and EEA. Fines for certain breaches of the GDPR are significant: up to the greater of EUR 20 million or 4% of total global annual turnover. In addition to the foregoing, a breach of the GDPR could result in regulatory investigations, reputational damage, orders to cease/ change our processing of our data, enforcement notices, assessment notices (for a compulsory audit), as well potential civil claims including class action type litigation where individuals suffer harm.

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.

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

The United Kingdom held a referendum in June 2016 in which a majority of voters voted to exit the European Union, which is generally referred to as Brexit. Negotiations are continuing to determine the future terms of the United Kingdom's relationship with the European Union, including, among other things, the terms of trade between the United Kingdom and the European Union as well as other world trading partners. The effects of Brexit will depend on any agreements the United Kingdom makes to retain access to European Union markets either during a transitional period or more permanently. In addition, Brexit could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union and could require us to obtain separate approvals for our product candidates in the United Kingdom and the European Union. 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 the United Kingdom and/or the European Union 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 the United Kingdom and/or European Union 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 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 $3.95 per share through March 24, 2019. 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;
- 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.

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 will rely in part on the research and reports that equity research analysts publish about us and our business, if at all. 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.

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

If we or our existing shareholders, particularly certain of 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 March 7, 2016, the SEC declared effective our shelf registration statement on Form F-3, which registered the resale of 11,640,827 shares subject to registration rights. All shares sold pursuant to an offering covered by such registration statement (or a subsequent shelf registration that we file to replace it after it expired) will be freely transferable. See "ITEM 7.B. Related Party Transactions—Registration Rights Agreement." In September 2017, we completed an underwritten public offering of 5,037,664 of our ordinary shares. 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 to these registration rights, as of March 15, 2019, 2,409,082 ordinary shares were subject to outstanding option and RSU awards granted to employees and office holders under our share incentive plans, including 1,475,457 ordinary shares issuable under currently exercisable share options. 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 2,178,806 ordinary shares issuable upon the exercise of option awards previously granted under our 2003 Israeli Share Option Plan and 853,936 ordinary shares issuable under our 2014 Equity Incentive Plan. On January 1, 2015, 2018 and 2019, the shares available for issuance under our 2014 Equity Incentive Plan automatically increased by 431,006, 540,955 and 543,577 shares, respectively. As of March 15, 2019, 3,412,194 shares remained available for issuance under our share incentive plans, which amount includes 1,272,943 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, 2018, Clal Biotechnology Industries Ltd. ("CBI"), beneficially owns or controls, directly and indirectly, 34.7% 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 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 and (iii) independence requirement for the board of directors. 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, certain transactions other than a public offering involving issuances of a 20% or more interest in 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 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 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.

We are an "emerging growth company" and the reduced disclosure requirements applicable to emerging growth companies may make our ordinary shares less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act (the "JOBS Act"), and we may take advantage of certain exemptions from various requirements that are applicable to other public companies that are not emerging growth companies. Most of such requirements relate to disclosures that we would only be required to make if we cease to be a foreign private issuer in the future. Nevertheless, as a foreign private issuer that is an emerging growth company, we will not be required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act for up to five fiscal years after the date of our initial public offering. We will remain an emerging growth company until the earliest of: (a) the last day of our fiscal year during which we have total annual gross revenues of at least $1.07 billion; (b) December 31, 2019, the last day of our fiscal year following the fifth anniversary of the closing of our initial public offering; (c) the date on which we have, during the previous three-year period, issued more than $1.0 billion in non-convertible debt; or (d) the date on which we are deemed to be a "large accelerated filer" under the Exchange Act. When we are no longer deemed to be an emerging growth company, we will not be entitled to the exemptions provided in the JOBS Act discussed above. We cannot predict if investors will find our ordinary shares less attractive as a result of our reliance on exemptions under the JOBS Act. If some investors find our ordinary shares less attractive as a result, there may be a less active trading market for our ordinary shares and our share price may be more volatile.

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. Additionally, pursuant to Section 404(b) of the Sarbanes-Oxley Act, unless we lose our status as an "emerging growth company" under the JOBS Act prior to the end of the fiscal year in which the fifth anniversary of our IPO occurred, we will not be required to obtain an auditor attestation under Section 404 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, 2018. 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, 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 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."

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 and military instability in Israel and by conflicts between Israel and other 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, economic, and military instability in Israel, including hostilities between Israel and its Arab neighbors, Hezbollah (an Islamist militia and political group in Lebanon) and Hamas (an Islamist militia and political group in the Gaza strip).

Recent political uprisings, social unrest and violence in various countries in the Middle East and North Africa, including Israel's neighbors Egypt and Syria, are affecting the political stability in those regions. This instability may lead to deterioration of the political relationships that exist between Israel and these countries and have raised concerns regarding security in the region. In addition, Iran has threatened to attack Israel and is widely believed to be developing nuclear weapons, and 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. These events and any future political, economic and military instability have the potential to interrupt our operations by damaging our facilities 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, 2018, we had 61 employees based in Israel, certain of which may be called upon to perform up to 54 days of military service in each three-year period (and in the case of non-officer commanders or officers, up to 70 or 84 days, respectively, in each three-year period) of military reserve duty 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. Such actions, particularly if they become more widespread, 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 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 were and are 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 and net of royalties actually paid as of December 31, 2018, totaled approximately $13.7 million and the amortized cost (using the interest method) of the liability as of that date totaled approximately $7.7 million. As of December 31, 2018, we had accrued and paid royalties to the IIA $0.3. We expect to receive additional grants from the IIA and we applied for further grants for 2019. However, as the funds available for IIA grants out of the annual budget of the State of Israel have been reduced in the past and may be further reduced in the future, we cannot predict whether we will be entitled to any future grants, or the amounts of any such grants.

The grants 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 (and in an adjourned meeting, with some exceptions, any number of shareholders). 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.

Item 4. INFORMATION ON THE COMPANY

A. History and Development of the Company

Our History

MediWound Ltd. ("MediWound") was founded in January 2000 with the goal of developing, manufacturing and commercializing novel products to address unmet needs in the fields of severe burns as well as chronic and other hard-to-heal wounds and connective tissue disorders. Our innovative biopharmaceutical product, NexoBrid, received marketing authorization from the EMA and the Israeli, Argentinian, South Korean and Russian Ministries of Health, for removal of dead or damaged tissue in adults with severe burns.

In March 2014, we listed our shares on the Nasdaq Global Market. We are a company limited by shares organized under the laws of the State of Israel. 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 fully integrated biopharmaceutical company focused on developing, manufacturing and commercializing novel therapeutics products to address unmet needs in the fields of severe burns, chronic and other hard-to-heal wounds, connective tissue disorders and other indications. Our first innovative biopharmaceutical product, NexoBrid, received marketing authorization from the EMA and the Israeli, Argentinean, South Korean and Russian 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. NexoBrid, which is based on our patented proteolytic enzyme technology, 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 have established a commercial organization for the marketing, sales and distribution of NexoBrid, including European headquarters in Germany and sales and marketing teams throughout Europe. We sell NexoBrid in Europe and Israel through our commercial organization, and we have launched NexoBrid in Argentina and South Korea and expect to launch in Russia in the first half of 2019, through our local distributor. We have recently announced the positive top-line results from our U.S. Phase 3 pivotal (DEDECT) study to support BLA submission to the FDA, has met its primary and all secondary endpoints and we are conducting a pediatric Phase 3 (CIDS) study to broaden the approved indication of NexoBrid, which we have recently expended to United States burn centers. Both the DETECT and the CIDS studies as well as the intended BLA submission to the FDA are funded by BARDA. We manufacture NexoBrid in our state-of-the-art, EMA-certified, cGMP-compliant, sterile pharmaceutical products manufacturing facility at our headquarters in Yavne, Israel.

NexoBrid is an easy to use, topically-applied product that removes eschar in four hours without harming the surrounding healthy tissues. The removal of eschar is a procedure also known as debridement. Debridement 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 15 countries and four continents in seven completed Phase 2 and Phase 3 clinical studies. 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 50 peer-reviewed papers, resulting in support of burn specialists and key opinion leaders. Awareness of NexoBrid continues to grow through our marketing efforts and continued multinational clinical development.

Our second innovative product candidate, EscharEx, is a topical biological drug being developed for debridement of chronic and other hard-to-heal wounds and is complementary to the large number of existing wound healing products, which require a clean wound bed in order to heal the wound. EscharEx contains the same proteolytic enzyme technology as NexoBrid, and benefits from the wealth of existing development data on NexoBrid. We have reported final results from our second Phase 2 study evaluating EscharEx for the debridement of chronic and other hard-to-heal wounds. In two Phase 2 studies that we conducted, this technology demonstrated safety and efficacy in the debridement of chronic and other hard-to-heal wounds, in a few applications.

The market opportunities for our patented proteolytic enzyme technology include both eschar removal of severe burns using NexoBrid and debridement of chronic and other hard-to-heal wounds using EscharEx. Approximately 100,000 patients with severe burns are hospitalized every year in the United States and Europe. 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.

In addition to marketing NexoBrid in Europe, we have signed local distribution agreements for distribution in Argentina, Russia, South Korea, Mexico, Colombia, Peru, Chile, Ecuador, Panama, India, Bangladesh, Sri Lanka, Japan, and Taiwan. We plan to target other international markets, such as Latin America, certain Asia-Pacific countries and members of the Commonwealth of Independent States ("CIS"), 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 a 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 fast debridement 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 potential solution for treatment of burns in the event of a MCI. In September 2015, we were awarded a contract by BARDA valued at up to $112 million for the advancement of the development and manufacturing, as well as the procurement, of NexoBrid as a medical countermeasure as part of BARDA's preparedness for mass casualty events. In July 2017, BARDA expanded its committed funds to support our research and development activities by an additional $32 million, bringing potential total non-dilutive funding to a maximum of $132 million.

In addition, in September 2018 we awarded a new contract to develop NexoBrid for the treatment of Sulfur Mustard injuries as part of BARDA preparedness for mass casualty events. The 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 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. See "—BARDA Contract" below.

We believe that the indication of debridement of chronic wound and other hard-to-heal-wounds with EscharEx represents a significant opportunity, having what is believed to be a total addressable patient base of more than 14 million patients in the United States and Europe alone, suffering from disorders such as diabetic foot ulcers ("DFUs"), venous leg ulcers ("VLUs"), pressure ulcers and surgical/traumatic hard-to-heal wounds. Currently, surgery is an effective method to debride a wound, however, sharp debridement 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 such as current enzymes, hydrogels and other topical dressings, which require numerous application sessions and a long time to achieve a clean wound bed, if they achieve this at all. Thus, there is an unmet need for a non-surgical product that will be effective like surgery, but without its limitations, and will significantly enhance the rate of, and time to achieve, complete debridement. As documented in the Phase 2 study described above, EscharEx significantly improves the rate of complete debridement after few once-daily applications, thus facilitating wound debridement without the need for surgery.

We are also using our patented proteolytic enzyme technology, which underlies NexoBrid, and our wealth of data and experience gained during the NexoBrid development, to support the development of additional indications such as treatment of connective tissue disorders. In ex-vivo model studies, which are laboratory studies conducted on tissues or cells extracted from a living organism, which in our case were conducted on diseased contracted cords that had been surgically removed from patients with a Dupuytren contracture, our technology confirmed with statistical significance that it could dissolve the pathological cords. We are developing an injectable formulation and conducted toxicology studies to enable initiation of clinical studies. We continue to explore additional indications as well.

Our Focus:

Burn Wounds

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. We believe these patients can benefit from NexoBrid's effective and selective, non-surgical eschar removal.

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 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 fast 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.

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 DFUs, VLUs and 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:

- *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. In the United States alone, over 23 million people, or approximately 8% of the population, suffer from diabetes, a chronic, life-threatening disease. 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, every year, in the United States alone, over 900,000 people develop a DFU and over 600,000 undergo debridement of DFUs.

- *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, in the United States alone, affect approximately 1.25 million people per year, out of which over 650,000 undergo debridement of VLUs. 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.

- *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.

Connective Tissue Disorders

In addition to severe burns and chronic and other hard-to-heal wound indications, we are developing an injectable product based on our patented proteolytic enzyme technology for connective tissue pathologies and indications, such as:

- *Dupuytren's disease:* a condition where one or more fingers are permanently flexed, caused by the formation of scar-like tissues below the palmar skin (Palmar Fascia), forming hard "cords" that freeze the fingers in non-functional flexion contraction. This condition affects approximately 6.2 million people in the United States alone.

- *Peyronie's disease:* the development of scar-like tissue, similar to Dupuytren's cords in the shaft of the penis, causing pain and distortion on erection, preventing intercourse. Peyronie's disease is typically caused by trauma and affects men over 50 years old. Surgical treatment may be an option in some cases, but can cause complications and may result in a shortening and even greater distortion of the penis. Approximately 3.7% to 7.1% of the male population above the age of 50 suffers from Peyronie's disease in the United States and approximately 3.2% of such age group suffer from the disease in Europe.

- *Frozen shoulder syndrome:* a disorder that causes the smooth tissues of the shoulder capsule to become thick, stiff and inflamed, affecting approximately 2% to 5% of the worldwide population and 10% to 20% of people with diabetes according to industry sources.

- *Excessive/unaesthetic scars:* A scar is a mark on the skin which is formed due to infection, injury, surgery, inflammation of tissue, burns, and acne. Scars can be of various sizes, shapes, and colors, depending on the age of the scar, the site of the scar and family history. Scar formation is unpredictable and varies from person to person. Excessive scarring can have unpleasant physical, aesthetic, psychological and social consequences. Estimates indicate that each year around 100 million people in the developed world acquire scars following elective surgery and surgery for trauma. Of these, approximately 15% have excessive or unaesthetic scars.

Currently, SOC for connective tissue disorders involves surgery, with a very high recurrence rate, and some non-surgical alternatives. One such alternative for the treatment of Dupuytren's and Peyronie's diseases is Xiaflex, a collagenase-based injectable enzyme that has received orphan drug status in the United States.

BARDA Contract

In September 2015, BARDA awarded us a contract valued at up to $112 million. In July 2017, BARDA expanded its commitment by an additional $32 million, bringing potential total non-dilutive funding to a maximum of $132 million. The contract is for the advancement of the development and manufacturing, as well as the procurement, of NexoBrid as a medical countermeasure as part of BARDA preparedness for mass casualty events.

The contract includes $56 million of funding to support development activities to complete the FDA approval process for NexoBrid for use in thermal burn injuries, as well as $16.5 million for procurement of NexoBrid, which is contingent upon FDA Emergency Use Authorization ("EUA") or FDA marketing authorization for NexoBrid. In addition, the contract includes options for further funding of up to $10 million for expanding NexoBrid's indications and up to $50 million for additional procurement of NexoBrid. The agreement may be terminated by BARDA at any time at BARDA's discretion.

In September, 2018, BARDA awarded us an additional new contract to develop NexoBrid for the treatment of Sulfur Mustard injuries as part of BARDA preparedness for mass casualty events. The 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 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, 2018 the Company has recorded $28.2 million in funding from BARDA under both contracts.

NexoBrid and Our Clinical History

NexoBrid, our innovative biopharmaceutical product, received marketing authorization from the EMA and the Israeli, Argentinean, South Korean and Russian Ministries of Health for the removal of eschar in adults with deep partial- and full-thickness thermal burns. The active ingredient in NexoBrid is a mixture of proteolytic enzymes enriched in bromelain prepared from an extract of pineapple plant stems. Proteolysis is a breakdown of proteins into smaller building blocks, polypeptides or amino acids. Our research and development team further developed and optimized this patented proteolytic enzyme technology, which is the basis for NexoBrid and all of our current 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 100cm^2.

We developed NexoBrid to fulfill the previously unmet need for an 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 15 countries and four continents in seven completed Phase 2 and Phase 3 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
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
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
Main Objectives	• Safety • Efficacy	• Comparison of efficacy and safety	• Safety • Efficacy	• Safety	• Safety • Efficacy	• Long-term scar assessment • Quality of life	• Safety and pharmacokinetics • 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
Number of Patients	• 154	• 20	• 140	• 30	• 182	• 89	• 36
Study Length	• 1985-2000	• 2002-2005	• 2003-2004	• 2006-2007	• 2006-2009	• 2011	• 2009-2015
Location	• Israel	• Israel	• International	• United States	• International	• International	• International

Trial 1: Retrospective Phase 2—Israel

Trial 1 evaluated the safety and efficacy of NexoBrid in hospitalized subjects between six months and 82 years of age with severe burns of up to 67% TBSA. Data from 154 subjects with complete file documentation were analyzed, including a signed informed consent form and pre- and post-eschar removal photographs. According to the trial, NexoBrid allowed early and fast debridement, reduced surgical burden and was determined to be safe locally and systemically.

Trial 2: Dose Range Phase 2—Israel

Trial 2 evaluated the efficacy and safety of three doses of NexoBrid. Twenty hospitalized adult subjects with severe burns of 1-15% TBSA were randomized and provided a one-, two- or four-gram dose of NexoBrid powder per 20 grams of a sterile gel substance ("Gel Vehicle"). The study confirmed that the use of two grams of NexoBrid mixed with 20 grams of Gel Vehicle per 100cm2 was a safe and effective dose.

Trial 3: Prospective Phase 2—International/Investigational New Drug ("IND")

Trial 3 evaluated the safety and enzymatic eschar removal efficacy of NexoBrid as compared to the Gel Vehicle and SOC. A total of 140 hospitalized adult subjects with severe burns of 2-15% TBSA (but not more than 30% TBSA in total), were randomized in a 2:1:1 ratio to NexoBrid, Gel Vehicle and SOC treatment. The trial results showed that NexoBrid was a fast and effective enzymatic debriding agent, combining the advantage of early eschar removal with reduced surgical burden.

Trial 4: Prospective Phase 2—United States/IND

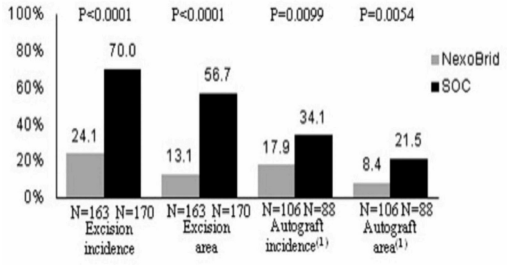
Trial 4 evaluated the safety and exploratory efficacy of NexoBrid in comparison to the Gel Vehicle and SOC in hospitalized adult subjects with severe burns of 1-5% TBSA. Thirty hospitalized subjects were randomized and provided NexoBrid, the Gel Vehicle or SOC treatment. Although this study was designed as a safety study and was conducted in a limited number of patients, the results suggest that NexoBrid provided effective debridement and may be an alternative to surgical debridement. According to the trial, NexoBrid had a similar safety profile to the Gel Vehicle and SOC and the Gel Vehicle was not shown to have any deleterious effect.

Trial 5: Phase 3—EMA

Trial 5 evaluated the safety and efficacy of NexoBrid. The study was a prospective, controlled, two-arm, parallel, open-label, randomized, multi-center design. It included 182 enrolled patients between the ages of four and 55, who were hospitalized with severe burn wounds covering from 5-30% TBSA. The two arms consisted of patients who were treated with NexoBrid and patients who were treated with SOC, which included surgical and non-surgical eschar removal. The treatment of the study arms differed only by the studied eschar removal modalities. The co-primary endpoints were the percentage of wound area that was excised and the percentage of wound area that was autografted. The secondary endpoints included need for and extent of eschar excision, time to wound closure, time to complete eschar removal (≥ 90%) and blood loss. The study was successfully concluded when pre-planned interim analysis demonstrated a statistically significant difference in both primary endpoints between the groups.

The results showed that NexoBrid significantly reduced both the percentage of wounds requiring excision or autografting and the percentage of wound area requiring excision or autografting. P-value is a measure of statistical significance, with P<0.05 considered statistically significant.

In patients who received NexoBrid, 24.5% of wounds required excision, whereas, in patients who received SOC, 70.0% of wounds required excision (P<0.0001). With regard to the proportion of wound area excised when excision was required, patients who received NexoBrid had 13.1% of wound area excised, compared to 56.7% of wound area excised for patients receiving SOC (P<0.0001). The results were similar for autografting, although this endpoint could only be evaluated for deep partial-thickness wounds, as full-thickness wounds always require autografting due to the lack of viable dermis, regardless of the technique used to remove the eschar. In patients receiving NexoBrid, 17.9% of deep partial-thickness wounds required autografting, compared to 34.1% for patients receiving SOC (P=0.0099). With regard to the proportion of wound area autografted, patients who received NexoBrid had 8.4% of deep partial-thickness wound area autografted, compared to 21.5% for patients receiving SOC (P<0.0054).

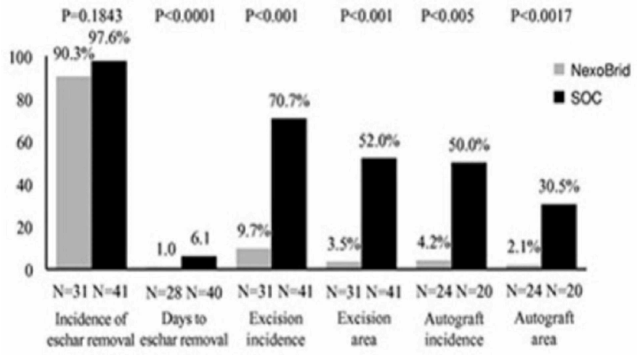


(1) Only deep partial-thickness wounds are presented, as full-thickness wounds always require autografting due to the lack of viable dermis, regardless of the technique used to remove the eschar.

NexoBrid successfully removed the eschar in 96.3% of the wounds compared to 93.5% of the wounds debrided by SOC.

The results also showed that NexoBrid significantly reduced the time required to achieve successful eschar removal, allowing for early and direct assessment of the wound bed. For patients with successful eschar removal, defined as at least 90%, those who received NexoBrid achieved successful eschar removal in 0.8 days, compared to 6.7 days for patients receiving SOC, as measured from the time of signing informed consent (P<0.0001), which represents the time at which a patient can start being treated with an investigational product in a clinical trial setting.

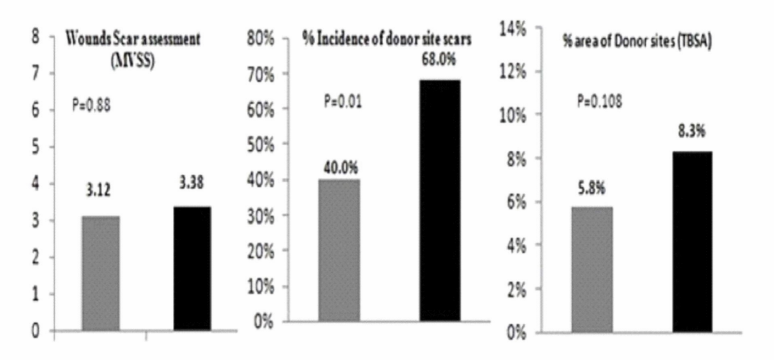
With regard to hand burns, results showed that the use of NexoBrid significantly reduced surgical burden in terms of the need for excision, grafting or escharotomy. In patients who received NexoBrid, 9.7% required excision, compared to 70.7% for patients receiving SOC (P<0.0001). When excision was required, the proportion of wound area excised was 3.5% for patients receiving NexoBrid and 52.0% for patients receiving SOC (P<0.0001). As for autografting, 4.2% of patients treated with NexoBrid required autografting, compared to 50.0% of patients treated with SOC (P=0.0005). When autografting was performed, the proportion of wound area autografted was 2.1% for patients who received NexoBrid and 30.5% for patients who received SOC (P=0.0017). With respect to escharotomies, no escharotomy was needed for hand burns treated with NexoBrid, whereas 9.7% of hand burns treated with SOC required escharotomies (P=0.07).



Trial 6: Phase 3b—EMA

Trial 6 assessed long-term scar formation and quality of life in adults and children who received NexoBrid or SOC during the Phase 3 clinical study. The follow-up was completed two to four years after injury. The study was a prospective, controlled, two-arm, parallel, blinded, multi-center design and included 89 patients. Scar quality was assessed using the Modified Vancouver Scar Scale ("MVSS"). The MVSS measures pliability, height, vascularity, and pigmentation, as well as pain and pruritus, on a scale of 0 to 18, with a higher score indicating a more severe scar. To assess quality of life, the study used the Short Form-36 questionnaire ("SF-36") for adults and the Burn Outcome Questionnaire ("BOQ") for children.

The results confirmed that based on the MVSS the quality of scars was comparable between the patients who received NexoBrid and those who were treated with SOC (3.12 and 3.38, respectively, P=0.88). However, patients who received NexoBrid experienced a significantly reduced overall quantity of scarring as compared to those who received SOC; with NexoBrid, 40% of patients had donor site scars, as compared to 68% of patients with SOC (P=0.01). Donor site scars on those who received NexoBrid were also 30% smaller than scars on those who received SOC (P=0.108). It was also confirmed that quality of life using the SF-36 and BOQ was comparable in both groups.



Clinical development overall safety assessment

The most commonly reported adverse reactions when using NexoBrid are local pain and transient pyrexia/hyperthermia. The data from its clinical development showed that the frequency of pain and pyrexia/hyperthermia was reduced through precautionary measures, including preventive analgesia as routinely practiced for extensive dressing changes in burn patients as well as antibacterial soaking of the treatment area before and after NexoBrid application. NexoBrid was not found to be associated with a significantly increased risk of serious or severe adverse events compared to SOC. Serious infections occurred with similar frequency in the SOC and NexoBrid cohorts and the incidence was low. Adverse events occurring in ≥3.0% of treated subjects (e.g. pruritus, or itching, anemia, insomnia, nausea, vomiting and skin graft failure) are common in burn patients and their rate was comparable between NexoBrid and SOC treated patients and below the rates reported in the literature. NexoBrid debridement was associated with a slightly higher rate of wound complications, general infections, wound infections/wound cultures and extent in antibiotic-use. The imbalances were small, wound infections were only mild to moderate in severity and each responded well to treatment. No detrimental effect on long-term outcome has been detected for the NexoBrid treated patients.

During the above mentioned completed trials, there were five deaths (four reported in the Phase 2 study) resulting from medical reasons in NexoBrid patients compared to one non-related death in the SOC group. Neither the analysis of the narratives contained in the death investigative report, nor the opinions of the physicians who treated the patients, nor the Data Safety Monitoring Board have associated NexoBrid with the deaths in patients who received the treatment. The EMA concluded that the benefit-risk of NexoBrid for the removal of eschar in adults with deep partial, mixed and full-thickness burns is positive.

Trial 7: Phase 2—EMA

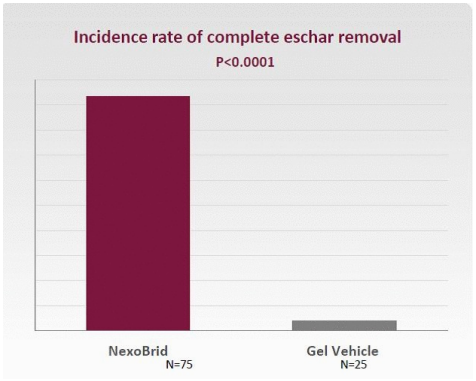
Trial 7 evaluated the safety, pharmacokinetics (transcutaneous absorption) and efficacy of NexoBrid in hospitalized children and adults with thermal burns. The multicenter, open-label, single-arm study was conducted in Europe, Israel and India and included 36 patients with severe burns of 4% to 30% total body surface area (TBSA). NexoBrid was applied to burns of up to 15% TBSA in one session, and when the wound area to be treated was more than 15% TBSA, NexoBrid was applied in two separate sessions, each up to 15% TBSA. Trial results showed that the use of NexoBrid was safe and effective. Furthermore, the pharmacokinetic profile following NexoBrid's first and second topical application was comparable, suggesting no concern with accumulation following a second topical application of NexoBrid.

Ongoing and future clinical trials

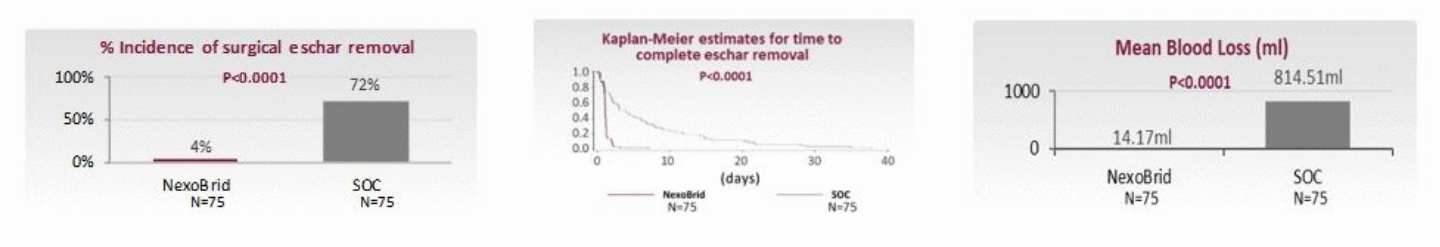
U.S. Phase 3 Study – DETECT study

The DEDECT 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 patients 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 involves 44 burn centers. The study objectives are 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. On January 2019 we announced positive top-line results. 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]).

[1] Fisher's exact test



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 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[2]); Patients treated with NexoBrid demonstrated a significantly shorter time to achieve complete eschar removal compared with patients treated with SOC (median time - NexoBrid: 1.0 days vs. SOC: 3.8 days, p<0.0001[3]); 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 have been treated, that the overall safety profile of NexoBrid in the study is good, and consistent with the safety data known from previous studies.



The planned twelve-month and twenty four-month safety follow-ups for cosmesis, function, quality of life and safety measurements are ongoing, and the Company expects to submit to the FDA the analysis of the twelve-month safety follow up in the first half of 2020 and of the twenty four months safety follow-up in the first half of 2021.

We plan to submit the Biological License Application (BLA) in the second half of 2019 based on the above available acute primary, secondary, and safety data with the twelve-month safety follow-up data submitted during the BLA review, subject to FDA concurrence at a pre BLA meeting planned for first half of 2019.

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

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

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 recently expended 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 study includes three pre-defined stages: Stage 1 includes patients from age four to 18; Stage 2 includes patients from age one to 18; and Stage 3 includes patients from birth to age 18. The study is currently in Stage 2. Recently, after reviewing the data of 50 pediatric patients, the study Data Safety Monitoring Board (DSMB) recommended to lower the study exclusion criteria age even further, to include pediatric patients also from new born to one years old. Based on this recommendation, we intend to approach the study sites' Institutional Review Boards and ask to allow to include into the CIDS study pediatric patients of all ages, from new born 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 24-month follow-up. Interim results with predefined stopping rules after a 12-month follow-up of all patients are expected to be available in the second half of 2022, with final results available in the second half of 2023. This study is funded by BARDA. See "—BARDA Contract" above.

European observational retrospective data collection study

As part of our post marketing commitment in Europe and as is customary for recently approved drugs, we agreed with European regulatory authorities to conduct an observational retrospective data collection study to assess risk minimization measures in burn patients who were treated with NexoBrid. The data was collected by investigators who will fill in report based on medical records of patients who received NexoBrid treatment at burn centers in the first two years from product launch and signed on inform consent form. Data was collected retrospectively from 160 burned patients which were treated with NexoBrid during 2 years period from launch date in 6 E.U. countries (Germany, Belgium, Sweden, Poland, Spain and Slovak Republic). The main objective of this study is assessing the effectiveness of the risk minimization activities and their effect on the incidence rate of pain and pyrexia compared to the incidence rate reported during Trial 5 (Phase 3—EMA). We recently completed the survey data collection and overall, the study met its co-primary endpoints showing non-inferiority in incidence rates of reported events of pain and pyrexia in the NexoBrid treated patients as compared with the events reported in clinical development of NexoBrid. Final results shall be reported to EMA on the second half of 2019. This study is funded by BARDA. See "—BARDA Contract" above.

EscharEx and Our 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 an effective and non-surgical debridement mean. EscharEx is based on the same patented proteolytic enzyme technology as NexoBrid but differs in other aspects, such as in formulation and presentation.

We completed a first Phase 2 feasibility study in Israel for chronic and other hard-to-heal wound technology. In January 2017 we 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 technology 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 prospective study was conducted in Israel and Europe 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. This was a prospective, controlled, assessor-blinded, randomized, multi-center Phase 2 study in Israel and Europe.

The primary endpoint assessed incidence of complete non-viable tissue removal (debridement) at the end of the debridement period (up to 10 treatment days) 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 EscharExwere older than wounds treated with gel vehicle (72.8 vs. 30.8 weeks), the study met its primary endpoint, as 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 vehicle (29% or 7/24) with p=0.047.

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

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 over extended periods of application to further support the product's convenient application. In this second cohort, we recruited patients from two etiologies, either DFUs or VLUs, over extended periods of application (24-72 hours) in 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.

In September 2017 we reported final results of the second cohort of 38 patients.

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.

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

Following discussions with the FDA regarding the clinical program for EscharEx to treat chronic and hard-to-heal wounds, we were able to obtain FDA concurrence that complete debridement will be the primary endpoint of the studies and wound closure will be measured as a safety outcome to document that EscharEx has no deleterious effect on wound closure. This design was used in our recently reported successful second Phase 2 study as well as in our on-going NexoBrid U.S. Phase 3 study in burns. We recently met with the Agency to discuss EscharEx development, received concurrence on many aspects, and suggested additional secondary efficacy endpoints on which we were requested to provide additional information. We recently submitted the information, and subject to FDA concurrence, plan to initiate EscharEx clinical program in the first half of 2019.

In tandem, we have been working on a second generation of EscharEx, or EX-02. This advanced formulation is designed to have several advantages. Based on our current pre-clinical studies, EX-02 demonstrated even higher potency in lower doses, which should further contribute to EscharEx's efficacy and tolerability. In addition, we believe EX-02 would be even easier to prepare and applied, which will further support compliance by the patient or caregiver and finally, EX-02 is more differentiated from NexoBrid, which further limits the chances for inter-competition between the two products.

The development of EscharEx for chronic and other hard-to-heal wound indications is in Phase 2 studies, and there is no certainty that EscharEx will achieve all the objectives of the trials as required or that 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. See "ITEM 3.D. Risk Factors—Development and commercialization of NexoBrid in the United States and our pipeline product candidates worldwide requires successful completion of the regulatory approval process, and may suffer delays or fail."

MWPC003 and Our Pre-Clinical History

We have performed preclinical model studies in Israel for the use of our patented proteolytic enzyme technology in treating connective tissue disorders. Our technology has shown promising results in preclinical model studies for the treatment of connective tissue pathologies. We are advancing the in-house production capacity of the injectable formulation and completed local toxicology studies to potentially allow us to initiate the clinical development of our pipeline product candidate, MWPC003, for connective tissue disorders.

We have 6 patents (in the United States and in other international markets) and 8 patent applications for MWPC003. These patents provide broad protection for the specific mixture of proteolytic enzymes in the treatment of a variety of connective tissue diseases. The patents are nominally set to expire on July 19, 2032.

Preclinical model study—Israel

In preclinical model studies, excised Dupuytren cords were injected with either MWPC003 or a saline solution (control) following Starkweather's ex-vivo validated model. MWPC003 repeatedly provided enzymatic degradation of Dupuytren cords (fasciotomy) in a tearing test model confirming with statistical significance that MWPC003 completely dissolves Dupuytren's cords (Fisher Exact test $p<0.0001$). In a second *ex vivo* study conducted in 71 cords injected with MWPC003 in descending doses, it was demonstrated that even very small doses of MWPC003 can dissolve the pathological cord in more than 80% of cases with the Cochran-Armitage test ($p=0.0021$) indicating that the probability for cord dissolution increases as the dose increases. Toxicology studies conducted in two species did not indicate systemic toxicity and the intra-dermal local effect was reversible.

Although we have conducted preclinical trials, the development of MWPC003 for connective tissue disorder 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 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 on developing our patented proteolytic enzyme technology, 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."

Clinical Trials

We conduct clinical tests 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 profile. As of the date hereof, we had conducted more than 20 preclinical studies, 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 28 employees as of December 31, 2018. 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 and the Israeli Ministry of Health. Our facility was approved and, after passing a periodic ministry of health audit in May 2017, reapproved as cGMP-compliant for an additional three-year term as of the audit date, until 2020 during which the Israeli Ministry of Health is scheduled to conduct its periodic audit for assessment of cGMP compliance renewal. Additionally, as we seek regulatory approval in the United States and other international jurisdictions for NexoBrid, the FDA or other regional applicable authorities may inspect our plant to confirm it meets all regulatory requirements. 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, which we estimate will be valid and qualified, subject to successful authorities cGMP audit, during 2022, and which we expect to cost approximately $8-12 million.

The intermediate drug substance used by us in the manufacturing of NexoBrid 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 gel substance by combining water for injections produced by us at our facility and additional excipients. The powder and gel are kept in separate containers in one package of NexoBrid and are simply mixed by a healthcare professional prior to use. NexoBrid is authorized to be sold in Europe, Israel and Argentina in packages containing either a vial of two grams of powder and a jar of 20 grams of gel, or a vial of five grams of powder and a jar of 50 grams of gel. Once the powder and gel are mixed, NexoBrid should be applied within 15 minutes at a ratio of either 2 grams of powder and 20 grams of gel to a burn wound area of 100 cm2 or 5 grams of powder and 50 grams of gel to a burn wound area of 250 cm2, as applicable; however, under current usage, NexoBrid's label provides that it should not be applied to more than 15% TBSA. Prior to mixture and application, NexoBrid has a shelf life of three years when stored under refrigeration.

Marketing, Sales and Distribution

We sell NexoBrid in Europe and Israel through our own commercial organization and launched NexoBrid in Argentina, South Korea and in the coming months in Russia through our local distributors. We are marketing NexoBrid by targeting a focused segment of burn specialists treating patients with severe burns in burn centers throughout the European Union. 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. In Europe, the marketing, sales and distribution of NexoBrid is carried out by our wholly-owned German subsidiary, MediWound Germany GmbH, which consists of a marketing team of specialized and knowledgeable sales representatives in Europe. We obtained national reimbursement in Belgium and Italy and we continue to locally execute our market access strategy for most of Europe to obtain procurement by hospitals as part of their budget, or under local, regional or national reimbursement, depending on the specific process required in each country. See "—Government Legislation and Regulation—Pharmaceutical Coverage, Pricing and Reimbursement." 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 50 peer-reviewed papers.

As part of the awarded contract with BARDA, we believe that, contingent upon the FDA Emergency Use Authorization and/or FDA marketing authorization for NexoBrid, BARDA's procurement of $16.5 million of NexoBrid as a medical countermeasure for preparedness for mass casualty events will be initiated in the second half of 2019, following the completion of the DETECT study acute phase.

In addition, upon FDA marketing authorization, we anticipate that NexoBrid will require a focused commercial team on the ground in the United States to cover the specialty hospital call point and maximize NexoBrid's commercial value.

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. We have signed local distribution agreements for distribution in Argentina, Russia, South Korea, Mexico, Colombia, Peru, Chile, Ecuador, Panama, India, Bangladesh, Sri Lanka, Japan and Taiwan. Our distributors in Argentina, South Korea and Russia obtained marketing authorization and launched NexoBrid. 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 2019.

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, 2018, we had been granted a total of 96 patents and have 37 pending patent applications. The family of patents that covers NexoBrid specifically includes 35 granted patents worldwide and 1 pending national phase application. EscharEx is covered by 30 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 family patents are nominally set to expire in 2025 in Europe and 2029 in the United States. Patents issued in other foreign jurisdictions will nominally expire in 2025. The national phase applications relating to EscharEx, if 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 allowed or enforced in our patents nor be certain of the priority of inventions covered by pending third-party patent applications. 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 have expired or 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, 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, 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.

LR License Agreement

In August 2016, we signed an exclusive, perpetual, worldwide license agreement with L.R. Research and Development Ltd. ("LR"), an entity controlled by Prof. Rosenberg, for use of a certain patent and related intellectual property (the "LR License Agreement"). For additional information, see "ITEM 7.B. Major Shareholders and Related Party Transactions – Related Party Transactions."

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, 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 debridement 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 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 other debriding agents and wound bed preparation techniques, such as sharp debridement and surgery and topical medication such as gels and enzymes, such as Smith & Nephew Plc's Santyl.

In addition to the currently available products, other products may be introduced to debride chronic and other hard-to-heal wounds or treat 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 convince 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 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. NexoBrid has completed the EMA's preclinical and clinical trials and other pre-marketing approval requirements and received marketing authorization for the European Union on December 18, 2012. Our pipeline product candidates would also have to complete such steps in the European Union. Additionally, we must also complete the approval processes in the United States and other jurisdictions in order to market NexoBrid, EscharEx or our pipeline product candidates.

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 national 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 cGMP;
- 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.

Clinical trial approval

Pursuant to the Clinical Trials Directive 2001/20/EC, as amended, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, approval must be obtained from the competent national authority of a European Union member state in which a study is planned to be conducted. To this end, a CTA is submitted, which must be supported by an investigational medicinal product dossier and additional supporting information prescribed by the Clinical Trials Directive and other applicable guidance documents. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

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. For example, as part of the EMA regulatory approval process, we agreed to provide further data from our post-marketing clinical trial of NexoBrid, the U.S. Phase 3 study (DEDCET). While we believe that the EMA will accept this study to satisfy one of our post-marketing commitments, if the EMA does not accept the study or is not satisfied by the study results, we will need to perform another costly study to provide such data.

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.

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 European Union 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 a marketing authorization application 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 European Union with the results of PIP studies included in the product information are eligible for an extension of their patent protection 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.

Marketing authorization

Authorization to market a product in the European Union 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 for all E.U. member states as well as the European Economic Area ("EEA") member states, Norway, Iceland and Lichtenstein. The centralized procedure is compulsory for medicines produced by certain biotechnological processes, products designated as orphan medicinal products and products with a new active substance indicated for the treatment of certain diseases, and is optional for products that are highly innovative or for which a centralized process is in the interest of patients. Products that have received orphan designation in the European Union, such as NexoBrid, will qualify for this centralized procedure, under which each product's marketing authorization application is submitted to the EMA. Under the centralized procedure in the European Union, the maximum time frame for the evaluation of a marketing authorization application 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.

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 European Union, the Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the investment necessary to develop the drug or biological product.

In the European Union, 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 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.

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. 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.

Data Privacy and Security Laws

We are also subject to data privacy and security laws in the E.U. as well as the EEA, including Regulation (EU) 2016/679 (General Data Protection Regulation, or GDPR) in relation to our collection, control, processing, sharing, disclosure and other use of personal data (i.e. data relating to an identifiable living individual). The GDPR is directly applicable in each E.U. and EEA Member State, however, it provides that E.U. and EEA Member States may introduce further conditions, including limitations, which could limit our ability to collect, control, process, share, disclose and otherwise use personal data (including health and medical information), and/or could cause our compliance costs to increase, ultimately having an adverse impact on our business. The GDPR imposes a strict data protection compliance regime including: providing detailed disclosures about how personal data is collected and processed (in a concise, intelligible and easily accessible form); demonstrating that valid consent or another an appropriate legal basis is in place or otherwise exists to justify data processing activities; appointing data protection officers in certain circumstances (and there are specific local law requirements, such as those in Germany, on the same); granting strengthened rights for data subjects in regard to their personal data (including the right to be "forgotten" and the right to data portability); introducing the obligation to notify data protection regulators or supervisory authorities (and in certain cases, affected individuals) of significant data breaches; imposing limitations on retention of personal data; maintaining a record of data processing; defining for the first time pseudonymized (i.e., key-coded) data; and complying with principal of accountability and complying with the obligation to demonstrate compliance through policies, procedures, training and audit. We are also subject to GDPR rules with respect to cross-border transfers of personal data out of the E.U. and EEA, which are evolving (for example, the European Commission has the ability to review adequacy decisions, such as the one in place for Israel).

We depend on a number of third parties in relation to the operation of our business, a number of which process personal data on our behalf. There is no assurance that our own privacy and security-related safeguards and/or any contractual measures that we enter into with these providers will protect us from the risks associated with the third-party processing, storage and transmission of such information. Any violation of data or security laws by our third party processors could have a material adverse effect on our business and result in the fines and penalties outlined below.

We are subject to the supervision of local data protection authorities in those E.U. and EEA jurisdictions where we are established or otherwise subject to the GDPR. Fines for certain breaches of the GDPR are significant: up to the greater of EUR 20 million or 4% of total global annual turnover. In addition to the foregoing, a breach of the GDPR could result in regulatory investigations, reputational damage, orders to cease/ change our processing of our data, enforcement notices, assessment notices (for a compulsory audit), as well potential civil claims including class action type litigation where individuals suffer harm.

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 enforces its cGMP 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 European Union 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 European Union cGMP 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 European Union 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, as amended by Directive 2004/27. 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. 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 drugs and biologics under the FDCA and implementing regulations and other laws, including the Public Health Service Act. 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, 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 or 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 or supplemental 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 identity, strength, quality and purity; and

- payment of user fees and FDA review and approval of the BLA.

We commenced the process of seeking FDA approval for NexoBrid for the removal of eschar in adults with severe burns by submitting an IND briefing package to the FDA on July 30, 2002.

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.

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 drug 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 drug 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 drug 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.

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, as amended, applicants are required to pay fees to the FDA for reviewing a BLA. These user fees, as well as the annual 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 90% of priority original BLA applications and priority original efficacy supplements within six months of the 60-day filing date and receipt date, respectively. The FDA's established goals are to review and act on 90% of original BLA applications and standard original efficacy supplements with 10 months of the 60-day filing date and receipt date, respectively. The FDA, however, may not be able to approve a biologic within these established goals, and its review goals are subject to change from time to time. Further, the outcome of the review, even if generally favorable, may not be an actual approval but rather an "action letter" that describes additional work that must be completed before the application can be approved.

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. 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 in the form of a risk management plan, or impose other limitations.

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 drug or biologic products for which we receive FDA approvals are subject to 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 is 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. Drug and 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 requirement, 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, suspension of a product 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 risk minimization action plans and 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 status 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 (generally 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 entitles a party to seven years of market exclusivity following drug or biological product approval, but 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 indication for seven years, except in certain limited circumstances. 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.

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. With enactment of the Food and Drug Administration Safety and Innovation Act (the "FDASIA") in 2012, 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.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a 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.

Biosimilar products

As part of the Patient Protection and Affordable Care Act of 2010, Public Law No. 111-148 (the "Affordable Care Act"), under the subtitle of Biologics Price Competition and Innovation Act of 2009 ("BPCI"), a statutory pathway has been created for licensure, or approval, of biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. 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 approval of a biologic product biosimilar to NexoBrid could have a materially adverse impact on our business, may be significantly less costly to bring to the market and may be priced significantly lower than NexoBrid, but such approval may only occur after our 12-year exclusivity period.

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, European Union 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, EMA 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 Affordable Care Act substantially changed the way healthcare is financed by both governmental and private insurers and significantly impacted the pharmaceutical industry. The Affordable Care Act 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 Affordable Care Act:

- 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 "branded prescription drugs" to specified federal government programs.

There have been judicial and congressional challenges to certain aspects of the Affordable Care Act, and we expect the current U.S. presidential administration to continue to seek amendments to or repeal of the Affordable Care Act. While Congress has not passed repeal legislation, the Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the Affordable Care Act are invalid as well. While the Trump Administration and CMS have both stated that the ruling will have no immediate effect, it is unclear how this decision, subsequent appeals, if any, and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act and our business. Congress may consider other legislation to repeal or replace elements of the Affordable Care Act in the future. We cannot predict what legislation, if any, to repeal or replace the Affordable Care Act will become law, or what impact any such legislation may have on our product candidate.

In the European Union, pricing and reimbursement schemes vary widely from country to country and often within regions or provinces of countries. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed and 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 European Union 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

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 and state 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, 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, 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).

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. 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.

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, 2022. The facilities consist of approximately 32,300 square feet of space, and the yearly lease fee is approximately $385 thousands. These facilities house our administrative headquarters, our research and development laboratories and our manufacturing plant. The sub-lease agreement include an option to extend the lease period for additional 3 years at our sole discretion.

We also lease offices at Eisenstrasse 5, 65428 Rüsselsheim, Germany. We lease these facilities pursuant to a lease agreement with a term of three years that expires on April 30, 2022. The facilities consist of approximately 2,670 square feet of space, and lease payments are approximately €2,800 (or $3,100) per month. These facilities house our European headquarters.

Legal Proceedings

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

On September 15, 2014, a statement of claim was filed against the company by certain shareholders of PolyHeal. The plaintiffs allege that the company is obligated to pay them a total amount of approximately $1.3 million plus applicable interest (totaled in $1.5 million as of the ruling date) in exchange for their respective portion of PolyHeal's shares, following the milestone occurrence under the 2010 PolyHeal Agreement. This claim arose out of a dispute with Teva under the 2010 PolyHeal Agreement. On December 14, 2014, the company filed a petition for a right to defend with the Tel Aviv-Jaffa District Court, in which the company: (i) rejected the arguments raised against it in the statement of claim; (ii) emphasized that its obligation under the 2010 PolyHeal Agreement to purchase the 7.5% of PolyHeal's shares is subject to the consumption of the deferred closing, as defined in the 2010 PolyHeal Agreement, including the receipt of the funds from Teva on a "back to back" basis; and (iii) stated that since no such payment has been made by Teva, the company is not subject to any obligation to purchase PolyHeal shares and/or make any payments to PolyHeal's shareholders.

On November 13, 2017, the Tel Aviv-Jaffa District Court issued a ruling in favor of the plaintiffs. The court ruled that the we are obligated to purchase PolyHeal's shares for approximately $6.75 plus applicable interest (totaled in $7.5 million as of the ruling date) million plus applicable interest, which represents the purchase price for the total number of shares that the PolyHeal Agreements contemplate would be acquired by the Company from all the shareholders of PolyHeal. The Court ordered that we are obligated to purchase shares in PolyHeal from the plaintiffs, on the basis of their actual share holdings in PolyHeal as of January 15, 2013, for approximately $1.5 million, within 15 days from the date of the Court's ruling. On December 27, 2017, we filed an appeal to the Supreme Court over the said ruling, alleging, among other things, that the agreement according to which the ruling was granted was misinterpreted by the District Court. We further alleged that both the wording of the agreement and the conduct of the parties thereunder prove that our obligation to purchase PolyHeal's shares was subject to the prior receipt of funds, which were never received, from Teva. On January 30, 2018, certain PolyHeal shareholders filed a cross appeal, alleging that they are entitled to receive from us a full repayment of their counsel's fees in a sum equal to 12.5% of the consideration to be paid for their shares.

Accordingly, a full provision for the purchase price of the shares plus the accrued interest, totaling $7.5 million, was recorded within the loss from discontinued operations in respect of this claim, of which approximately $1.5 million was paid to plaintiffs in consideration for PolyHeal's shares.

On March 24, 2019, we entered into a settlement agreement and mutual general release (the "PolyHeal Settlement Agreement") with the plaintiffs, which contingent upon the Israeli Supreme Court's approval of this settlement agreement, settles any and all debts, obligations or liabilities that we and the plaintiffs had, has or may have to the other party under, in connection with or arising out of the transactions described above. Pursuant to the terms of this PolyHeal Settlement Agreement, the plaintiffs will repay to the company a non-material portion of the amount that was ruled in their favor under the 2017 Ruling, and the Israeli Supreme Court will approve and accept the appeal that was filed by us on December, 2017, cancel the 2017 Ruling that was issued by the District Court against us, and reject the Cross-Appeal. However, if the Israeli Supreme Court does not approve of the PolyHeal Settlement Agreement or refuses to take the actions requested from the court in the PolyHeal Settlement Agreement, these matters may result in the continuation of the existing litigation or new litigation or arbitration proceedings, any of which would materially increase our expenses and may disrupt our management's focus on our business.

See "ITEM 8.A. Consolidated Statements and Other Financial Information—Legal Proceedings" and "ITEM 3.D. Risk Factors- We may have liabilities under our former agreements with PolyHeal Ltd."

On March 24, 2019, we entered into a settlement agreement and mutual general release (the "Teva Settlement Agreement") with Teva, which contingent upon the Supreme Court's approval of the PolyHeal Settlement Agreement, which settles any and all debts, obligations or liabilities that each party or any of its controlled affiliates had or has to the other party or any of its controlled affiliates under, in connection with or arising out of certain transactions and agreements entered into between us and Teva from 2007 to 2012 (collectively, the "Collaboration Agreements"), which have terminated effective as of December 31, 2012 and September 2, 2013, as applicable, and which related to NexoBrid, and PolyHeal, including the above PolyHeal milestone and certain payments, which are primarily reimbursement for development and manufacturing costs, that we believed were to be borne by Teva through the effective date of termination of such Collaboration Agreements in December 2012.

Pursuant to the terms of the Teva Settlement Agreement, Teva has agreed to pay us $4.0 million in cash, and to reduce the contingent consideration that is payable to Teva pursuant to the our repurchase of our shares from Teva in 2013, so that we will be 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, defend and hold harmless Teva and its controlled affiliates 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 million, if a notice of such claim has been received by us prior to December 31, 2023.

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 and (ii) MediWound UK Limited, our inactive wholly-owned subsidiary, which was incorporated on July 26, 2004 under the laws of England. To the best of our knowledge, we also hold approximately 8% ownership interest in Polyheal Ltd.

D. Property, Plants and Equipment

See "ITEM 4.B. Business Overview—Properties" and "ITEM 4.B. Business Overview—Manufacturing, Supply and Production."

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, 2018 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 fully integrated biopharmaceutical company focused on developing, manufacturing and commercializing novel therapeutics products to address unmet needs in the fields of severe burns, chronic and other hard-to-heal wounds, connective tissue disorders and other indications. Our first innovative biopharmaceutical product, NexoBrid, received marketing authorization from the EMA and the Israeli, Argentinean, South Korean and Russian 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. NexoBrid, which is based on our patented proteolytic enzyme technology, 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 established a commercial organization for the marketing, sales and distribution of NexoBrid, including European headquarters in Germany and sales and marketing teams throughout Europe. We sell NexoBrid in Europe and Israel through our commercial organization, and we have launched NexoBrid in Argentina and South Korea, through our local distributor. We are conducting an on-going U.S. Phase 3 pivotal study to support a BLA submission to the FDA and a European pediatric study to broaden the approved indication of NexoBrid, both of which are funded by BARDA. We manufacture NexoBrid in our state-of-the-art, EMA-certified, cGMP-compliant, sterile pharmaceutical products manufacturing facility at our headquarters in Yavne, Israel.

The Company's securities are listed for trading on NASDAQ since March 2014 following our Initial Public Offering. In 2017, we completed an underwritten public offering of 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.

Our revenue was $1.6 million, $2.5 million and $3.4 million in 2016, 2017 and 2018, respectively. In addition, we have signed local distribution agreements for distribution of NexoBrid in Argentina, Russia, South Korea, Mexico, Colombia, Peru, Chile, Ecuador, Panama, India, Bangladesh, Sri Lanka, Japan and Taiwan. Our future growth will depend, in part, on our ability to expand the commercialization of NexoBrid throughout Europe and receive marketing approval in the United States and other jurisdictions for NexoBrid and EscharEx. However, our net operating losses were $20.2 million, $13.7 million and $4.0 million for the years ended December 31, 2016, 2017 and 2018, respectively. As of December 31, 2018, we had an accumulated deficit of $130.7 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future as Research and Development activities are central to our operation.

We expect to continue to invest in our research and development efforts, including continuing our NexoBrid ongoing clinical trials, as well as the clinical development of EscharEx and our pipeline product candidates. In addition, we expect to continue to advance NexoBrid as a standard of care, expend its commercial reach to additional important international markets and its potential use by countries for preparedness for mass casualty events.

Key Components of Statements of Operations

Revenues

Sources of revenues. We derive revenues from direct and indirect 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. Therefore, our ability to generate revenues will depend on the successful commercialization of NexoBrid.

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, rental fees, utilities and depreciation, changes in inventory of finished products and other manufacturing expenses, which is partially offset by an allotment of manufacturing costs associated with research and development activities to research and development expenses. We expect that our cost of revenues will increase as we expand the sale of NexoBrid throughout the European Union and internationally. We expect that our cost of revenues as a percentage of our total revenues will decrease to the extent that our sales from NexoBrid increase.

Operating Expenses

Research and Development Expenses, gross

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

Since 2016, we have cumulatively spent approximately $47.3 million on research and development primarily of NexoBrid and EscharEx, of which $30.7 million was funded by participation by BARDA funds and the Israeli government grants. Our total research and development expenses, net of participations, were approximately $7.1 million, $5.5 million and $4.1 million in 2016, 2017 and 2018, respectively. Our research and development expenses related primarily to the development of NexoBrid and EscharEx. We charge all research and development expenses to operations as they are incurred.

The successful development of our patented proteolytic enzyme technology used in NexoBrid, EscharEx and additional pipeline product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of our technology for additional indications. This uncertainty is due to numerous risks and uncertainties associated with developing products, including the uncertainty of:

- the scope, rate of progress and expense of our research and development activities;
- preclinical results;
- clinical trial results;
- the terms and timing of regulatory approvals;
- the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights; and
- the ability to market, commercialize and achieve market acceptance for NexoBrid or any other product candidate that we may develop in the future.

A change in the outcome of any of these variables with respect to the development of other products that we may develop could result in a significant change in the costs and timing associated with their development. For example, if the EMA, the FDA or other regulatory authority were to require us to conduct preclinical and clinical studies beyond those which we currently anticipate for the completion of clinical development of our product candidates or if we experience significant delays in enrollment in any clinical trials, we could be required to expend significant additional financial resources and time on the completion of the clinical development.

Participation by Third Parties

Our research and development expenses are net of the following participations by third parties:

Participation by the IIA. We receive grants, subject to repayment through future royalty payments, as part of the NexoBrid and EscharEx research and development programs approved by the IIA. The requirements and restrictions for such grants are found in the Innovation Law. Under the Innovation Law, royalties of 3% on the revenues derived from sales of products or services developed in whole or in part using IIA grants are payable to the IIA. The maximum aggregate royalties paid generally cannot exceed 100% of the grants made to us, plus annual interest generally equal to the 12-month LIBOR applicable to dollar deposits, as published on the first business day of each calendar year. The total gross amount of grants actually received by us from the IIA, including accrued LIBOR interest and net of royalties actually paid as of December 31, 2018, totaled approximately $13.7 million and the amortized cost (using the effective interest method) of the liability as of that date totaled approximately $7.7 million. As of December 31, 2018, we had accrued and paid royalties to the IIA totaling $0.3 million.

In addition to paying any royalty due, we must abide by other restrictions associated with receiving such grants under the Innovation Law that continue to apply following repayment to the IIA. These restrictions may impair our ability to outsource manufacturing, engage in change of control transactions or otherwise transfer our know-how outside of Israel and may require us to obtain the approval of the IIA for certain actions and transactions and pay additional royalties and other amounts to the IIA. In addition, any change of control and any change of ownership of our ordinary shares that would make a non-Israeli citizen or resident an "interested party," as defined in the Innovation Law, requires prior written notice to the IIA. If we fail to comply with the Innovation Law, we may be subject to criminal charges. See "Item 3.D. Risk Factors – We 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."

Research and development grants received from the IIA are recognized upon receipt as a liability if future economic benefits are expected from the project that will result in royalty-bearing sales. The amount of the liability for the loan is first measured at fair value using a discount rate that reflects a market rate of interest that reflects the appropriate degree of risks inherent in our business. The change in the fair value of the liability associated with grants from the IIA is reflected as an increase or decrease in our research and development expenses for the relevant period.

Participation by BARDA. On September 29, 2015, we were awarded a contract by BARDA valued up to $112 million for the advancement of the development and manufacturing, as well as the procurement, of NexoBrid in the United States. On July 17, 2017, we entered into an amendment to our contract with BARDA that increased its potential value to a maximum of $132 million. See "ITEM 4.B. Business Overview—BARDA Contract." Pursuant to the contract, BARDA has committed to fund all development costs of NexoBrid required for achieving marketing authorization by the FDA, either directly or indirectly by reimbursing actual costs incurred by us. In September 2018, we were awarded a new contract to develop NexoBrid for the treatment of Sulfur Mustard injuries as part of BARDA preparedness for mass casualty events. The 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 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, 2018, we have recorded $28.2 million in funding from BARDA out of the $68 million of committed funds provided for under those two contracts.

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, advertising, market access, medical, sales and distribution activities. These expenses also include costs related to the maintenance of our offices in Germany, which is focused primarily on marketing NexoBrid, and marketing authorization holder related costs.

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 and exchange rate differences. The 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, 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 operations of the development, manufacturing and sales of PolyHeal, including impairments of inventories, our exclusive global license of the PolyHeal product and other assets, and any legal process profit or loss are reported separately as a discontinued operation in our statement of operations for the periods presented below, as well as for all historical periods to be presented in future quarterly and annual releases of our results of operations.

Taxes on Income

The standard corporate tax rate in Israel was 25% and 24%, in the years 2016 and 2017 tax years, respectively and as of January 1, 2018 and thereafter, the corporate tax rate 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 $133 million as of December 31, 2018. 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 a 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

The following table sets forth our results of operations in dollars for the periods indicated:

	Years Ended December 31,		
	2016	**2017**	2018
Consolidated statements of operations data:			
Revenues	1,558	$ 2,496	$ 3,401
Cost of revenues	2,158	1,578	2,088
Gross (loss) profit	(600)	918	1,313
Operating expenses:			
Research and development, gross	14,779	14,625	17,915
Participation by BARDA and IIA	(7,711)	(9,163)	(13,843)
Research and development, net of participations	7,068	5,462	4,072
Selling and marketing	8,403	5,362	4,188
General and administrative	4,084	3,781	3,799
Other income from settlement agreement			(7,537)
Other expenses	-	-	751
Operating loss	(20,155)	(13,687)	(3,960)
Financial income	2,166	406	412
Financial expense	(896)	(1,252)	(2,117)
Loss from continuing operations	(18,885)	(14,533)	(5,665)
Profit (loss) from discontinued operation	-	(7,616)	4,608
Net loss	(18,885)	$ (22,149)	$ (1,057)

Year Ended December 31, 2017 Compared to Year Ended December 31, 2018

Revenues

We generated revenues from sales of NexoBrid in 2017 of approximately $2.5 million, compared to approximately $3.4 million in revenues from the sale of NexoBrid in 2018.

Costs and Expenses

Cost of revenues

Cost of revenues as a percentage of revenues decreased from approximately 63% in the year ended December 31, 2017 to approximately 61% in the year ended December 31, 2018.

Allotment of manufacturing costs to research and development increased $0.6 million in the year ended December 31, 2018, primarily due to the development activities of NexoBrid and EscharEx in 2018. Change in inventory of finished products increased from $(1.0) million in 2017 to $0.3 in 2018

Research and development expenses, net of participations

Research and development expenses, gross, increase 22% from approximately $14.6 million in the year ended December 31, 2017 to approximately $17.9 million in the year ended December 31, 2018. The expenses primarily related to development of NexoBrid, which was predominantly funded by BARDA participation, and EscharEx. The increase resulted primarily from an increase in subcontractors costs and in the allotment cost of manufacturing for research and development purposes related to NexoBrid and EscharEx.

Salary and related expenses remained stable in the years ended December 31, 2017 and 2018. Subcontracting costs increased $2.6 million in the year ended December 31, 2018 primarily due to clinical development activity of NexoBrid.

Allotment of manufacturing costs for research and development purposes increased $0.6 million in the year ended December 31, 2018 primarily due to development activities of NexoBrid and EscharEx.

Moreover, participation from BARDA and the Israeli Innovation Authority increased by approximately $4.6 million from $9.2 million in the year ended December 31, 2017 to $13.8 in the year ended December 31, 2018, primarily due to increase of BARDA funds.

Selling and marketing expenses

Selling and marketing expenses decreased 22%, from approximately $5.4 million in the year ended December 31, 2017 to approximately $4.2 million in the year ended December 31, 2018. The decrease was primarily due to a decrease in marketing activities associated with the launch of NexoBrid in the E.U. and a decrease of headcount of employees focused on selling and marketing.

General and administrative expenses

General and administrative expenses remained stable at $3.8 million in the years ended December 31, 2017 and 2018.

Financial income

Financial income remained in the same level of about $0.4 million in the year ended December 31, 2017 and 2018.

Financial expense

Financial expense increased from approximately $1.3 million in the year ended December 31, 2017 to approximately $2.1 million in the year ended December 31, 2018. The increase in financial expenses in 2018 included $0.4 million due to the revaluation of contingent consideration for purchase of shares, $0.2 million of exchange differences and $0.2 million of finance expenses in respect of deferred revenues.

Year Ended December 31, 2016 Compared to Year Ended December 31, 2017

Revenues

We generated revenues from sales of NexoBrid in 2016 of approximately $1.6 million, compared to approximately $2.5 million in revenues from the sale of NexoBrid in 2017. The increase was primarily due to an increase in the volume of sales in the EU.

Costs and Expenses

Cost of revenues

Cost of revenues decreased 27% from approximately $2.2 million in the year ended December 31, 2016 to approximately $1.6 million in the year ended December 31, 2017.

The cost of revenues consisted primarily of employee related expenses, including salaries and benefit and equity-based compensation, cost of materials, changes in inventory of finished products and other manufacturing expenses, which is partially offset by an allotment of manufacturing costs associated with research and development activities to research and development expenses. Allotment of manufacturing costs to research and development decreased $1.0 million in the year ended December 31, 2017, primarily due to a reduction in the development activities of EscharEx in 2017. Change in inventory of finished products decreased $1.8 million from $0.8 million in 2016 to $(1.0) in 2017.

Research and development expenses, net of participations

Research and development expenses, gross, decreased 1% from approximately $14.8 million in the year ended December 31, 2016 to approximately $14.6 million in the year ended December 31, 2017. The expenses primarily related to development of NexoBrid, which was predominantly funded by BARDA participation, and EscharEx. The decrease resulted primarily from a decrease in the allotment of cost of manufacturing for research and development purposes related to NexoBrid and EscharEx.

Salary and related expenses increased $0.6 million in the year ended December 31, 2017 due to an increased headcount of employees focused on research and development. Subcontracting costs increased $0.2 million in the year ended December 31, 2017 primarily due to clinical development activity of NexoBrid.

Allotment of manufacturing costs for research and development purposes decreased $1.0 million in the year ended December 31, 2017 primarily due to reduction in the development activities of EscharEx.

Moreover, participation from BARDA and the Israeli Innovation Authority increased by approximately $1.5 million from $7.7 million in the year ended December 31, 2016 to $9.2 in the year ended December 31, 2017.

Selling and marketing expenses

Selling and marketing expenses decreased 36%, from approximately $8.4 million in the year ended December 31, 2016 to approximately $5.4 million in the year ended December 31, 2017. The decrease was primarily due to a decrease in marketing activities associated with the launch of NexoBrid in the E.U. and a decrease of headcount of employees focused on selling and marketing.

General and administrative expenses

General and administrative expenses decreased 7% from approximately $4.1 million in the year ended December 31, 2016 to approximately $3.8 million in the year ended December 31, 2017.

Financial income

Financial income decreased from approximately $2.2 million in the year ended December 31, 2016 to approximately $0.4 million in the year ended December 31, 2017. Financial income in 2016 included $1.6 million due to revaluation of contingent consideration for purchase of shares.

Financial expense

Financial expense increased from approximately $0.9 million in the year ended December 31, 2016 to approximately $1.3 million in the year ended December 31, 2017. Financial expenses in 2017 included $0.4 million due to the revaluation of contingent consideration for the purchase of shares.

B. Liquidity and Capital Resources

Our primary uses of cash are to fund working capital requirements, research and development expenses of NexoBrid and EscharEx and sales and marketing activities associated with the commercialization of NexoBrid in Europe. In March 2014, we closed our IPO, resulting in net proceeds to us of approximately $71.7 million. In September 2015, we were awarded a contract by BARDA, which was modified in July 2017 and is currently valued at up to $132 million, for the advancement of the development and manufacturing, as well as the procurement, of NexoBrid in the United States. In addition, we were recently awarded a new contract to develop NexoBrid for the treatment of Sulfur Mustard injuries as part of BARDA preparedness for mass casualty events. The 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 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. See “ITEM 4.B. Business Overview—BARDA Contract.” Since we expect a significant portion of the funding for our NexoBrid development plan will be funded by BARDA, we intend to use a portion of our proceeds raised during our IPO initially intended for the development of NexoBrid to further advance the development of EscharEx. Furthermore, on March 7, 2016, the SEC declared our shelf registration statement on Form F-3 effective. Under this shelf registration statement, we could 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 September 2017, we completed an underwritten public offering of 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. We currently intend to use the net proceeds from the sale of securities offered by us pursuant to our registration statement on Form F-3 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.

The table below summarizes our sources of financing for the periods presented.

	Issuance of Ordinary Shares and Warrants	Government Grants and BARDA Funding, net	Total
		(in thousands)	
Year ended December 31, 2018	$ -	$ 13,784	$ 13,784
Year ended December 31, 2017	$ 22,665	$ 8,895	$ 31,560
Year ended December 31, 2016	$ 7	$ 6,466	$ 6,473

Our sources of financing in the year ended December 31, 2018 totaled $13.3 million and consisted primarily of funding under the BARDA contract totaling $13.2 million and the IIA government grants, net of repayments totaling $0.1 million.

Our sources of financing in the year ended December 31, 2017 totaled $31.6 million and consisted primarily of the underwritten public offering proceeds of $22.7 million, IIA government grants totaling $0.3 million and funding under the BARDA contract totaling $8.6 million.

Our sources of financing in the year ended December 31, 2016 totaled $6.5 million and consisted primarily of IIA government grants totaling $0.9 million and funding under the BARDA contract totaling $5.6 million.

As of December 31, 2018, we had $23.6 million of cash, cash equivalents and short-term deposits. Our net operating losses were $20.2 million. $13.7 million and $4.0 million for the years ended December 31, 2016, 2017, and 2018 respectively. As of December 31, 2018, we had an accumulated deficit of $130.7 million. We expect to continue 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 2016, 2017, and 2018 amounted to $0.7 million, $1.0 million, and $0.5 million, respectively. Capital expenditures consist primarily of investments in manufacturing and laboratory equipment.

Our future capital requirements will depend on many factors, including our revenue growth, 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 12 months.

Cash Flows

The following table summarizes our consolidated statement of cash flows for the periods presented:

	Year Ended December 31,		
	2016	2017	2018
		(in thousands)	
Net cash provided by (used in):			
Continuing operating activities	$ (16,445)	$ (14,892)	$ (12,154)
Continuing investing activities	1,816	437	(17,040)
Continuing financing activities	907	22,995	46
Discontinued operating activities	—	(1,563)	-

Net cash used in continuing operating activities

The use of cash in all periods resulted primarily from our net losses adjusted for non-cash charges and measurements and changes in components of working capital. Adjustments to net income for non-cash items include depreciation and amortization, equity-based compensation, revaluation of contingent liabilities and changes in assets and liabilities items.

Net cash used in continuing operating activities was approximately $14.9 million in the year ended December 31, 2017 compared to approximately $12.2 million in the year ended December 31, 2018. The decrease was attributed primarily to the decrease in operating loss as a result of BARDA support and a decrease in change of working capital assets, net.

Net cash used in continuing operating activities was approximately $16.4 million in the year ended December 31, 2016 compared to approximately $14.9 million in the year ended December 31, 2017. The decrease was attributed primarily to the decrease in operating loss, which was partially offset by an increase in change of working capital assets, net.

Net cash used in discontinued operating activities

Net cash used in discontinued operating activities was approximately $1.6 million in the year ended December 31, 2017, attributed primarily to the consideration paid to PolyHeal's shareholders following the district court ruling. See "ITEM 8.A. Consolidated Statements and Other Financial Information —Legal Proceedings" and "ITEM 3.D. Risk Factors—We may have continuing obligations or liabilities under our former agreements with Teva Pharmaceutical Industries Ltd. and PolyHeal Ltd.

Net cash provided by (used in) continuing investing activities

The use of cash in continuing investing activities has historically been primarily related to investments in short-term banks deposits and purchases of property and equipment. Net cash provided by investing activities was $0.4 million during the year ended December 31, 2017 compared to cash used by investing activities of $17.0 million during the year ended December 31, 2018. The decrease was attributable primarily to $16.6 million investment in short-term bank deposits and a decrease in purchase of property and equipment.

Net cash provided by investing activities was $1.8 million during the year ended December 31, 2016 compared to cash provided by investing activities of $0.4 million during the year ended December 31, 2017. The decrease was attributable primarily to decrease of proceeds from short-term bank deposits and an increase in purchase of property and equipment.

Net cash provided by continuing financing activities

Net cash provided by continuing financing activities was $23.0 million during the year ended December 31, 2017 compared to $0 million during the year ended December 31, 2018. The decrease was attributed primarily to our receipt of $22.7 million net proceeds from our underwritten public offering in 2017.

Net cash provided by continuing financing activities was $0.9 million during the year ended December 31, 2016 compared to $23.0 million during the year ended December 31, 2017. The increase was attributed primarily to our receipt of $22.7 million net proceeds from our underwritten public offering in 2017.

Application of Critical Accounting Policies and Estimates

Our accounting policies and their effect on our financial condition and results of operations are more fully described in our consolidated financial statements included elsewhere in this annual report. We have prepared our financial statements in accordance with IFRS as issued by the IASB. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. Actual results may differ from these estimates under different assumptions or conditions. See "ITEM 3.D. Risk Factors" for a discussion of the possible risks which may affect these estimates.

While our significant accounting policies are more fully described in the notes to our consolidated financial statements appearing elsewhere in this annual report, we believe that the accounting policies discussed below are critical to our financial results and to the understanding of our past and future performance, as these policies relate to the more significant areas involving management's estimates and assumptions. We consider an accounting estimate to be critical if: (a) it requires us to make assumptions because information was not available at the time or it included matters that were highly uncertain at the time we were making our estimate; and (b) changes in the estimate could have a material impact on our financial condition or results of operations.

Revenue Recognition

We currently generate revenues from direct and indirect sales of NexoBrid to burn centers and hospital burn units in Europe and Israel as well as to local distributors in other countries. Revenues are recognized to the extent that it is probable that the economic benefits will flow to the company and the revenues can be reliably measured, regardless of when the payment is being made. Revenues are measured at the fair value of the consideration received or receivable, taking into account contractually defined terms of payment and excluding taxes or duty and net of returns and allowances, trade discounts and volume rebates.

Revenues from the sale of products are 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 to the buyer.

Revenues from distributor's agreements which are comprised of multiple elements and provide for varying consideration terms, such as upfront payments and milestone payments, are recognized when the criteria for revenue recognition have been met and only to the extent of the consideration that is not contingent upon completion or performance of future services under the contract.

Deferred revenues include unearned amounts received from customers not yet recognized as revenues.

In May 2014, IFRS 15, "Revenue from Contracts with Customers" ("the new Standard") was issued by the IASB. The new Standard introduces a five-step model that will apply to revenue earned from contracts with customers and is effective for the Company beginning January 1, 2018.

The new Standard allows the option of modified retrospective adoption. Under this option, the Company is required to recognize the cumulative effect of the initial adoption of the new Standard as an adjustment to the opening balance of retained earnings as of the date of initial application. According to the new Standard, when long-term advances (exceeding one year) are received for a future service, the Company is required to accrue interest and recognize finance expense on the advances over the period of the contract.

We adopted this standard using the modified retrospective method rather than full retrospective method. The accumulated effect of implementing the new Standard as of January 1, 2018 was an increase of deferred revenues by $249 thousands and increase of accumulated deficit by $249 thousands.

Research and Development Expenses

Research expenses are recognized as expenses when incurred. Costs incurred on development projects are recognized as intangible assets as of the date as of which it can be established that it is probable that future economic benefits attributable to the asset will flow to us considering its commercial feasibility. This is generally the case when regulatory approval for commercialization is achieved and costs can be measured reliably. Given the current stage of the development of our products, no development expenditures have yet been capitalized. Intellectual property-related costs for patents are part of the expenditure for the research and development projects. Therefore, registration costs for patents are expensed when incurred as long as the research and development project concerned does not meet the criteria for capitalization.

Equity-Based Compensation

We account for our equity-based compensation for employees in accordance with the provisions of IFRS 2 "Share-based Payment," which requires us to measure the cost of equity-based compensation based on the fair value of the award on the grant date.

We have selected the binominal pricing model as the most appropriate method for determining the estimated fair value of our equity-based awards. The resulting cost of an equity incentive award is recognized as an expense over the requisite service period of the award, which is usually the vesting period. We recognize compensation expense over the vesting period using the accelerated method pursuant to which each vesting tranche is treated as a separate amortization period from grant date to vest date, and classify these amounts in the consolidated financial statements based on the department to which the related employee reports.

The determination of the grant date fair value of options using an option pricing model is affected by estimates and assumptions regarding a number of complex and subjective variables. These variables include the expected volatility of our share price over the expected term of the options, share option exercise and cancellation behaviors, risk-free interest rates and expected dividends, which are estimated as follows:

- *Fair value of our ordinary shares*. After March 20, 2014, the date our ordinary shares began trading on Nasdaq, the grant date fair value for equity-based awards is based on the closing price of our ordinary shares on Nasdaq on the date of grant and fair value for all other purposes related to share-based awards is the closing price of our ordinary shares on Nasdaq on the relevant date.

- *Volatility*. The expected share price volatility was based on the historical equity volatility of the ordinary shares of comparable companies that are publicly traded.

- *Early exercise factor*. Since adequate historical experience is not available to provide a reasonable estimate, the early exercise factor is determined based on peer group imperial studies.

- *Risk-free rate*. The risk-free interest rate is based on the yield from U.S. Treasury zero-coupon bonds with a term equivalent to the contractual life of the options.

- *Expected dividend yield*. We have never declared or paid any cash dividends and do not presently plan to pay cash dividends in the foreseeable future. Consequently, we used an expected dividend yield of zero.

If any of the assumptions used in the option pricing models change significantly, equity-based compensation for future awards may differ materially compared with the awards granted previously.

Government Grants from the Israeli Innovation Authority

Research and development grants received from the IIA are recognized upon receipt as a liability if future economic benefits are expected from the project that will result in royalty-bearing sales. The amount of the liability for the loan is first measured at fair value using a discount rate that reflects a market rate of interest that reflects the appropriate degree of risks inherent in our business. We used a discount rate of 12% based in part on our cost of capital determined by an independent valuation analysis conducted at the time of our initial recognition of IIA grants as a liability on our balance sheets. The difference between the amount of the grant received and the fair value of the liability is accounted for as a government grant and recognized as a reduction of research and development expenses. After initial recognition, the liability is measured at amortized cost using the effective interest method. Royalty payments are treated as a reduction of the liability. If no economic benefits are expected from the research activity, the grant receipts are recognized as a reduction of the related research and development expenses. In that event, the royalty obligation is treated as a contingent liability in accordance with IAS 37, "Provisions, Contingent Liabilities and Contingent Assets."

At the end of each reporting period, we evaluate whether there is reasonable assurance that the liability recognized will be repaid based on our best estimate of future sales and, if not, the appropriate amount of the liability is derecognized against a corresponding reduction in research and development expenses.

Government Funding from BARDA

Non-royalty bearing funds from BARDA for funding research and development activities of NexoBrid are recognized at the time we are entitled to such funds on the basis of the related costs incurred and are recorded as a reduction from our research and development expenses.

Contingent Consideration for Purchase of Shares

On September 2, 2013, in accordance with the terms of the Teva Shareholders' Rights Agreement entered into in 2007 and amended in 2010, we exercised our rights to repurchase all of our shares held by Teva in consideration for an obligation to pay Teva future royalty payments of 20% of our revenues from the sale or license of NexoBrid resulting in royalty payments up to a total amount of $30.6 million and from the sale or license of the PolyHeal Product resulting in royalty payments up to a total amount of $10.8 million. We account for this obligation as a liability on our balance sheet in an amount equal to the fair value of the future royalty payments. In order to determine the fair value, we estimated the amount and timing of the future payments to Teva based on our projected results of operations. The obligation to pay Teva future royalty payments no longer includes amounts from the sale or license of the PolyHeal Product since the license to the PolyHeal Product has expired. The resulting liability as of the exercise date was estimated at approximately $19.2 million. The contingent consideration was revalued as of December 31, 2017 and 2018 to be approximately $14.4 million and $14.5 million, respectively, and we recorded financial expenses of $0.4 million and $0.8 million in 2017 and 2018 respectively.

Pursuant to the terms of the Teva Settlement Agreement signed in March 2019, Teva has agreed to reduce the contingent consideration that is payable to Teva pursuant to the our repurchase of our shares from Teva in 2013, so that we will be obligated to pay Teva annual future royalty payments of 15% of our revenues from the sale or license of NexoBrid starting from January 1, 2019, up to a total amount of $10.2 million and to pay us $4.0 million in cash.

Pursuant to a Settlement Agreement with Teva, the fair value of the revised future royalty obligation to Teva was estimated at $ 6.3 million as of December 31, 2018 using a discounted cash flow model based on sales projections. In addition, a one-time net income of $7,537 was recorded as other income and a one-time income of $4,608 was recorded within the profit from discontinued operation in the fourth quarter and full year ending December 31, 2018.

Impairment of Non-Financial Assets

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. We evaluate 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.

An impairment loss of an asset, other than goodwill, 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.

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 24 employees as of December 31, 2018 and is supported by highly experienced consultants in various research and development disciplines.

We have received government grants (subject to payment of royalties) as part of NexoBrid and EscharEx research and development programs approved by the IIA (in 2017 and 2018 only for EscharEx). The total gross amount of grants actually received by us from the IIA, including accrued LIBOR interest and net of royalties actually paid as of December 31, 2018, totaled approximately $13.7 million and the amortized cost (using the interest method) of the liability totaled approximately $7.4 million and $7.7 million as of December 31, 2017 and 2018, 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, 2018, we had accrued and paid royalties to the IIA totaling $0.3 million.

We received funds from BARDA in accordance with the terms of our BARDA contract. As of December 31, 2018 we had accrued $28.2 million.

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

D. Trend Information

Other than 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, 2018 to December 31, 2018 that are reasonably likely to have a material adverse effect on our net revenue, income, profitability, liquidity or capital resources, or that caused the disclosed financial information to be not necessarily indicative of future operating results or financial condition.

E. Off-Balance Sheet Arrangements

We do not currently engage in off-balance sheet financing arrangements. In addition, we do not have any interest in entities referred to as variable interest entities, which includes special purposes entities and other structured finance entities.

F. Contractual Obligations

Our significant contractual obligations as of December 31, 2018 are summarized in the following table:

	Payments Due by Period			
	Total	2019	2020	2021 and thereafter
		(in thousands)		
Operating lease obligations[1]	$ 1,824	$ 592	$ 476	$ 756

(1) Operating lease obligations consist of payments pursuant to lease agreements for office and laboratory facilities, as well as lease agreements for 16 vehicles, which generally run for a period of three years.

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, 2019:

Name	Age	Position
Executive Officers		
Gal Cohen[5]	46	President and Chief Executive Officer
Sharon Malka[5]	47	Chief Financial and Operations Officer
Lior Rosenberg M.D.	73	Chief Medical Technology Officer
Ety Klinger Ph.D.	57	Chief Research and Development Officer
Carsten Henke	53	Chief Commercial Officer EU
Yaron Meyer	40	General Counsel and Corporate Secretary
Directors		
Stefan T. Wills[3][5]	62	Active Chairman of the Board of Directors
Ofer Gonen	46	Director
Assaf Segal	47	Director
Vickie R. Driver M.D[1][2][3]	65	Director
Nissim Mashiach[1][2][3][4]	58	Director
Sharon Kochan[1][2][3][4]	50	Director

(1) Member of our audit committee.

(2) Member of our compensation committee.

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

(4) External director under the Companies Law.

(5) On March 12, 2019, we announced that Gal Cohen has decided to step down as the Chief Executive Officer of the company by the end of May 2019. Following Gal Cohen's departure from the company, Sharon Malka, the company's Chief Financial Officer and Chief Operations Officer, will be appointed as Chief Executive Officer of the company, and Stephen T. Wills, the company's Chairman of the board of directors, will serve as Active Chairman.

Executive Officers

Gal Cohen has served as our President and Chief Executive Officer since November 2006. From 2004 to 2006, Mr. Cohen served as Director of Strategic Business Planning and New Ventures at Teva, a public Israeli pharmaceutical company. He also launched Copaxone in Europe and the United States while he served as Projects Manager for Teva's Global Products Division from 2000 to 2004 and for its Corporate Industrial Engineering Department from 1998 to 2000. Mr. Cohen holds a B.Sc. in Industrial Engineering and Management (cum laude) from the Technion—Israel Institute of Technology and an M.B.A. (*cum laude*) from Tel Aviv University.

Sharon Malka has served as our Chief Financial and Operations Officer since 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.

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.

Carsten Henke has served as our Chief Commercial Officer for the European organization since October 2014 and is acting as the Managing Director of our wholly-owned subsidiary, MediWound Germany GmbH, since July 2013. From February 2009 to December 2012, Mr. Henke served as Teva's General Manager in Spain, and from January 2004 to January 2009, he served as Teva's Director of Marketing and Sales in Germany. Mr. Henke holds a B.Sc. in European Management from the ESB Business School at Reutlingen University and a Graduado Superior in International Business Administration—E-4 from Comillas Pontifical University ICAI—ICADE in Madrid, Spain.

Yaron Meyer has served 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

Stefan T. Wills has served as a member of our board of directors since May 2017 and as Chairman of our board since October 2017. Mr. Wills has served, since 1997, as Executive Vice President, Secretary, Treasurer and Chief Financial Officer of Palatin Technologies, Inc. ("Palatin"), a publicly-held biopharmaceutical company developing targeted, receptor-specific peptide therapeutics for the treatment of diseases with significant unmet medical need and commercial potential. He has served in various roles at Palatin since 1997, including as Executive Vice President of Operations from 2005 until June 2011 and as Chief Operating Officer and Executive Vice President from 2011 to present. Mr. Wills served as Executive Chairman and Interim Principal Executive Officer of Derma Sciences, Inc. ("Derma"), a publicly-held company providing advanced wound care products, from December 2015 until February 2017 when Derma was acquired by Integra Life Sciences Holding Corporation. Mr. Wills also served as the lead director and chairman of the audit committee of Derma until February 2017 and as Derma's Chief Financial Officer from 1997 to 2000. Mr. Wills serves on the board of trustees and executive committee of The Hun School of Princeton since 2013 and its chairman since June 2018, and, from 1991 to 2000, he was the President and Chief Operating Officer of Golomb, Wills & Company, P.C., a public accounting firm. Mr. Wills, a certified public accountant, received his B.S. in accounting from West Chester University, and an M.S. in taxation from Temple University.

Ofer Gonen has served as a member of our board of directors since September 2003. Mr. Gonen is also the Chief Executive Officer of Clal Biotechnology Industries Ltd. ("CBI"). Mr. Gonen manages CBI's life science investments, business development, U.S.-based operations and investment support of CBI's portfolio companies. Mr. Gonen serves as an executive chairman and board member of several companies, including Gamida Cell Ltd., CureTech Ltd., Campus Bio L.P., Clal Life Sciences L.P. and Clal Application Center Ltd. Prior to joining CBI, Mr. Gonen was the general manager of Biomedical Investments as well as a technology consultant to various Israeli venture capital funds and an Academic Aide to the Governor of the Bank of Israel. Mr. Gonen gained extensive experience in R&D the management in defense-oriented projects within the prestigious "Talpiot" program of the Israel Defense Forces, for which he was awarded the Israeli National Security Medal. Mr. Gonen 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, Israel.

Assaf Segal has served as a member of our board of directors since October 2017. Mr. Segal has served as the Chief Financial Officer at Clal Biotechnology Industries Ltd. since July 2015. 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.

Vicki 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 has served as Executive Vice President & President Rx Pharmaceuticals, for Perrigo Company Plc., a global, over-the-counter, consumer goods and specialty pharmaceutical company listed on the New York Stock Exchange, since 2007, and has been a member of the Perrigo Executive Committee since 2007. 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.

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, 2018. All amounts reported in the table reflect the cost to the company, as recognized in our financial statements for the year ended December 31, 2018.

Name and Position	Salary & Social Benefits[1]	Bonus	Share-Based Payment[2]	Other Compensation[3]	Total
			(U.S. dollars)[4]		
Gal Cohen, *President and Chief Executive Officer*	406,008	145,351	39,893	20,982	570,269
Sharon Malka, *Chief Financial and Operations Officer*	286,350	111,985	44,28	9,534	452,155
Lior Rosenberg, M.D., *Chief Medical Technology Officer*	301,75	92,067	22,143	4,106	420,073
Carsten Henke, *Chief Commercial Officer EU & Managing Director of MediWound Germany GmbH*	284,163	73,203	22,143	25,596	405,105
Ety Klinger, *Chief Research & Development Officer*	231,549	70,737	53,035	18,707	374,028

(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, 2018 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, (ii) vacation benefits and (iii) severance pay.

(4) Converted (i) from NIS into U.S. dollars at the rate of 3.58 = U.S.$1.00, based on the average representative rate of exchange between the NIS and the U.S. dollar in the year ended December 31, 2018 and (ii) from Euro into U.S. dollars at the rate of Euro 1.185 = U.S$1.00, based on the average representative rate of exchange between the Euro and the U.S. dollar as reported by the Bank of Israel in the year ended December 31, 2018.

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, 2018 was $2.9 million. As of December 31, 2018, options to purchase 1,283,039 ordinary shares granted to our directors and executive officers were outstanding under our share option plans at a weighted average exercise price of $9.24 per share. 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 Mr. Gal Cohen, our CEO and Prof. Rosenberg, our Chief Medical Technology 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 their employment, Mr. Cohen is entitled to a one-time termination payment equal to two times our CEO's monthly fixed compensation if our CEO's employment as our CEO is terminated without cause, and to five times our CEO's monthly fixed compensation if terminated as our CEO in connection with a change of control in our Company; in addition 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. 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 (the "2014 Plan"). The 2014 Plan provides for the grant of options, restricted shares, restricted share units 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. The reserved pool was increased by 431,006, 540,955 and 423,577 ordinary shares as of January 1, 2015, January 1, 2018 and January 1, 2019, 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 held by each of our directors and executive officers who beneficially own greater than 1% of our ordinary shares or options to purchase more than 1% of our ordinary shares as of March 15, 2019:

Name	Number of Options	Number of RSUs	Grant Date	Exercise Price	Vested Options as of March 15, 2019	Expiration Date
Gal Cohen, *President and Chief Executive Officer*						
	45,600		1/15/2011	$ 9.82	45,600	1/14/2021
	152,000		12/24/2013	$ 12.89	152,000	12/23/2023
	70,000		1/28/2016	$ 9.58	52,500	12/22/2025
Sharon Malka, *Chief financial and operation Officer*						
	49,172		1/15/2011	$ 7.97	49,172	1/14/2021
	38,000		1/15/2011	$ 9.82	38,000	1/14/2021
	121,600		12/24/2013	$ 12.89	121,600	12/23/2023
	50,000		12/23/2015	$ 9.58	37,500	12/22/2025
	135,000		12/31/2018	$ 5.15	-	12/30/2028
		45,000	12/31/2018			
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	18,750	12/22/2025
	20,000		12/31/2018	$ 5.15	-	12/30/2028
		6,667	12/31/2018			

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 directors are independent under the Nasdaq Stock Market rules. The definition of "independent director" under the Nasdaq Stock Market 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 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 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 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 recently 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 the new regulations.

External Directors

Under the Israeli Companies Law, we are 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, 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, 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 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.

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 Stefan T. Wills to serve as chairman of the board of directors.

Audit Committee

Israeli Companies Law 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.

Nasdaq listing rules

Under the Nasdaq Stock Market 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 or, if we choose to follow requirements under Israeli law, we must disclose that fact in this annual report.

Our audit committee consists of Sharon Kochan (chairperson), Vickie R. Driver and Nissim Mashiach, 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 rules. All members of our audit committee meet the requirements for financial literacy under the applicable 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 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

Our Compensation Committee consists of Sharon Kochan (chairperson), Vickie R. Driver and Nissim Mashiach, each of whom is independent under the Nasdaq Stock Market rules.

Under the Israeli Companies Law, the board of directors of a public company must appoint a compensation committee. The compensation committee 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. However, subject to certain exceptions, Israeli companies whose securities are traded on stock exchanges such as the Nasdaq Global Market, and who do not have a controlling shareholder, do not have to meet this majority requirement so long as the compensation committee meets other Israeli Companies Law composition requirements, as well as the requirements of the jurisdiction where the company's securities are traded. 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.

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. 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 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.

We have adopted a compensation policy, which 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.

Nasdaq listing rules

Under Nasdaq corporate governance rules, we are required to maintain a 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 Nasdaq rules relating to compensation committee members, which are different from the general test for independence of board and committee members. Each of the members of our compensation committee satisfies those requirements.

Compensation committee 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.

Approval of Related Party Transactions Under Israeli Law

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, 2019, Clal Biotechnology Industries Ltd. beneficially owned or controlled, directly and indirectly, 34.7% of our issued and outstanding ordinary shares.

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 such agreements is limited to an amount equal to the greater of (x) 25% of our total shareholders' equity based on our most recently financial statements of the time of the actual payment of the indemnification or (y) $25 million. The maximum amount set forth in such 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, 2018, we had 73 employees, 61 based in Israel and 12 (including 1 full time service providers) based throughout Europe and employed by our German subsidiary. The total number of our full-time employees and the distribution of our employees according to main areas of activity, as of the end of each of the last three years, are set forth in the following table:

	As of December 31,		
	2016	**2017**	**2018**
Department			
Administrative	7	8	9
Research and development	22	26	24
Manufacturing	23	26	28
Sales and marketing	20	16	12
Total	**72**	**76**	**73**

During the periods covered by the above table, 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, 2019 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 27,178,839 ordinary shares outstanding as of March 15, 2019. We have deemed our ordinary shares subject to stock options that are currently exercisable or exercisable within 60 days of March 15, 2019 to be outstanding and to be beneficially owned by the person holding the stock option for the purpose of computing the percentage ownership of that person. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

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 and executive officers will have 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		
Stefan T. Wills	*	*
Ofer Gonen	*	*
Assaf Segal	*	*
Vickie R. Driver	*	*
Nissim Mashiach	*	*
Sharon Kochan	*	*
Gal Cohen(1)	381,202	1.4%
Sharon Malka	*	*
Lior Rosenberg(2)	1,945,322	7.1%
Carsten Henke	*	*
Ety Klinger	*	*
Yaron Meyer	*	*
All executive officers and directors as a group (11 persons)(3)	2,861,336	10.5%
Principal Shareholders		
Clal Biotechnology Industries Ltd.(4)	9,429,555	34.7%
Wellington Management Group LLP(5)	3,432,542	12.6%
Migdal Insurance & Financial Holdings Ltd.(6)	2,126,058	7.8%
Yelin Lapidot(7)	1,703,081	6.3%

* Less than 1%.

(1) Shares beneficially owned consist of: (i) 131,102 ordinary shares held directly by Gal Cohen; and (ii) 250,100 ordinary shares issuable upon exercise of outstanding options that are currently exercisable or exercisable within 60 days of March 15, 2019.

(2) As reported on a Schedule 13G/A filed on February 8, 2018, shares beneficially owned consist of: (i) 140,367 ordinary shares held directly by Prof. Rosenberg; (ii) 94,750 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, 2019; 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.

(3) Shares beneficially owned consist of 1,987,131 ordinary shares held directly or indirectly by such executive officers and directors and 874,205 ordinary shares issuable upon exercise of outstanding options that are currently exercisable or exercisable within 60 days of March 15, 2019.

(4) As reported on a Schedule 13G/A filed on February 12, 2019, 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; and (ii) 1,220,582 ordinary shares held by CBI. 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.

(5) As reported on a Schedule 13G/A filed on February 12, 2019, shares beneficially owned consist of 3,432,542 ordinary shares owned of record by clients of one or more investment advisers directly or indirectly owned by Wellington Management Group LLP. As reported on a Schedule 13G/A filed on February 12, 2019, of the 3,432,542 shares beneficially owned, Wellington Management Group LLP has shared voting power with respect to 3,128,149 ordinary shares and shared dispositive power with respect to all 3,432,542 ordinary shares; Wellington Group Holdings LLP has shared voting power with respect to 3,128,149 ordinary shares and shared dispositive power with respect to all 3,432,542 ordinary shares; Wellington Investment Advisors Holdings LLP has shared voting power with respect to 3,128,149 ordinary shares and shared dispositive power with respect to all 3,432,542 ordinary shares; and Wellington Management Company LLP has shared voting power with respect to 3,128,149 ordinary shares and shared dispositive power with respect to 3,326,736 ordinary shares. The address of Wellington Management Group is c/o Wellington Management Company LLP, 280 Congress Street, Boston, MA 02210.

(6) As reported on a Schedule 13G/A filed on February 14, 2019, shares beneficially owned consist of: (i) 1,909,112 ordinary shares held for members of the public through, among others, provident funds, mutual funds, pension funds and insurance policies, which are managed by direct and indirect subsidiaries of Migdal Insurance & Financial Holdings Ltd ("Migdal"), and (ii) 216,946 ordinary shares are beneficially held for their own account (Nostro account). Migdal is a widely held public company listed on the Tel Aviv Stock Exchange. The address of Migdal is 4 Efal Street, Petah Tikva 49512, Israel.

(7) As reported on a Schedule 13G/A filed on February 14, 2019, shares beneficially owned consist of: 1,423,081 ordinary shares beneficially owned by mutual funds managed by Yelin Lapidot Mutual Funds Management Ltd., and (ii): 280,000 ordinary shares beneficially owned by Yelin Lapidot Provident Funds Management Ltd., each a wholly-owned subsidiary of Yelin Lapidot Holdings Management Ltd. ("Yelin Lapidot Holdings"), for the benefit of the members of the mutual funds. As reported on a Schedule 13G/A filed on February 14, 2019, Dov Yelin and Yair Lapidot each own 24.38% of the share capital and 25% of the voting rights of Yelin Lapidot Holdings, and are responsible for the day-to-day management of Yelin Lapidot Holdings. As reported on a Schedule 13G/A filed on February 14, 2019, each of Yelin Lapidot Mutual Funds Management Ltd. and Yelin Lapidot Provident Funds Management Ltd. operates under independent management and makes its own independent voting and investment decisions. The address of Yelin Lapidot Holdings is 50 Dizengoff St., Dizengoff Center, Gate 3, Top Tower, 13th floor, Tel Aviv 64332, Israel.

Changes in Ownership of Major Shareholders

Prior to our IPO in March 2014, CBI (and its affiliated entities, including Access Industries Holdings LLC) owned 9,789,555, or 63.4%, of our ordinary shares. As of March 15, 2019, primarily due to our issuance of ordinary shares, CBI's (and its affiliated entities') ownership of our ordinary shares decreased to 34.7%.

The beneficial ownership of our ordinary shares by other current major shareholders of our company has also fluctuated over the course of the past three years. The beneficial ownership of each of Migdal, Lior Rosenberg and Wellington Management Group LLP has been reported as follows as of the end of 2016, 2017 and 2018, respectively:

- Migdal: 7.9%, 8.4% and 8.1%
- Lior Rosenberg: 8.7%, 7.2% and 7.1%
- Wellington Management Group LLP: 8.9%, 13.5% and 12.6%

The beneficial ownership of an additional current major shareholder—Yelin Lapidot (and its affiliated entities)—has increased over the last two years, going from 1,252,381 ordinary shares (5.7%) as of March 2017 to 1,432,381 ordinary shares (5.3%) and 1,703,081 ordinary shares (6.3%) as of the end of 2017 and 2018, respectively.

Harel Insurance Investments & Financial Services Ltd., a former 5% shareholder of our company, ceased to hold 5% over the course of 2016, having dropped to 2.9% as of December 31, 2016.

Registered Holders

As of March 15, 2019, 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 57.2% of the 17,178,839 ordinary shares outstanding as of December 31, 2018. 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 have entered into a registration rights agreement with certain of our shareholders (the "Registration Rights Agreement"). The Registration Rights Agreement replaces the shareholders' right agreement, dated August 2, 2007, as amended on December 30, 2010, among us and certain of our shareholders. The Registration Rights Agreement provides that certain holders of our ordinary shares have 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. On March 7, 2016, the SEC declared effective our shelf registration statement on Form F-3, which registered the resale of the 11,640,827 shares subject to registration rights. Under SEC rules, shelf registration statement terminated upon the third anniversary of its effectiveness. The registration rights will terminate on March 24, 2021. The registration rights are described in more detail under "ITEM 10.B. Articles of Association."

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.

Patent Purchase Agreement

In November 2010, we entered into a patent purchase agreement (the "Patent Purchase Agreement"), with LR. In accordance with the Patent Purchase Agreement, we acquired from LR a patent family covering an occlusive dressing system for use in the treatment of burns, which is not a part of NexoBrid, EscharEx or our pipeline product candidates, in consideration of our reimbursement of his costs of filing and obtaining the patents and a one-time payment, in a total amount of $88,000, and in addition, fixed annual payments of $30,000 for every 12 months until the expiration of the patent in May 2018.

LR License Agreement

In September 2016, we signed an exclusive, perpetual, worldwide license agreement with LR for use of a certain patent and related intellectual property (the "LR License Agreement"). Under the LR License Agreement, we received an exclusive license to use LR's patent and intellectual property to develop, manufacture, market and commercialize a wound dressing that is advantageous for application of a debrided wound bed for the treatment of burns and other wounds. The LR License Agreement may be terminated by LR or us, subject to the dispute resolution procedures contained in the LR License Agreement, as a result of a material breach by the other party when such breach has not been cured within thirty days of written notification, or the other party's liquidation or entering into any arrangement with its creditors. We may also terminate the LR License Agreement at any time, in whole or in part, by giving LR 90 days' written notice and we shall have no obligation to compensate LR as a result of such termination.

In consideration for the LR License Agreement, we have agreed to make a one-time payment of $64,000 within 60 days following the receipt of marketing authorization with respect to products we develop pursuant to the LR License Agreement in the US or the EU. In addition, we undertook to pay royalties of 10% from net sales of product developed pursuant to the LR License Agreement and 10% of all consideration actually received by us from sublicensing the Licensed Products. In the event that a Competitor Product, as defined in the LR License Agreement, is marketed in certain territories, the royalty payments or sublicense fees paid by us to LR in that territory will be reduced to 5%.

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 indirect parent company, 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 $385,000. The Sub-Lease Agreement is scheduled to expire on October 30, 2022. The sub-lease agreement include an option to extend the lease period for additional 3 years at our sole discretion.

Agreements with Directors and Officers

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 officers and certain of our directors. 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 grants dated December 23, 2015, June 22, 2017, January 16, 2018 and December 31, 2018.

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."

Family Relationships

We are not aware of any familial relationships between any of our 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

We have appended our consolidated financial statements at the end of this annual report, starting at page F-2, as part of this annual report.

Legal Proceedings

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

On September 15, 2014, a statement of claim was filed against the company by certain shareholders of PolyHeal. The plaintiffs allege that the company is obligated to pay them a total amount of approximately $1.5 million in exchange for their respective portion of PolyHeal's shares, following the milestone occurrence under the 2010 PolyHeal Agreement. This claim arises out of a dispute with Teva under the 2010 PolyHeal Agreement. On December 14, 2014, the company filed a petition for a right to defend (the "Petition") with the Tel Aviv-Jaffa District Court, in which the company: (i) rejected the arguments raised against it in the statement of claim; (ii) emphasized that its obligation under the 2010 PolyHeal Agreement to purchase the 7.5% of PolyHeal's shares is subject to the consumption of the deferred closing, as defined in the 2010 PolyHeal Agreement, including the receipt of the funds from Teva on a "back to back" basis; and (iii) stated that since no such payment has been made by Teva, the company is not subject to any obligation to purchase PolyHeal shares and/or make any payments to PolyHeal's shareholders.

On November 13, 2017, the Tel Aviv-Jaffa District Court issued a ruling in favor of the plaintiffs. The court ruled that we are obligated to purchase PolyHeal's shares for approximately $6.75 million plus applicable interest (totaled in $7.5 million as of the ruling date), which represents the purchase price for the total number of shares that the PolyHeal Agreements contemplate would be acquired by the Company from the shareholders of PolyHeal. The Court ordered that we are obligated to purchase shares in PolyHeal from the plaintiffs, on the basis of their actual share holdings in PolyHeal as of January 15, 2013, for approximately $1.3 million plus applicable interest (totaled in $1.5 million as of the ruling date), within 15 days from the date of the Court's ruling. On December 27, 2017, we filed an appeal to the Supreme Court over the said ruling, alleging, among other things, that the agreement according to which the ruling was granted was misinterpreted by the District Court. We further alleged that both the wording of the agreement and the conduct of the parties thereunder prove that our obligation to purchase PolyHeal's shares was subject to the prior receipt of funds, which were never received, from Teva. On January 30, 2018, certain PolyHeal shareholders filed a cross appeal, alleging that they are entitled to receive from us a full repayment of their counsel's fees in a sum equal to 12.5% of the consideration to be paid for their shares.

Accordingly, a full provision for the purchase price of the shares plus the accrued interest, totaling $7.5 million was recorded within the loss from discontinued operations in 2017 in respect of this claim, of which approximately $1.5 million was paid to plaintiffs in consideration for PolyHeal's shares.

On March 24, 2019, we entered into the PolyHeal Settlement with the plaintiffs, which contingent upon the Supreme Court's approval of the PolyHeal Settlement Agreement, settles any and all debts, obligations or liabilities that we and the plaintiffs had, has or may have to the other party under, in connection with or arising out of the transactions described above. Pursuant to the terms of this PolyHeal Settlement Agreement, the plaintiffs will repay to the company a non-material portion of the amount that was ruled in their favor under the 2017 Ruling, and the Israeli Supreme Court will approve and accept the appeal that was filed by us on December, 2017, cancel the 2017 Ruling that was issued by the District Court against us, and reject the Cross-Appeal. However, if the Israeli Supreme Court does not approve of the PolyHeal Settlement Agreement or refuses to take the actions requested from the court in the PolyHeal Settlement Agreement, these matters may result in the continuation of the existing litigation or new litigation or arbitration proceedings, any of which would materially increase our expenses and may disrupt our management's focus on our business. See "ITEM 3.D. Risk Factors—We may have liabilities under our former agreements with Teva Pharmaceutical Industries Ltd. and PolyHeal Ltd."

On March 24, 2019, we entered into a settlement agreement and mutual general release (the "Teva Settlement Agreement") with Teva, which contingent upon the Supreme Court's approval of the PolyHeal Settlement Agreement, which settles any and all debts, obligations or liabilities that each party or any of its controlled affiliates had or has to the other party or any of its controlled affiliates under, in connection with or arising out of certain transactions and agreements entered into between us and Teva from 2007 to 2012 (collectively, the "Collaboration Agreements"), which have terminated effective as of December 31, 2012 and September 2, 2013, as applicable, and which related to NexoBrid, and PolyHeal, including the above PolyHeal milestone and certain payments, which are primarily reimbursement for development and manufacturing costs, that we believed were to be borne by Teva through the effective date of termination of such Collaboration Agreements in December 2012.

Pursuant to the terms of the Teva Settlement Agreement, Teva has agreed to pay us $4.0 million in cash, and to reduce the contingent consideration that is payable to Teva pursuant to the our repurchase of our shares from Teva in 2013, so that we will be 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, defend and hold harmless Teva and its controlled affiliates 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 million, if a notice of such claim has been received by us prior to December 31, 2023.

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, 2018, except as otherwise disclosed in this annual report.

Item 9. THE OFFER AND LISTING

A. Listing Details

Our ordinary shares have been traded on Nasdaq under the symbol "MDWD".

As of March 15, 2019, we had 9 holders of record of our ordinary shares. The actual number of shareholders is greater than this number of record holders, and includes shareholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

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

Our authorized share capital consists of 37,244,508 ordinary shares, par value NIS 0.01 per share, of which 27,178,839 shares are issued and outstanding as of March 15, 2019.

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.

Our prior articles were replaced in March 2014 by new articles of association and at which time all of our issued and outstanding preferred shares converted into ordinary shares. On June 2018, we amended the articles by increasing the share capital of the Company to NIS 372,445.08 divided into 37,244,508 of our ordinary shares. The description below is a summary of the material provisions of our new articles of association and of the Companies Law.

Voting rights and conversion.

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.

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 all 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. In addition, 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 recently 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."

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. This 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.

Exchange controls

There are currently no Israeli currency control restrictions on remittances of dividends on our ordinary shares, proceeds from the sale of the shares or interest or other payments to non-residents of Israel, except for shareholders who are subjects of countries that are, or have been, in a state of war with Israel.

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 generally be between four and 21 days prior to the date of the meeting and in certain circumstances, 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 passed 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 director's 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 under 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 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 shall constitute a lawful quorum.

Vote requirements

Our articles of association provide that all resolutions of our shareholders require a simple majority vote, 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 and (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) requires the approval described above under "ITEM 6.C. Board Practices—Approval of Related Party Transactions Under Israeli Law—Disclosure of personal interests of controlling shareholders and approval of certain transactions." 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), in addition to the ordinary majority vote of all classes of shares voting together as a single class at a shareholder meeting.

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 have entered into the Registration Rights Agreement with certain of our shareholders. Pursuant to the Registration Rights Agreement, holders of a total of 11,640,827 of our ordinary shares have the right to require us to register these shares under the Securities Act under specified circumstances and will have incidental registration rights as described below. After registration pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act. On March 7, 2016, the SEC declared effective our shelf registration statement on Form F-3, which registered the resale of the 11,640,827 shares subject to registration rights.

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 will not be deemed approved if a majority of the votes of shares represented at the meeting of shareholders that are held by parties other than the other party to the merger, or by 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, vote against 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 (as described under "ITEM 6.C. Board Practices—Approval of Related Party Transactions Under Israeli Law—Disclosure of personal interests of controlling shareholders and approval of certain transactions.")

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.

In addition, 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 March 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."

Transfer Agent and Registrar

The transfer agent and registrar for our ordinary shares is American Stock Transfer & Trust Company, New York, New York.

C. Material Contracts

For a description of the registration rights present in 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. Business Overview—BARDA Contract."

For a description of our license agreement with Mark Klein, see "ITEM 4.B. Business Overview—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 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. This summary does not discuss all the aspects of Israeli tax law that may be relevant to a particular investor in light of his or her personal investment circumstances or to some types of investors subject to special treatment under Israeli law. Examples of such investors include residents of Israel or traders in securities who are subject to special tax regimes not covered in this discussion. 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. In 2017 the corporate tax rate was 24%. 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 Investments 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). In 2017-2019 dividends paid out of preferred income attributed to a Special Preferred Enterprise, directly to a foreign parent company, are subject to withholding tax at source at the rate of 5% (temporary provisions).

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).

Taxation of 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 an Approved Enterprise or a Beneficiary Enterprise and 20% if the dividend is distributed from income attributed to a Preferred 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 NIS 641,880 for 2018, 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 2019, the additional tax will be at a rate of 3% on annual income exceeding NIS 649,560.

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 subject to special tax accounting rules as a result of any item of gross income with respect to the shares being taken into account in an applicable financial statement;
- 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, 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 own tax advisers 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:

- 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 advisers 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 reported 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, 2018. 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 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. Because a mark-to-market election generally would not be available with respect to any lower-tier PFICs that we may own, 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 a PFIC for U.S. federal income tax purposes.

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 we are determined to be 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 of our subsidiaries that also may be determined to be PFICs.

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.

Medicare Tax

Certain U.S. Holders that are individuals, estates or trusts are subject to a 3.8% tax on all or a portion of their "net investment income," which may include all or a portion of their dividend income and net gains from the disposition of ordinary shares. Each U.S. Holder that is an individual, estate or trust is urged to consult its tax advisors regarding the applicability of the Medicare tax to its income and gains in respect of its investment in our ordinary shares.

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. 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 currently subject to the informational requirements of the Exchange Act applicable to foreign private issuers and fulfill the obligations of these requirements by filing reports with the SEC. As a foreign private issuer, we are exempt from the rules under the Exchange Act relating 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 periodic reports and financial statements with the SEC as frequently or as promptly as U.S. companies whose securities are registered under the Exchange Act. However, we are required to file with the SEC, within 120 days after the end of each subsequent fiscal year, an annual report on Form 20-F containing financial statements which will be examined and reported on, with an opinion expressed, by an independent public accounting firm. We also file with the SEC reports on Form 6-K containing quarterly unaudited financial information.

You may read and copy any document we file with the SEC without charge at the SEC's public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. The SEC also maintains an Internet site that contains reports and other information regarding issuers that file electronically with the SEC. Our filings with the SEC are also available to the public through this web site at http://www.sec.gov. As permitted under Nasdaq Stock Market Rule 5250(d)(1)(C), we will post our annual reports filed with the SEC on our website at http://www.mediwound.com. We will not furnish hard copies of such reports to our shareholders unless we are requested to do so in writing. Upon receipt of such a request, we will provide a hard copy of such reports to such requesting shareholder free of charge. The information contained on our website is not part of this or any other report filed with or furnished to the SEC.

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 portion of our expenses are denominated in Israeli shekels, accounting for approximately 28%, 40% and 45% of our expenses in the years ended December 31, 2016, 2017 and 2018, respectively. We also have expenses in other non-dollar currencies, in particular the Euro, and for the next few years, we expect that the substantial majority of our revenue, if any, will be denominated in Euros from the sale of NexoBrid in the European Union. 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 the shekel (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:

	Change in Exchange Rate	
Period	Shekel against the U.S. dollar (%)	Euro against the U.S. dollar (%)
2014	(12.0)	(11.8)
2015	(0.3)	(10.4)
2016	1.5	(3.4)
2017	9.8	13.9
2018	(8.1)	(4.4)

A 10% increase (decrease) in the value of the NIS and Euro against the U.S. dollar would have decreased (increased) our net loss by approximately $0.1 million in 2018.

As we are marketing and sales of NexoBrid in Europe and clinical trials of NexoBrid 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 borrowings.

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 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

Initial Public Offering

The effective date of the registration statement (File No. 333-193856) for our IPO of ordinary shares, par value NIS 0.01, was March 19, 2014. The offering commenced on March 19, 2014 and was closed on March 25, 2014. In our IPO, we issued and sold a total of 5,750,000 ordinary shares at a price per share of $14.00 with aggregate gross proceeds of approximately $80.5 million. Under the terms of the offering, we incurred aggregate underwriting discounts of approximately $5.6 million and expenses of approximately $3.2 million in connection with the offering, resulting in net proceeds to us of approximately $71.7 million.

From the effective date of the registration statement and until December 31, 2018, we have used existing cash and the net proceeds from the offering, in the amount of approximately $23.2 million to expand our marketing infrastructure, $25.2 million on research and development and $28.5 million to maintain our manufacturing capabilities, for working capital and other general corporate purposes. Under the modified BARDA contract, BARDA has agreed to fund up to $56 million of the development costs of NexoBrid and we expect that almost all NexoBrid development programs, including clinical and non-clinical development as well as regulatory submission, will be funded by BARDA. In addition, under the new BARDA contract, BARDA has agreed to fund up to $12 million of the development costs of NexoBrid for the treatment of Sulfur Mustard injuries under the Animal Rule. Therefore, we intend to use a portion of our proceeds raised during our IPO together with the net proceeds raised in our September 2017 follow-on offering, to further advance our research and development activities, primarily the clinical development of EscharEx and the remainder, if any, for working capital and other general corporate purposes. See ITEM 4.B. Business Overview—BARDA Contract." We may also use a portion of the net proceeds to make acquisitions or investments in complementary companies or technologies, although we do not have any agreement or understanding with respect to any such acquisition or investment at this time.

None of the net proceeds of the offering was paid directly or indirectly to any director, officer, general partner of ours or to their associates, persons owning 10% or more of any class of our equity securities, or to any of our affiliates, except as a compensation and general and administrative expenses.

Item 15. CONTROLS AND PROCEDURES

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, 2018. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2018, our disclosure controls and procedures were effective.

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, 2017. 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, 2018.

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.

Attestation Report of the Registered Public Accounting Firm

This annual report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting because the JOBS Act provides an exemption from such requirement as we qualify as an emerging growth company.

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 ethics and proper business conduct 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. 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 2018.

Item 16C. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Principal Accountant Fees and Services

We paid the following fees for professional services rendered Kost Forer Gabbay & Kasierer, a member of Ernst & Young Global, an independent registered public accounting firm, for the years ended December 31, 2018 and 2017:

	2017	2018
Audit Fees	$ 290,000	$ 160,000
Audit-Related Fees	—	
Tax Fees	—	
Total	$ 290,000	$ 160,000

"**Audit fees**" are the aggregate fees paid for the audit of our annual financial statements. 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, including the registration statement filed in connection with our September 2017 equity offering.

"**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 accountant.

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

Not applicable.

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 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 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 rules.

- *Majority of independent directors*. Under the Companies Law, we are only required to appoint at least two external directors, within the meaning of the Companies Law, to our board of directors. Currently, four of our directors (of which two are external directors, within the meaning of the Companies Law) qualify as independent directors under the rules of the U.S. federal securities laws and the Nasdaq Stock Market 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.

Item 16H. MINE SAFETY DISCLOSURE

Not applicable.

PART III

Item 17. FINANCIAL STATEMENTS

Not applicable.

Item 18. FINANCIAL STATEMENTS

See pages F-2 through F-40 of this annual report.

Item 19. EXHIBITS

Exhibit No.	Description
1.1	Amended and Restated Articles of Association of the Registrant(2)
1.2	First Amendment to the Amended and Restated Articles of Association, effective as of June 12, 2014(6)
1.3	Second Amendment to the Amended and Restated Articles of Association, effective as of June 18, 2018
1.4	Memorandum of Association of the Registrant(3)
4.1	Form of Registration Rights Agreement by and among the Registrant and certain shareholders of the Registrant(3)
4.2	Form of Information Rights Agreement by and between Clal Biotechnology Industries Ltd. and the Registrant(3)
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(4)
4.4	Patent Purchase Agreement, dated November 24, 2010, by and between the Registrant and L.R. R & D Ltd.(4)
4.5	Form of Indemnification Agreement(3)
4.6	Supply Agreement, dated January 11, 2001, as amended, by and between the Registrant and Challenge Bioproducts Corporation Ltd.†(4)
4.7	License Agreement, dated September 22, 2000, as amended, by and between the Registrant and Mark Klein†(4)
4.8	2003 Israeli Share Option Plan(4)
4.9	2014 Equity Incentive Plan(3)
4.10	First Amendment to the 2014 Equity Incentive Plan, effective as of December, 2018
4.11	Letter Agreement, dated February 18, 2014, by and between the Registrant and Teva Pharmaceutical Industries Ltd.(3)
4.12	MediWound Ltd.'s Compensation Policy for Executive Officers and Directors(5)
4.13	BARDA Contract, dated September 29, 2015, by and between the Registrant and the U.S. Biomedical Advanced Research and Development Authority†(7)
4.14	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)
4.15	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)
4.16	Modification to the BARDA Contract, dated July 19, 2017, by and between the Registrant and the U.S. Biomedical Advanced Research and Development Authority(1)
4.17	BARDA Contract, dated September 30, 2018, by and between the Registrant and the U.S. Biomedical Advanced Research and Development Authority*
4.18	License Agreement, dated November 11, 2016 by and between the registrant and L.R. Research and Development Ltd.(8)
4.19	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)(1)
4.20	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)
4.21	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.
8.1	List of subsidiaries of the Registrant(4)
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 Kost Forer Gabbay and Kasierer, a member of Ernst & Young Global, an independent registered public accounting firm
100	The following financial information from the Registrant's Annual Report on Form 20-F for the year ended December 31, 2017 formatted in XBRL (eXtensible Business Reporting Language): (i) Consolidated Balance Sheets at December 31, 2016 and 2017; (ii) Consolidated Statements of Profit or Loss or Other Comprehensive Loss for the years ended December 31, 2015, 2016 and 2017; (iii) Consolidated Statements of Changes in Equity (Deficiency) for the years ended December 31, 2015, 2016 and 2017; (iv) Consolidated Statements of Cash Flows for the years ended December 31, 2015, 2016 and 2017; and (v) Notes to Consolidated Financial Statements, tagged as blocks of text. Users of this data are advised, in accordance with Rule 406T of Regulation S-T promulgated by the SEC, that this Interactive Data File is deemed not filed or part of a registration statement or prospectus for purposes of Sections 11 or 12 of the Securities Act, is deemed not filed for purposes of Section 18 of the Exchange Act, and otherwise is not subject to liability under those sections.

† Confidential treatment previously requested and granted with respect to certain portions, which portions were omitted and filed separately with the Securities and Exchange Commission.

* Portions of this exhibit have been omitted pursuant to a request for confidential treatment by the Securities and Exchange Commission and the non-public information has been filed separately with the Securities and Exchange Commission.

(1) Previously filed with the SEC on March 19, 2018 pursuant to the registrant's Form 20-F and incorporated by reference herein.

(2) Previously filed with the SEC on March 14, 2014 pursuant to a registration statement on Form F-1 (File No. 333-193856) and incorporated by reference herein.

(3) Previously filed with the SEC on March 3, 2014 pursuant to a registration statement on Form F-1 (File No. 333-193856) and incorporated by reference herein.

(4) Previously filed with the SEC on February 10, 2014 pursuant to a registration statement on Form F-1 (File No. 333-193856) and incorporated by reference herein.

(5) Previously filed with the SEC on August 5, 2014 as Annex A to Exhibit 99.1 to the Registrant's Form 6-K and incorporated by reference herein.

(6) Previously filed with the SEC on February 12, 2015 pursuant to the Registrant's Annual Report on Form 20-F for the year ended December 31, 2014 (File No. 001-36349) and incorporated by reference herein.

(7) Previously filed with the SEC on January 25, 2016 pursuant 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 pursuant 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.

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 25, 2019

By: /s/ Sharon Malka
Sharon Malka
Chief Financial and Operation Officer

MEDIWOUND LTD. AND ITS SUBSIDIARIES

CONSOLIDATED FINANCIAL STATEMENTS

DECEMBER 31, 2018

INDEX

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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 sheets of MediWound Ltd. and its subsidiaries (the "Company") as of December 31, 2017 and 2018 and the related consolidated statements of comprehensive profit or loss, changes in equity and cash flows for each of the three years in the period ended December 31, 2018 and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the consolidated financial position of the Company at December 31, 2017 and 2018, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, 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.

/s/ KOST FORER GABBAY & KASIERER
A Member of Ernst & Young Global
We have served as the Company's auditor since 2001.

Tel-Aviv, Israel
March 25, 2019

CONSOLIDATED BALANCE SHEETS

U.S. dollars in thousands

	Note	December 31, 2017	December 31, 2018
CURRENT ASSETS:			
Cash and cash equivalents	5	36,069	6,716
Short-term bank deposits	6	-	16,917
Trade receivables		369	560
Inventories	7	1,886	1,680
Other receivables	8, 22	3,196	6,840
		41,520	32,713
LONG-TERM ASSETS:			
Long term deposits		56	48
Property, plant and equipment, net	9	1,924	2,020
Intangible assets, net	10	635	495
		2,615	2,563
		44,135	35,276
CURRENT LIABILITIES:			
Trade payables and accrued expenses		3,251	2,715
Other payables	11, 22	2,182	2,182
		5,433	4,897
LONG-TERM LIABILITIES:			
Deferred revenues		988	1,158
Liabilities in respect of IIA grants	12,13	7,380	7,568
Contingent consideration for purchase of shares	13,15e,23b	14,381	6,330
Liability in respect of discontinued operation	19	6,003	6,003
Severance pay liability, net	14	330	348
		29,082	21,407
SHAREHOLDERS' EQUITY:	16		
Ordinary shares of NIS 0.01 par value:			
Authorized: 32,244,508 shares as of December 31, 2017 and 37,244,508 shares as of December 31, 2018; Issued and Outstanding 27,047,737 and 27,178,839 shares as of December 31, 2017 and 2018, respectively.		75	75
Share premium		138,992	139,637
Foreign currency translation adjustments		(38)	(25)
Accumulated deficit		(129,409)	(130,715)
		9,620	8,972
		44,135	35,276

The accompanying notes are an integral part of the consolidated financial statements.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE PROFIT OR LOSS

U.S. dollars in thousands (except of share and per share data)

	Note	Year ended December 31, 2016	2017	2018
Revenues		1,558	2,496	3,401
Cost of revenues	20a	2,158	1,578	2,088
Gross profit (loss)		(600)	918	1,313
Operating expenses:				
Research and development, gross		14,779	14,625	17,915
Participations by BARDA and IIA		(7,711)	(9,163)	(13,843)
Research and development, net of participations	20b	7,068	5,462	4,072
Selling and marketing	20c	8,403	5,362	4,188
General and administrative	20d	4,084	3,781	3,799
Other income from settlement agreement	23	-	-	(7,537)
Other expenses	20e	-	-	751
Total operating expenses		19,555	14,605	5,273
Operating loss		(20,155)	(13,687)	(3,960)
Financial income	20f	2,166	406	412
Financial expense	20f	(896)	(1,252)	(2,117)
Loss from continuing operations		(18,885)	(14,533)	(5,665)
Profit (loss) from discontinued operation	19,23b	-	(7,616)	4,608
Net loss		(18,885)	(22,149)	(1,057)
Other comprehensive income (loss):				
Items to be reclassified to profit or loss in subsequent periods:				
Foreign currency translation adjustments		7	(29)	13
Total comprehensive loss		(18,878)	(22,178)	(1,044)
Basic and diluted net loss per share:	21			
Basic and diluted net loss per share from continuing operations		(0.86)	(0.62)	(0.21)
Basic and diluted net profit (loss) per share from discontinued operations		-	(0.33)	0.17
Total Basic and diluted net loss per share		(0.86)	(0.95)	(0.04)

The accompanying notes are an integral part of the consolidated financial statements.

CONSOLIDATED STATEMENTS OF CHANGES IN EQUITY

U.S. dollars in thousands

	Share capital	Share premium	Foreign currency translation Adjustments	Accumulated deficit	Total Equity
Balance as of January 1, 2016	60	111,801	(16)	(88,375)	23,470
Loss for the period	-	-	-	(18,885)	(18,885)
Other comprehensive income	-	-	7	-	7
Total comprehensive (loss) income	-	-	7	(18,885)	(18,878)
Exercise of options	*	7	-	-	7
Share-based compensation	-	3,171	-	-	3,171
Balance as of December 31, 2016	60	114,979	(9)	(107,260)	7,770
Loss for the period	-	-	-	(22,149)	(22,149)
Other comprehensive loss	-	-	(29)	-	(29)
Total comprehensive (loss) income	-	-	(29)	(22,149)	(22,178)
Exercise of options	*	7	-	-	7
Issuance of ordinary shares of NIS 0.01 par value net of issuance expenses	15	22,643	-	-	22,658
Share-based compensation	-	1,363	-	-	1,363
Balance as of December 31, 2017	75	138,992	(38)	(129,409)	9,620
Accumulated effect of adopting IFRS 15	-	-	-	(249)	(249)
Balance as of January 1, 2018	75	138,992	(38)	(129,658)	9,371
Loss for the period	-	-	-	(1,057)	(1,057)
Other comprehensive income	-	-	13	-	13
Total comprehensive (loss) income	-	-	13	(1,057)	(1,044)
Exercise of options	*	-	-	-	*
Share-based compensation	-	645	-	-	645
Balance as of December 31, 2018	75	139,637	(25)	(130,715)	8,972

* 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,		
	2016	**2017**	**2018**
Cash Flows from Operating Activities:			
Net loss	(18,885)	(22,149)	(1,057)
Adjustments to reconcile net loss to net cash used in continuing operating activities:			
Adjustments to profit and loss items:			
Loss (profit) from discontinued operation	-	7,616	(4,608)
Depreciation and amortization	589	567	577
Share-based compensation	3,171	1,363	645
Revaluation of liabilities in respect of IIA grants	(1,298)	229	287
Revaluation of contingent consideration for purchase of shares	(1,621)	351	758
Other income from settlement agreement	-	-	(7,537)
Increase in severance pay liability, net	125	111	19
Net financing income	(414)	(349)	(412)
Un-realized foreign currency (gain) loss	(94)	(185)	182
	458	9,703	(10,089)
Changes in asset and liability items:			
Decrease (increase) in trade receivables	(107)	28	(211)
Decrease (increase) in inventories	873	(1,042)	206
Decrease (increase) in other receivables and long term deposits	33	(1,227)	(306)
Increase (decrease) in trade payables and accrued expenses	2,195	(135)	(536)
Decrease in other payables and deferred revenues	(1,012)	(70)	(161)
	1,982	(2,446)	(1,008)
Net cash used in continuing operating activities	(16,445)	(14,892)	(12,154)
Net cash used in discontinued operating activities	-	(1,563)	-
Net cash used in operating activities	(16,445)	(16,455)	(12,154)

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,		
	2016	**2017**	**2018**
Cash Flows from Investing Activities:			
Purchase of property and equipment	(671)	(1,045)	(522)
Purchase of intangible assets	(30)	(30)	(12)
Interest received	407	349	106
Proceeds from (investments in) short term bank deposits, net	2,110	1,163	(16,612)
Net cash provided by (used in) investing activities	1,816	437	(17,040)
Cash Flows from Financing Activities:			
Proceeds from exercise of options	7	7	*
Proceeds from issuance of shares, net	-	22,658	-
Proceeds from the IIA grants, net of re-payment	900	330	46
Net cash provided by financing activities	907	22,995	46
Exchange rate differences on cash and cash equivalent balances	86	226	(205)
Increase (decrease) in cash and cash equivalents from continuing activities	(13,636)	8,766	(29,353)
Decrease in cash and cash equivalents from discontinued activities	-	(1,563)	-
Balance of cash and cash equivalents at the beginning of the year	42,502	28,866	36,069
Balance of cash and cash equivalents at the end of the year	28,866	36,069	6,716

* Represents an amount lower than $1.
The accompanying notes are an integral part of the consolidated financial statements.

NOTE 1: GENERAL

a. General description of the Company and its operations:

MediWound Ltd. (the "Company" or "MediWound"), is a fully integrated biopharmaceutical company focused on developing, manufacturing and commercializing novel products to address unmet needs in the fields of severe burns, chronic and other hard to heal wounds, connective tissue disorders and other indications.

The Company's innovative biopharmaceutical product, NexoBrid, received marketing authorization from the European Medicines Agency ("EMA") as well as the Israeli, Argentinean, South-Korean and Russian 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 Europe and in Israel through its commercial organizations and in other territories through local distributers.

The Company second investigational innovative product, EscharEx, is a topical biological drug being developed for debridement of chronic and other hard-to-heal wounds.

The Company has a contract with the U.S. Biomedical Advanced Research and Development Authority ("BARDA"), which was modified in July 2017, for the advancement of the development and manufacturing, as well as the procurement of NexoBrid, as a medical countermeasure as part of BARDA preparedness for mass casualty events. In September 2018, the Company has awarded additional contract with BARDA to develop NexoBrid for the treatment of Sulfur Mustard injuries as part of BARDA preparedness for mass casualty events (see Note 15d).

b. The Company has two wholly owned subsidiaries: MediWound Germany GmbH, acting as Europe (“EU”) marketing authorization holder and EU sales and marketing arm and MediWound UK Limited, an inactive company. In addition, the Company owns approximately 8% of PolyHeal Ltd., a private life sciences company ("PolyHeal").

c. The Company's securities are listed for trading on NASDAQ since March 2014. In September 2017, the Company completed a follow-on public offering. A total of 5,037,664 new ordinary shares were issued in consideration to net proceeds of $22,658, after deducting underwriter’s discounts, commissions and other offering expenses (see Note 16).

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES

a. Basis of presentation of financial statements:

These financial statements have been prepared in accordance with International Financial Reporting Standards ("IFRS") as issued by the International Accounting Standards Board ("IASB").

The Company's consolidated financial statements have been prepared on a cost basis, except for financial instruments which are measured at fair value through profit or loss.

b 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.

c. 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 raised in U.S. dollars including the public offering completed in 2014, the follow-on offering completed in 2017 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.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

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.

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.

d. 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.

e. 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.

f. 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 including materials, labor and other direct and indirect manufacturing costs based on practical capacity.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

g. Participation by governments support:

(i) Israeli Innovation Authority grants:

Government grants are recognized when there is reasonable assurance that the grants will be received and the Company will comply with the attendant conditions.

Research and development grants received from the Israeli Innovation Authority ("IIA"), are recognized upon receipt as a liability if future economic benefits are expected from the project that will result in royalty-bearing sales. In that event, the royalty obligation is treated as a contingent liability in accordance with IAS 37, "*Provisions, Contingent Liabilities and Contingent Assets*" ("IAS 37").

A liability for the grant is first measured at fair value (Level 3 of the fair value hierarchy) using a discount rate that reflects a market interest rate. The difference between the amount of the grant received and the fair value of the liability is accounted for as a government grant and recognized as a deduction from research and development expenses. After initial recognition, the liability is measured at amortized cost using the effective interest method. Royalty payments are treated as a reduction of the 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, if so, the appropriate amount of the liability is derecognized against a corresponding reduction in research and development expenses.

(ii) Funding by BARDA:

Non-royalty bearing funds from BARDA for funding research and development projects are recognized at the time the Company is entitled to such grants on the basis of the related costs incurred and recorded as a deduction from research and development expenses.

h. Leases:

The criteria for classifying leases as finance or operating leases depend on the substance of the agreements and are made at the inception of the lease in accordance with the following principles as set out in IAS 17.

Operating leases:

Leases in which substantially all the risks and rewards of ownership of the leased asset are not transferred to the Company 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.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

i. 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
Electronic machinery and laboratory equipment	15-20
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.

j. Intangible assets, net:

Separately acquired intangible assets with finite useful life are measured on initial recognition at cost.

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.

k. Revenue recognition:

The Company currently generates revenues from direct and indirect sales of its innovative biopharmaceutical product, NexoBrid, to burn centers and hospital burn units in Europe and Israel as well as to local distributors in other countries. Revenues are recognized to the extent that it is probable that the economic benefits will flow to the Company and the revenues can be reliably measured, regardless of when the payment is being made. Revenues are measured at the fair value of the consideration received or receivable, taking into account contractually defined terms of payment and excluding taxes or duty and net of returns and allowances, trade discounts and volume rebates.

Revenues from the sale of products are 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.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

Revenues from distributors agreements which comprised of multiple elements (including license to access the Company's intellectual property and exclusive distribution rights), provide for varying consideration terms, such as upfront payments and milestone payments, are recognized when the criteria for revenue recognition have been met and only to the extent of the consideration that is not contingent upon completion or performance of future services under the contract. The Company concluded that the components do not have "stand alone value" to the customer and accordingly they are accounted for as one unit of account. Consequently, revenues from these components are recognized on the straight line basis over the license period.

Deferred revenues include unearned amounts received from customers not yet recognized as revenues. As of December 31, 2018, the aggregate amount of the deffered revenue was $1,356, which is expected to be recognized over 12 years.

Effective of January 1, 2018, the Company adopted IFRS 15, "Revenue from Contracts with Customers" ("the Standard"). The Company elected to adopt the provisions of the Standard which replaces IAS 18, using the modified retrospective method with the application of certain practical expedients and without restatement of comparative data.

The new Standard introduces a five-step model that applies to revenue earned from contracts with customers:

Step 1: Identify the contract with a customer, including reference to contract combination and accounting for contract modifications.

Step 2: Identify the distinct performance obligations in the contract.

Step 3: Determine the transaction price, including reference to variable consideration, significant financing components, non-cash consideration and any consideration payable to the customer.

Step 4: Allocate the transaction price to the distinct performance obligations on a relative stand-alone selling price basis using observable prices, if s available, or using estimates and assessments.

Step 5: Recognize revenue when a performance obligation is satisfied, either at a point in time or over time.

The Company generates revenues from direct and indirect sales of its products and from license agreements with its distributors.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

1. Revenue from the Sale of products:

   Revenue 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.

2. Revenue from distribution agreements with Multiple- element:

   According to the new Standard, entities need to determine whether the licenses for intellectual property is a performance obligation which is distinct from other goods and services included in the contract. An analysis of the Company's contracts with its distributors indicates that in the majority of contracts, the Company grants its distributors a right to access its intellectual property as it exists throughout the license period. Accordingly, the Company recognizes revenue from the granting of licenses over the license period, which is identical to the legacy accounting treatment.

   In addition, in accordance with terms of some license agreements, the Company is entitled for up-front payments which are accounted for as deferred revenues and recognized in profit and loss over the license period. According to the new Standard, when long-term advances (exceeding one year) are received for a future service, the Company is required to accrue interest and recognize finance expense on the advances over the period of the contract. Under the legacy revenue recognition guidance the Company did not recognize finance expenses in respect of deferred revenue.

   On January 1, 2018, the Company adopted the new standard for all its distribution agreements at the date of initial application, with the cumulative effect of applying the new guidance recognized as an adjustment to the opening retained earnings balance. Results for reporting periods beginning after January 1, 2018 are presented under the new guidance, while prior period amounts are not adjusted and continue to be reported under the accounting standards in effect for the prior period. The Company recorded a net increase to opening accumulated deficit of $249 as of January 1, 2018 due to the cumulative impact of adopting the new guidance and an increase of deferred revenues by $249.

U.S. dollars in thousands (except of share and per share data)

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

The following table summarizes the impacts of adopting IFRS 15 on the Company's statement of financial position as of December 31, 2018 and its consolidated statements of comprehensive loss for the period ended December 31, 2018 for each of the line items affected.

Impact on the condensed consolidated statement of financial position:

	As reported	Adjustments	Amounts without adoption of IFRS 15
Deferred revenues*	1,356	(369)	987
Accumulated deficit	(130,715)	369	(130,346)

* Comprised of short term deferred revenues classified in other payable and long term deferred revenues.

Impact on the condensed consolidated statements of comprehensive loss for the year ended December 31, 2018:

	As reported	Adjustments	Amounts without adoption of IFRS 15
Revenues	3,401	(44)	3,357
Financial expense	(2,117)	164	(1,953)
Net loss	(1,057)	120	(937)
Total Basic and diluted net loss per share	(0.04)	(0.0)	(0.04)

l. 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.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

m. 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.

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.

n. Financial instruments:

Effective of January 1, 2018 the Company adopted IFRS 9, "Financial Instruments" ("the Standard"), which replaced IAS 39. The Company elected to adopt the provisions of the Standard retrospectively without restatement of comparative data.

1. Financial assets:

Financial assets are classified, at initial recognition, and subsequently measured at amortized cost, fair value through other comprehensive income (OCI), and fair value through profit or loss.

The classification of financial assets at initial recognition depends on the financial asset's contractual cash flow characteristics and the Company's business model for managing them. With the exception of trade receivables that do not contain a significant financing component or for which the Company has applied the practical expedient, the Company initially measures a financial asset at its fair value plus, in the case of a financial asset not at fair value through profit or loss, transaction costs.

Receivable:

The Company has receivables that are financial assets with fixed or determinable payments that are not quoted in an active market.

2. Financial liabilities:

Financial liabilities within the scope of IFRS 9 are initially measured at fair value.

After initial recognition, the accounting treatment of financial liabilities is based on their classification as follows:

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

Financial liabilities measured at amortized cost:

Loans and other contingent liabilities are measured at amortized cost using the effective interest method taking into account directly attributable transaction costs.

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.

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).

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

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.

6. De-recognition of financial instruments:

a) Financial assets:

A financial asset is derecognized when the contractual rights to the cash flows from the financial asset expire or the Company has transferred its contractual rights to receive cash flows from the financial asset or assumes an obligation to pay the cash flows in full without material delay to a third party and has transferred substantially all the risks and rewards of the asset, or has neither transferred nor retained substantially all the risks and rewards of the asset, but has transferred control of the asset.

b) Financial liabilities:

A financial liability is derecognized when it is extinguished, that is when the obligation is discharged or cancelled or expires. A financial liability is extinguished when the debtor (the Company) discharges the liability by paying in cash, other financial assets, goods or services; or is legally released from the liability.

7. Contingent consideration for purchase of shares:

The contingent consideration liability for purchase of shares is measured at fair value(Level 3 of the fair value hierarchy) and initially recorded against equity. Subsequent changes in the fair value are recognized in profit or loss.

o. 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.

The Company accounts for this obligation as a liability on the balance sheet in an amount equal to the fair value of the future royalty payments. In order to determine the fair value, the Company estimated the amount and timing of the future payments based on our projected results of operations.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

p. 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 EU 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.

Contributions to the defined contribution plan in respect of severance or retirement pay are recognized as an expense when contributed concurrently with performance of the employee's services.

q. 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.

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

r. 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 profit or loss.

s. Loss per share:

Loss per share is calculated by dividing the 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.

NOTE 3:- SIGNIFICANT ACCOUNTING JUDGMENTS, ESTIMATES AND ASSUMPTIONS USED IN THE PREPARATION OF THE FINANCIAL STATEMENTS

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 JUDGMENTS, ESTIMATES AND ASSUMPTIONS USED IN THE PREPARATION OF THE FINANCIAL STATEMENTS (Cont.)

- Contingent consideration for the purchase of shares:

  Contingent consideration for the purchase of shares was first measured at fair value. After initial recognition, the liability is measured at amortized cost using the effective interest method. As the contingent consideration 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 fair value of this liability.

- Legal claims:

  In estimating the likelihood of outcome of legal claims filed against the Company and its investees, the companies rely on the opinion of their legal counsel. These estimates are based on the legal counsel's best professional judgment, taking into account the stage of proceedings and legal precedents in respect of the different issues. Since the outcome of the claims will be determined in courts, the results could differ from these estimates.

NOTE 4:- DISCLOSURE OF NEW STANDARDS IN THE PERIOD PRIOR TO THEIR ADOPTION

IFRS 16, "Leases":

In January 2016, the IASB issued IFRS 16, "Leases" ("the new Standard"). According to the new Standard, a lease is a contract, or part of a contract, that conveys the right to use an asset for a period of time in exchange for consideration.

The effects of the adoption of the new Standard are as follows:

- According to the new Standard, lessees are required to recognize all leases in the statement of financial position (excluding certain exceptions, see below). Lessees will recognize a liability for lease payments with a corresponding right-of-use asset, similar to the accounting treatment for finance leases under the existing standard, IAS 17, "Leases". Lessees will also recognize interest expense and depreciation expense separately.

- Variable lease payments that are not dependent on changes in the Consumer Price Index ("CPI") or interest rates, but are based on performance or use are recognized as an expense by the lessees as incurred and recognized as income by the lessors as earned.

- In the event of change in variable lease payments that are CPI-linked, lessees are required to remeasure the lease liability and record the effect of the remeasurement as an adjustment to the carrying amount of the right-of-use asset.

- The accounting treatment by lessors remains substantially unchanged from the existing standard, namely classification of a lease as a finance lease or an operating lease.

NOTE 4:- DISCLOSURE OF NEW STANDARDS IN THE PERIOD PRIOR TO THEIR ADOPTION (Cont.)

- The new Standard includes two exceptions which allow lessees to account for leases based on the existing accounting treatment for operating leases - leases for which the underlying asset is of low financial value and short-term leases (up to one year).

The new Standard is effective for annual periods beginning on or after January 1, 2019.

The new Standard permits lessees to use one of the following approaches:

1. Full retrospective approach - according to this approach, a right-of-use asset and the corresponding liability will be presented in the statement of financial position as if they had always been measured according to the provisions of the new Standard. Accordingly, the effect of the adoption of the new Standard at the beginning of the earliest period presented will be recorded in equity. Also, the Company will restate the comparative data in its financial statements. Under this approach, the balance of the liability as of the date of initial application of the new Standard will be calculated using the interest rate implicit in the lease, unless this rate cannot be easily determined in which case the lessee's incremental borrowing rate of interest on the commencement date of the lease will be used.

2. Modified retrospective approach - this approach does not require restatement of comparative data. The balance of the liability as of the date of initial application of the new Standard will be calculated using the lessee's incremental borrowing rate of interest on the date of initial application of the new Standard. As for the measurement of the right-of-use asset, the Company may choose, on a lease-by-lease basis, to apply one of the two following alternatives:

   - Recognize an asset in an amount equal to the lease liability, with certain adjustments.
   - Recognize an asset as if the new Standard had always been applied.

   Any difference arising on the date of first-time recorded in equity.

   The Company believes that it will apply the modified retrospective approach upon the initial adoption of the new Standard by measuring the right-of-use asset at an amount equal to the lease liability, as measured on the transition date.

   The Company has a substantial number of lease contracts, mainly leases of Vehicles and laboratory, office and clean room spaces (see also Note 15g). In assessing the impact of the new Standard on the financial statements, the Company is evaluating the following matters:

- Options to extend the lease- according to the new Standard, the non-cancellable period of a lease includes periods that are covered by options to extend the lease if the lessee is reasonably certain to exercise the option. The Company is reviewing whether such options exist in its lease agreements and whether it is reasonably certain that it will exercise the options. As part of its assessment, the Company is evaluating all relevant facts and circumstances that create an economic incentive to exercise the option, including significant leasehold improvements that have been or are expected to be undertaken, the importance of the underlying asset to the Company's operations and past experience in connection with the exercise of such options.

NOTE 4:- DISCLOSURE OF NEW STANDARDS IN THE PERIOD PRIOR TO THEIR ADOPTION (Cont.)

- Separation of lease components - according to the new Standard, all lease components within a contract should be accounted for separately from non-lease components. A lessee is allowed a practical expedient according to which it can elect, by class of underlying asset, not to separate non-lease components from lease components, and instead account for them as a single lease component. The Company is reviewing whether such non-lease components, such as management and maintenance services, exist in its current lease contracts and whether the above practical expedient should be applied to each class of underlying asset.

- Incremental interest rate - the Company estimates the incremental interest rate to be used for measuring the lease liability and right-of-use asset on the date of initial adoption of the new Standard, based on the lease term and nature of the leased asset.

The Company is also evaluating the need for making adjustments to its information systems, internal control, policies and procedures that will be necessary in order to apply the provisions of the new Standard.

The Company estimates that the effect of the initial adoption of the new Standard as of January 1, 2019, is expected to result in an increase in the Company's total assets and liabilities of approximately $ 2,500 and no change in its equity.

Moreover, the effect of the initial adoption of the new Standard in 2019 is expected to result in a decrease in the Company's lease expenses of approximately $ 590 and an increase in the Company's depreciation and finance expenses of approximately $ 530 and $ 150, respectively. The total effect of the initial adoption of the new Standard in 2019 is expected to result in a decrease of approximately $ 60 in operating expenses and a increase of approximately $ 90 in net loss.

In addition, as a result of the adoption of the new Standard, in 2019, the Company's cash flows from operating activities are expected to decrease by approximately $ 590 and its cash flows from financing activities are expected to increase by approximately $ 590.

U.S. dollars in thousands (except of share and per share data)

NOTE 5:- CASH AND CASH EQUIVALENTS

	December 31,	
	2017	2018
USD cash for immediate withdrawal	26,700	5,336
Non-USD cash for immediate withdrawal	9,369	1,380
	36,069	6,716

NOTE 6:- SHORT-TERM BANK DEPOSITS

	December 31,	
	2017	2018
USD bank deposits (1)	-	16,828
IL restricted bank deposits (2)	-	89
	-	16,917

(1) The USD deposits bear annual interest of 2.34%-2.60% for the period of 148-328 days for 2018.
(2) As of December 31, 2018, the Company had an amount of $ 89 that was restricted by the bank and may be used only when certain conditions are met.

NOTE 7:- INVENTORIES

	Year ended December 31,	
	2017	2018
Raw materials	339	432
Finished goods	1,547	1,248
	1,886	1,680

NOTE 8:- OTHER RECEIVABLES

	Year ended December 31,	
	2017	2018
Government authorities	226	126
BARDA funds	2,175	2,524
Prepaid expenses and other	129	132
Former shareholder, net (see Note 15e) *	666	4,000
Related parties	-	58
	3,196	6,840

* The 2018 balance includes $1,517 receivable in respect of discouninued operation (see Note 23b).

U.S. dollars in thousands (except of share and per share data)

NOTE 9:- PROPERTY, PLANT AND EQUIPMENT, NET

Balance as of December 31, 2018:

	Office furniture	Electronic machinery and laboratory equipment	Computers	Leasehold improvements	Total
Cost					
Balance as of January 1, 2018	248	3,561	139	2,120	6,068
Disposals	(7)	-	(55)	-	(62)
Additions	7	493	19	3	522
Foreign currency translation	(5)	-	(1)	-	(6)
Balance as of December 31, 2018	243	4,054	102	2,123	6,522
Accumulated Depreciation					
Balance as of January 1, 2018	154	1,802	93	2,095	4,144
Disposals	(7)	-	(55)	-	(62)
Additions	18	351	33	23	425
Foreign currency translation	(4)	-	(1)	-	(5)
Balance as of December 31, 2018	161	2,153	70	2,118	4,502
Depreciated cost as of December 31, 2018	82	1,901	32	5	2,020

Balance as of December 31, 2017:

	Office furniture	Electronic machinery and laboratory equipment	Computers	Leasehold improvements	Total
Cost					
Balance as of January 1, 2017	227	2,551	185	2,120	5,083
Disposals	-	-	(74)	-	(74)
Additions	9	1,010	26	-	1,045
Foreign currency translation	12	-	2	-	14
Balance as of December 31, 2017	248	3,561	139	2,120	6,068
Accumulated Depreciation					
Balance as of January 1, 2017	126	1,508	118	2,057	3,809
Disposals	-	-	(74)	-	(74)
Additions	20	294	47	38	399
Foreign currency translation	8	-	2	-	10
Balance as of December 31, 2017	154	1,802	93	2,095	4,144
Depreciated cost as of December 31, 2017	94	1,759	46	25	1,924

U.S. dollars in thousands (except of share and per share data)

NOTE 10:- INTANGIBLE ASSETS, NET

Balance as of December 31, 2018

	License and Knowhow
Cost	
Balance as of January 1, 2018	1,526
Additions	12
Balance as of December 31, 2018	1,538
Accumulated Amortization	
Balance as of January 1, 2018	891
Additions	152
Balance as of December 31, 2018	1,043
Amortized cost	
Balance as of December 31, 2018	495

Balance as of December 31, 2017

	License and Knowhow
Cost	
Balance as of January 1, 2017	1,496
Additions	30
Balance as of December 31, 2017	1,526
Accumulated Amortization	
Balance as of January 1, 2017	723
Additions	168
Balance as of December 31, 2017	891
Amortized cost	
Balance as of December 31, 2017	635

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 (see Note 15c).

U.S. dollars in thousands (except of share and per share data)

NOTE 11:- OTHER PAYABLES

	Year ended December 31,	
	2017	2018
Employees and payroll accruals	1,621	1,532
Current maturities of IIA grants	57	146
Related parties	324	227
Deferred revenues	131	198
Other	49	79
	2,182	2,182

NOTE 12:- LIABILITIES IN RESPECT OF IIA GRANTS

	Year ended December 31,	
	2017	2018
Balance as of January 1	6,888	7,437
Grants received	401	93
Royalties	(81)	(103)
Amounts carried to Profit or Loss	229	287
Balance as of Decmber 31	7,437	7,714
Current maturities	(57)	(146)
Long term liabilities in respect of IIA grants	7,380	7,568

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 actually received by the Company from the IIA including accrued LIBOR interest, net of royalties as of December 31, 2018 is approximately $ 13,692, while the amortized cost of this liability as of that date is $ 7,714, using the interest method.

U.S. dollars in thousands (except of share and per share data)

NOTE 13:- FINANCIAL INSTRUMENTS

a. Financial risk factors:

The Company's activities expose it to various market risks (mainly foreign currency risk and interest rate risk). The Company's Board of Directors has provided guidelines for risk management and specific policies for various risk exposures.

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 in Europe, and additionally due to marketing expenses incurred in Europe.

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 is based on a calculation of the present value of future royalty payments using a discount rate that reflects the applicable market rate of interest at the date of the initial recognition. The Company used a discount rate of 16% based in part on the Company's estimation, at the time of the Company's initial recognition of the contingent consideration. The amount and timing of the future royalty payments are based on the Company's projected revenues.

c. 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,		
	2016	2017	2018
Sensitivity test to changes in NIS and EURO exchange rates			
Gain (loss) from change:			
5% increase in exchange rate	$ 11	$ 346	$ 31
5% decrease in exchange rate	$ (11)	$ (346)	$ (31)

NOTE 13:- FINANCIAL INSTRUMENTS (Cont.)

Sensitivity tests and principal work assumptions:

The selected changes in the relevant risk variables were determined based on management's estimate as to reasonable possible changes in these risk variables.

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.

NOTE 14:- 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 15:- 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. 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 2016, 2017 and 2018 amounted to $ 57, $ 48 and $ 72, respectively.

NOTE 15:- CONTINGENT LIABILITIES AND COMMITMENTS (Cont.)

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 generally cannot exceed 100% of the grants received by the Company, plus annual interest generally equal to the 12-month LIBOR applicable to dollar deposits, as published on the first business day of each calendar year. The royalty amount payable by the Company as of December 31, 2018 is approximately $ 13,692, which represents the total amount of grants actually received by the Company from the IIA including accrued interest, net of royalties actually paid by the Company (see also Note 12).

c. On November 24, 2010, the Company signed an agreement with one of its shareholders, to purchase a patent for the production and sale of related products for the treatment of burns. In consideration for the transfer and assignment of all rights and title relating to the patent, the Company paid a one-time payment in the amount of $ 88 and undertook to pay annual fixed payments in the amount of $ 30 as long as the patent is valid in the US and/or in any EU member country. The patent expired in May 2018.

d. The Company has a contract with BARDA, which was modified in July 2017, for the advancement of the development and manufacturing, as well as the procurement of NexoBrid, as a medical countermeasure as part of BARDA preparedness for mass casualty events. The modified contract includes approximately $ 56,000 of funding to support development activities to complete the U.S. Food and Drug Administration (FDA) approval process for NexoBrid for use in thermal burn injuries, as well as approximately $ 16,500 for procurement of NexoBrid, which is contingent upon FDA Emergency Use Authorization (EUA) and/or FDA marketing authorization for NexoBrid. In addition, the contract includes options for further funding of up to approximately $ 10,000 for expanding NexoBrid's indications and of up to approximately $ 50,000 for additional procurement of NexoBrid.

As of December 31, 2018 the Company recorded accumulated $ 28,032 in funding from BARDA under this contract.

In September 2018, the Company has awarded additional contract with BARDA to develop NexoBrid for the treatment of Sulfur Mustard injuries as a medical countermeasure as part of BARDA preparedness for mass casualty events.

The contract provides approximately $ 12,000 of funding to support research and development activities up to pivotal studies in animals under the U.S. Food and Drug Administration (FDA) Animal Rule. The contract also contains options for additional funding of up to approximately $31,000 for additional development activities, animal pivotal studies, and the FDA Biologics License Application (BLA) submission for approval of NexoBrid for the treatment of Sulfur Mustard injuries

NOTE 15:- CONTINGENT LIABILITIES AND COMMITMENTS (Cont.)

As of December 31, 2018 the Company recorded accumulated $ 137 in funding from BARDA under this contract.

e. Contingent consideration for purchase of shares:

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 19a). 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 of 20% of the Company's revenues from the sale or license of NexoBrid up to a total amount of $ 30,600 and from the sale or license of the PolyHeal Product up to a total amount of $ 10,800. The obligation to pay Teva future royalty payments no longer includes amounts from the sale or license of the PolyHeal Product since the license to the PolyHeal Product has expired.

The total amortized cost of the future royalty obligation to Teva were initially accounted at their estimated fair value at the exercise date on September 2, 2013, using a discounted cash flow model based on sales projections. Subsequent changes in this liability are recorded in profit or loss within financial income of financial expenses.

Accordingly, the liability was remeasured to $ 14,381 and $ 14,460 as of December 31, 2017 and 2018, respectivaly, as a result of a revaluation in the amount of $ 351 and $ 758, in 2017 and 2018, respectivaly, which was recorded within financial expenses.

Pursuant to a Settlement Agreement with Teva entered in March 2019, the fair value of the revised future royalty obligation to Teva was estimated at $ 6,330 as of December 31, 2018 using a discounted cash flow model based on sales projections.

As a result of Teva Settlement Agreement, a one-time net income of $ 7,537 was recorded as other income from settlement agreement and a one-time income of $ 4,608 was recorded within the profit from discontinued operation in the fourth quarter and the year ending December 31, 2018 (see Note 23b).

f. In December 2010, the Company, Teva and PolyHeal, entered into a series of agreements to collaborate in the development, manufacturing and commercialization of PolyHeal's wound care product, or the PolyHeal Product (see also Note 19).

NOTE 15:- CONTINGENT LIABILITIES AND COMMITMENTS (Cont.)

On September 15, 2014, a Statement of Claim was filed against the Company by some shareholders of Polyheal (the "Plaintiffs"). The Plaintiffs allege that the Company is obligated to pay them a total amount of $1,475 in exchange for their respective portion of PolyHeal's shares, following the commencement of a feasibility study for the next generation of the PolyHeal Product in November 15, 2012, which constituted a milestone under a buyout option agreement between the Company, PolyHeal and its shareholders.

On November 12, 2017, the Tel Aviv District Court issued its ruling accepting the plaintiffs' claim and ruled that the Company is obligated to purchase PolyHeal's shares for approximately $6,750 plus applicable interest, which represents the purchase price for the total number of shares that the 2010 PolyHeal Agreements contemplate would be acquired by the Company from all the shareholders of PolyHeal. The Court ordered that the Company is obligated to purchase shares of PolyHeal from the plaintiffs, on the basis of their actual share holdings in PolyHeal as of January 15, 2013, for approximately $1,500, within 15 days from the date of the Court's ruling.

Accordingly, on Novemeber 12, 2017 a full provision for the shares purchase price plus the accrued interest, totaled $7,500 was recorded within the loss from discontinued operation in respect of this claim, of which approximately $1,497 was paid in December 2017 to plaintiffs in consideration for PolyHeal's shares. In addition, the Company born legal expenses totaled $116 for the year ended on December 31, 2017.

On December 27, 2017, the Company filed an appeal with the Israeli supreme court, in which it: (i) rejected the arguments raised against it in the Statement of Claim; (ii) emphasized that its obligation under the 2010 PolyHeal Agreement to purchase the 7.5% of PolyHeal's shares is subject to the consumption of the deferred closing, as defined in the buyout agreement, including the receipt of the funds from Teva on a "back to back" basis; and (iii) stated that since no such payment has been made by Teva, the Company is not subject to any obligation to purchase PolyHeal shares and/or make any payments to PolyHeal's shareholders.

In March 2019 the Company entered into a Settlement Agreement with the plaintiffs, which, contingent upon the Israeli Supreme Court's approval of the settlement agreement, will result in the acceptance of our appeal by the Supreme Court and the cancellation of the 2017 ruling that was issued by the District Court against MediWound (see also Note 23a).

g. Operating Lease Agreements:

1. The Company's offices and its production facility in Israel are located in a building that the Company leases from its Parent Company, 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 116,000 (approximately $31). This sub-lease agreement which was amended on January 1, 2019, expires in October 2022 and provides with 3 years extantion period at the sole discretion of the Company.

U.S. dollars in thousands (except of share and per share data)

NOTE 15:- CONTINGENT LIABILITIES AND COMMITMENTS (Cont.)

The Company's subsidiary offices are located in Germany. The monthly rent fee is currently €2,800 (approximately $3) and the lease agreement expires on April 30, 2022.

2. The Company and its subsidiary have operating lease agreements for 16 vehicles for a period of three years. As of December 31, 2018, the Company deposited $ 39 in respect of the vehicles operating leases.

3. Minimum future lease fees for both agreements as of December 31, 2018 are as follows:

2019	592
2020	476
2021	426
2022	330
	1,824

NOTE 16:- EQUITY

a. Share capital

	Year ended December 31,	
	2017	2018
Authorized number of shares	32,244,508	37,244,508
Issued and outstanding number of shares	27,047,737	27,178,839

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. In March 2014, the Company completed its IPO, and its securities are listed for trading on NASDAQ.

d. On September 21, 2017, the Company completed a follow-on public offering. A total of 4,400,000 new ordinary shares were issued in consideration to offering price of $5.00 per share. On September 29, 2017, the underwriters partially exercised their ‘green shoe’ option and purchased 637,664 additional ordinary shares. The net proceeds, including the underwriters' option, were $22,658, after deducting underwriter’s discounts, commissions and other offering expenses.

U.S. dollars in thousands (except of share and per share data)

NOTE 17:- SHARE-BASED COMPENSATION

a. Expense recognized in the financial statements:

The expenses that was recognized for services received from employees and directors is as follows:

	Year ended December 31,		
	2016	2017	2018
Cost of revenues	504	188	71
Research and development	752	488	181
Selling and marketing	765	204	63
General and administrative	1,150	483	330
Total share-based compensation	3,171	1,363	645

b. Share-based payment plan for employees and directors:

The Company has reserved for issuance stock options and restricted stock units ("RSUs") at total of 2,988,617 ordinary shares. As of December 31, 2018, 579,535 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 3-4 years.

U.S. dollars in thousands (except of share and per share data)

NOTE 17:- SHARE-BASED COMPENSATION (Cont.)

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

	2016		2017		2018	
	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	2,313,224	9.35	2,181,075	9.62	1,934,735	10.02
Option's Granted	47,500	8.56	40,000	6.72	665,000	5.12
Option's Exercised	(80,149)	0.09	(79,624)	0.09	(208,332)	2.63
Option's Forfeited	(99,500)	10.80	(206,716)	8.93	(78,154)	9.06
Outstanding options and at end of year	2,181,075	9.62	1,934,735	10.02	2,313,249	9.31
Option's Exercisable at end of year	1,401,866	9.35	1,562,235	10.25	1,475,451	11.23

The following table summarizes information about share options outstanding as of December 31, 2018:

	Options and outstanding as of December 31, 2018		
Range of exercise prices ($)	Number of options	Weighted Average Remaining contractual life	Weighted average exercise price
4.63 - 5.15	665,000	9.65	5.12
7.26 - 9.82	829,349	5.69	9.08
12.89 - 13.76	818,900	4.92	12.94
Total	2,313,249	6.56	9.31

The following table summarizes information about RSU's outstanding as of December 31, 2018:

	RSU's 2018
Outstanding at beginning of year	-
Granted	95,833
Forfeited	-
Vested	-
Outstanding at the end of the period	95,833
RSU's Exercisable at end of year	-

U.S. dollars in thousands (except of share and per share data)

NOTE 17:- SHARE-BASED COMPENSATION (Cont.)

The fair value of the options and RSU's granted to employees and directors at the grant date for the years ends December 31, 2016, 2017 and 2018 was $193, $172 and $1,650, respectively.

1. On June 9, 2016, the shareholders' general meeting of the Company approved to extend the exercise period of certain options previously granted to the CEO. The Fair Value of the extension of the Options, as of the modification date, was estimated at approximately $39.

2. On June 22, 2017, the Company's Board of Directors approved the grant of 40,000 options to purchase ordinary shares under the Plan, for an exercise price of $ 6.72 per share to certain new Board members of the Company. The fair value of the options granted, as of the grant date, was estimated at approximately $172.

3. On February 22, 2018, the general meeting of the Company approved to extend the exercise period of 208,332 options previously granted to CEO and in addition approved the grant of 40,000 options to purchase the Company's ordinary shares, for an exercise price of $ 4.63 per share, to certain of its directors. The fair value of the extended options was estimated at approximately $98 and the new options granted, as of the grant date, was estimated at approximately $76.

4. On June 27, 2018, a total of 208,332 options which were previously granted to the Company's CEO were exercised into 131,102 ordinary shares using cashless exercise mechanism.

5. On December 31, 2018, the Company's Board of Directors approved the grant of 625,000 options to purchase ordinary shares, for an exercise price of $ 5.15 per share, and the grant of 95,833 RSU's to its employees. The fair value of the options and RSU's granted, as of the grant date, was estimated at approximately $1,261 and $389, respectivaly.

d. The fair value of the Company's share options granted to employees and directors for the years ended December 31, 2016, 2017 and 2018 was estimated using the binomial option pricing models using the following assumptions:

	December 31,		
	2016	2017	2018
Dividend yield (%)	0	0	0
Expected volatility of the share prices (%)	72	63	44-54
Risk-free interest rate (%)	0.28-2.0	1.22-2.15	1.63-2.69
Early exercise factor (%)	100-150	150	100-150
Weighted average share prices (Dollar)	8.56	7.80	4.07

The expected share price volatility is based on the historical equity volatility of the share prices of comparable companies that are publicly traded, as there is no sufficient historical trading data for the Company.

NOTE 18:- TAXES ON INCOME

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 rates in Israel:

- The Israeli corporate income tax rate was 23% in 2018, 24% in 2017 and 25% in 2016.

  In December 2016, the Israeli Parliament approved the Economic Efficiency Law (Legislative Amendments for Applying the Economic Policy for the 2017 and 2018 Budget Years), which reduces the corporate income tax rate to 24% (instead of 25%) effective from January 1, 2017 and to 23% effective from January 1, 2018.

- Tax benefits under the Israel Law for the Encouragement of Capital Investments, 1959 (the "Investment Law"):

  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.

c. Corporate tax rate in Germany:

The statutory corporate tax rate in Germany was 29.79% in 2018, 30.53% in 2017 and 29.72% in 2016.

NOTE 18:- TAXES ON INCOME (Cont.)

d. Final tax assessments:

The Company has finalized its tax assessments through the 2012 tax year.

The Company's subsidiary has not received a final tax assessment since its incorporation.

e. Net operating carryforward losses for tax purposes and other temporary differences:

As of December 31, 2018, the Company had carryforward losses and other temporary differences mainly from R&D expenses together amounting to approximately $133,000.

f. Deferred taxes:

The Company did not recognize deferred tax assets for carryforward losses and other temporary differences because their utilization in the foreseeable future is not probable.

g. Current taxes on income:

The Company did not record any current taxes for the years ended December 31, 2016, 2017 and 2018 as a result of its carryforward losses.

h. 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 19:- DISCONTINUED OPERATION

a. In December 2010, the Company, Teva and PolyHeal, entered into a series of agreements to collaborate in the development, manufacturing and commercialization of PolyHeal's wound care product, or the PolyHeal Product ("2010 PolyHeal Agreement"). Under the 2010 PolyHeal Agreement, PolyHeal granted the Company an exclusive global license to manufacture, develop and commercialize all the Polyheal Products in consideration for royalty payments. Concurrently, the Company granted Teva an exclusive global sub license to commercialize the Polyheal Products in consideration for certain royalties and milestone payments. In addition, Teva undertook to finance the Company's future development of the Polyheal Product and all of its manufacturing costs. Under the 2010 PolyHeal Agreement, Teva initially invested $ 6,750 in the Company, and undertook to invest an additional $ 6,750 in the Company subject to the achievement of a development milestone. Concurrent with Teva's investment in the Company, the Company purchased shares of PolyHeal for total consideration of $ 6,750. Additionally, the Company undertook to purchase additional shares of PolyHeal for the same amount, subject to the achievement of the same abovementioned development milestone.

NOTE 19:- DISCONTINUED OPERATION (Cont.)

b. The Company has accounted this transaction as an acquisition of a group of assets since the assets acquired did not constitute a business as defined in IFRS 3. The Company allocated the consideration paid for the group of assets acquired based on their fair value to two identifiable assets: the license for the Polyheal Products in the amount of $ 6,333 and royalty rights arising from the Company's ownership of shares of PolyHeal in the amount of $ 417.

c. Following the termination of the Company's collaborations with Teva under the 2010 PolyHeal Agreement, the Company's exclusive license for the PolyHeal Product expired in September 2013. As a result of the expiration of the PolyHeal license, the Company accounted for the operation related to PolyHeal as a discontinued operation in accordance with IFRS accounting standard 5, "Non-current Assets Held for Sale and Discontinued Operations" and the Company has fully impaired the license for the PolyHeal Product.

d. On November 15, 2012, the Company informed Teva of the commencement of a feasibility study for the next generation of the PolyHeal Product, which constituted a milestone under the 2010 PolyHeal Agreement. In accordance with the terms of the agreement, Upon achievement of this milestone, Teva was to invest an additional $ 6,750 in exchange of the Company's ordinary shares and the Company was to purchase, following and pending the consummation of this investment, for an identical amount, ordinary shares of PolyHeal from its existing shareholders. The Company has not received the milestone investment from Teva.

On September 15, 2014, a Statement of Claim was filed against the Company by some shareholders of Polyheal and on November 12, 2017, the Tel Aviv District Court issued its ruling. During December 2017, the Company paid approximately $1,497 in consideration for PolyHeal's shares. Since the Company believes that the carrying amount of its royalty rights arising from the Company's ownership of shares of Polyheal would not be recoverable, a full impairment of these royalty rights is included within the loss from discontinued operation for the year ended December 31, 2017. In addition, the Company born legal expenses totaled $116 for the year ended December 31, 2017.

As of December 31, 2017, the Company 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 plus accrued interest. On December 27, 2017 the Company filed an appeal (see Note 15f).

In March 2019 the Company entered into a Settlement Agreement with the plaintiffs,which, contingent upon the Israeli Supreme Court's approval of the settlement agreement, will result in the acceptance of our appeal by the Supreme Court and the cancellation of the 2017 ruling that was issued by the District Court against MediWound (see also Note 23a).

As a result of a Settlement Agreement signed with the Teva in March 2019 (see also Note 23b), a one-time net income of $4,608 was recorded within the profit from discontinued operation in the fourth quarter and full year ending December 31, 2018.

U.S. dollars in thousands (except of share and per share data)

NOTE 20:- SUPPLEMENTARY INFORMATION TO THE STATEMENTS OF COMPREHENSIVE PROFIT OR LOST

a. Cost of revenues:

	Year ended December 31,		
	2016	2017	2018
Salary and benefits (including share-based compensation)	2,112	2,073	2,212
Subcontractors	66	121	72
Depreciation and amortization	475	457	474
Cost of materials	410	535	468
Other manufacturing expenses	892	989	783
Decrease (increase) in inventory of finished products	780	(999)	299
Allotment of manufacturing costs to R&D	(2,577)	(1,598)	(2,220)
	2,158	1,578	2,088

b. Research and development expenses, net of participations:

	Year ended December 31,		
	2016	2017	2018
Salary and benefits (including share-based compensation)	3,171	3,840	3,703
Subcontractors	8,517	8,780	11,423
Depreciation and amortization	28	42	51
Cost of materials	351	223	309
Allotment of manufacturing costs	2,577	1,598	2,220
Other research and development expenses	135	142	209
Research and development, gross	14,779	14,625	17,915
Participations:			
BARDA funds	(5,566)	(8,565)	(13,238)
Revaluation of liabilities in respect of IIA grants	(2,145)	(598)	(605)
	7,068	5,462	4,072

U.S. dollars in thousands (except of share and per share data)

NOTE 20:- SUPPLEMENTARY INFORMATION TO THE STATEMENTS OF COMPREHENSIVE INCOME (Cont.)

c. Selling and marketing expenses:

	Year ended December 31,		
	2016	2017	2018
Salary and benefits (including share based compensation)	5,438	3,062	2,343
Marketing and medical support	2,444	1,628	1,055
Depreciation and amortization	18	12	9
Shipping and delivery	111	236	192
Registration and marketing license fees	392	424	589
	8,403	5,362	4,188

d. General and administrative expenses:

	Year ended December 31,		
	2016	2017	2018
Salary and benefits (including share-based compensation)	2,361	2,032	2,035
Professional fees	1,241	1,224	1,361
Depreciation and amortization	66	56	43
Other	416	469	360
	4,084	3,781	3,799

e. Other expenses:

Other one-time expenses associated with the review of potential strategic transactions.

f. Financial income and expense:

	Year ended December 31,		
	2016	2017	2018
Financial income:			
Interest income	414	349	412
Revaluation of contingent consideration for the purchase of shares	1,621	-	-
Exchange differences, net	131	57	-
	2,166	406	412
Financial expense:			
Interest in respect of IIA grants	847	827	892
Revaluation of contingent consideration for the purchase of shares	-	351	758
Exchange differences, net	-	-	219
Finance expenses in respect of deferred revenue	-	-	164
Other	49	74	84
	896	1,252	2,117

U.S. dollars in thousands (except of share and per share data)

NOTE 21:- NET 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,					
	2016		2017		2018	
	Weighted average number of shares	Loss	Weighted average number of shares	Loss	Weighted average number of shares	Loss
Basic and diluted loss	21,862,169	(18,885)	23,341,040	(14,533)	27,113,617	(5,665)

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,					
	2016		2017		2018	
	Weighted average number of shares	Loss	Weighted average number of shares	Loss	Weighted average number of shares	Profit
Basic and diluted profit (loss)	-	-	23,341,040	(7,616)	27,113,617	4,608

c. Net profit (loss) per share from continuing and discontinued operations:

	Year ended December 31,		
	2016	2017	2018
Basic and Diluted loss per share:			
Net loss from continuing operations	(0.86)	(0.62)	(0.21)
Profit (loss) from discontinued operation	-	(0.33)	0.17
Net loss per share	(0.86)	(0.95)	(0.04)

U.S. dollars in thousands (except of share and per share data)

NOTE 22:- BALANCES AND TRANSACTIONS WITH RELATED PARTIES AND KEY OFFICERS

a. Related parties consist of:

- Clal Biotechnologies Industries Ltd.- Parent Company.
- Directors of the Company.
- CureTech Ltd.-Sister Company

b. Balances of related parties:

	Payables	Recievable
Parent Company (1):		
As of December 31, 2017	238	-
As of December 31, 2018	186	-
Other related parties:		
As of December 31, 2017	86	-
As of December 31, 2018	41	58

(1) The Company leases office space and a production facility from the Parent Company in accordance with a sublease agreement (see Note 15 (g)).

c. Transactions with related parties:

	Professional Fee (1)	Rent expenses and other
Parent company:		
2016	27	804
2017	35	817
2018	44	292
Other related parties:		
2016	159	-
2017	225	-
2018 (2)	162	(246)

(1) Professional fees do not include short-term employee benefits and share-based compensation to one of the Company's shareholders, who is a key officer, in the amounts of $420, $691 and $537 for the years 2016, 2017 and 2018, respectively, as well as payment for the purchasing of a patent in amount of $30, $30 and $12 for the years 2016, 2017 and 2018, respectively (see note 15c).

(2) Comprise of participation in building maintenance on amount of $246.

U.S. dollars in thousands (except of share and per share data)

NOTE 22:- BALANCES AND TRANSACTIONS WITH RELATED PARTIES AND KEY OFFICERS (Cont.)

d. Compensation of 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,		
	2016	2017	2018
Short-term employee benefits	2,108	2,324	2,304
Share-based compensation	1,445	731	276
	3,553	3,055	2,580
Number of officers	7	6	6

In December 2007, the Company's board of directors approved one-time bonus payments to the Chief Executive Officer and Chief Medical Officer in the amounts of $ 120 each, to be paid upon achieving marketing approval in the United States.

NOTE 23:- SUBSEQUENT EVENTS

a. On March 24, 2019, the Company entered into a settlement agreement and mutual general release with the Plaintiffs (the "Polyheal Settlement Agreement"), which settles any and all debts, obligations or liabilities that the Plaintiffs and MediWound had, has or may have to the other party in connection with the agreements among MediWound, Teva, PolyHeal, the Plaintiffs and other shareholders of PolyHeal.

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 contingent upon the Israeli Supreme Court approval of this Polyheal Settlement Agreement, it will result in the acceptance of the Company's appeal that was filed on December, 2017, and the cancellation of the 2017 Ruling that was issued by the District Court against MediWound. 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 USD 10 million, if a notice of such claim has been received by the Company prior to December 31, 2023.

b. On March 24, 2019, the Company entered into a settlement agreement and mutual general release with Teva (the “Teva Settlement Agreement”), which settles any and all debts, obligations or liabilities that each party or any of its controlled affiliates had or has to the other party or any of its controlled affiliates under, in connection with or arising out of certain transactions and agreements entered into between Teva and the Company from 2007 to 2012 (collectively, the “Collaboration Agreements”), which have terminated effective as of December 31, 2012 and September 2, 2013, as applicable, and which related to the Company's product, NexoBrid, and to PolyHeal Ltd. product, PolyHeal.

NOTE 23:- SUBSEQUENT EVENTS(Cont.)

During the recent years, the Company has been engaged in discussions with Teva regarding payments the Company believes Teva was obligated to make to the Company pursuant to these Collaboration Agreements.

Pursuant to the terms of the Teva Settlement Agreement, Teva has agreed to pay the Company $ 4,000 in cash, and to reduce the contingent consideration that is payable to Teva pursuant to the Company's repurchase of its shares from Teva in 2013, so that the Company will be 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.

As a result of Teva Settlement Agreement, a one-time net income from settlement agreement of $7,537 was recorded as other income and a one-time income of $4,608 was recorded within the profit from discontinued operation in the fourth quarter and the year ending December 31, 2018.

Exhibit 1.3

MediWound Ltd.

Second Amendment
to the Amended and Restated Articles of Association

Effective as of June 18, 2018

1. Capitalized terms not defined herein shall have the meaning ascribed to them in the Amended and Restated Articles of Association of MediWound Ltd. (the "Company"), which were adopted by the Company effective as of March 25, 2014 (the "Articles").

2. Article 6 of the Articles is hereby amended in its entirely to read as follows:

> "6. The authorized share capital of the Company is New Israeli Shekels 372,445.08 divided into 37,244,508 ordinary shares of 0.01 New Israeli Shekel (one Agora) nominal value each (**"Ordinary Shares"**)."

Exhibit 4.10

MediWound Ltd.

First Amendment
to the 2014 Equity Incentive Plan

Effective as of December 18, 2018

1. Capitalized terms not defined herein shall have the meaning ascribed to them in the 2014 Equity Incentive Plan of MediWound Ltd. (the "Company"), which were adopted by the Company effective as of March 9, 2014 (the "Plan").

2. Article 5 of the Plan is hereby amended in its entirely to read as follows:

> "5. The initial number of Shares reserved for the grant of Awards under the Plan, together with the number of Shares reserved for issuance under any share incentive plans previously adopted by the Company ("Prior Plans"), shall be 3,032,742 Shares, subject to adjustment due to certain changes as provided under the Plan. Subject to the provision at the end of this paragraph, The 'pool' of Shares reserved under the Plan will be automatically increased annually on each January 1 subsequent to the date of the adoption of the Plan, by a number of Shares equal to the lower of (i) 2% of the total number of outstanding shares of the Company as of immediately prior to such increase, (ii) 600,000 Shares, subject to adjustment due to certain changes as provided under the Plan, or (iii) a number of Shares determined by the Board to become reserved as of (or in lieu of) an upcoming January 1, if so determined prior to the January 1 on 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. All of the Shares reserved for issuance under the Plan may be issued pursuant to the exercise of Incentive Stock Options. The class of Shares shall be designated by the Board with respect to each Award and the notice of grant shall reflect such designation. Any Share underlying an Award granted hereunder or under a Prior Plan that has expired or was cancelled or terminated or forfeited for any reason without having been exercised shall be automatically, and without any further action on the part of the Company or any Grantee, returned to the "pool" of reserved Shares hereunder and shall again be available for grant for the purposes of the Plan (unless the Plan shall have been terminated) or unless the Board determines otherwise. Notwithstanding the other provisions of this Section 5, the Board may, subject to any other approvals required under any Applicable Law, increase or decrease the number of Shares to be reserved under the Plan. Such Shares may, in whole or in part, be authorized but unissued Shares, or Shares that shall have been or may be reacquired by the Company (to the extent permitted pursuant to the Companies Law) or by a trustee appointed by the Board under the relevant provisions of the Ordinance, the Companies Law or any equivalent provision of any other Applicable Law. Any Shares that are not subject to outstanding Awards at the termination of the Plan shall cease to be reserved for the purpose of the Plan, but until termination of the Plan, the Company shall at all times reserve a sufficient number of Shares to meet the requirements of the Plan."

Exhibit 4.17

Confidential Treatment Requested by Mediwound Ltd.

AWARD/CONTRACT	1. THIS CONTRACT IS A RATED ORDER UNDER DPAS (15 CFR 700)	RATING	PAGE OF PAGES 1 2
2. CONTRACT *(Proc. Inst. Ident.)* NO. HHSO100201800023C	3. EFFECTIVE DATE 09/30/2018	4. REQUISITION/PURCHASE REQUEST/PROJECT NO.	

5. ISSUED BY	CODE	ASPR-BARDA	6. ADMINISTERED BY *(If other than Item 5)*	CODE	ASPR-BARDA02
ASPR-BARDA 200 Independence Ave., S.W. Room 640–G Washington DC 20201			US DEPT OF HEALTH & HUMAN SERVICES ASST SEC OF PREPAREDNESS & RESPONSE ACQ MANAGEMENT, CONTRACTS, & GRANTS O'NEILL HOUSE OFFICE BUILDING Washington DC 20515		

7. NAME AND ADDRESS OF CONTRACTOR *(No., Street, City, Country, State and ZIP Code)*	8. DELIVERY FOB ORIGIN X OTHER *(See below)*
MEDIWOUND LTD 1477616 MEDIWOUND LTD 42 HAYARKON 42 HAYARKON YAVNE 00812	9. DISCOUNT FOR PROMPT PAYMENT

CODE 1477616	FACILITY CODE	10. SUBMIT INVOICES (4 copies unless otherwise specified) TO THE ADDRESS SHOWN IN	ITEM

11. SHIP TO/MARK FOR	CODE		12. PAYMENT WILL BE MADE BY	CODE	PSC
			PSC Program Support Center 7700 Wisconsin Ave Bethesda MD 20814		

13. AUTHORITY FOR USING OTHER THAN FULL AND OPEN COMPETITION: ☐10 U.S.C. 2304 (c) ( ) ☐41 U.S.C. 253 (c) ( )	14. ACCOUNTING AND APPROPRIATION DATA See Schedule

15A. ITEM NO	15B. SUPPLIES/SERVICES	15C. QUANTITY	15D. UNIT	15E. UNIT PRICE	15F. AMOUNT
	Continued				
			15G. TOTAL AMOUNT OF CONTRACT ▶		$11,942,818

16. TABLE OF CONTENTS

(X)	SEC.	DESCRIPTION	PAGE(S)	(X)	SEC.	DESCRIPTION	PAGE(S)
PART I - THE SCHEDULE				PART II - CONTRACT CLAUSES			
	A	SOLICITATION/CONTRACT FORM			I	CONTRACT CLAUSES	
	B	SUPPLIES OR SERVICES AND PRICES/COSTS		PART III - LIST OF DOCUMENTS, EXHIBITS AND OTHER ATTACH.			
	C	DESCRIPTION/SPECS./WORK STATEMENT			J	LIST OF ATTACHMENTS	
	D	PACKAGING AND MARKING		PART IV - REPRESENTATIONS AND INSTRUCTIONS			
	E	INSPECTION AND ACCEPTANCE			K	REPRESENTATIONS, CERTIFICATIONS AND OTHER STATEMENTS OF OFFERORS	
	F	DELIVERIES OR PERFORMANCE					
	G	CONTRACT ADMINISTRATION DATA			L	INSTRS., CONDS., AND NOTICES TO OFFERORS	
	H	SPECIAL CONTRACT REQUIREMENTS			M	EVALUATION FACTORS FOR AWARD	

CONTRACTING OFFICER WILL COMPLETE ITEM 17 (SEALED-BID OR NEGOTIATED PROCUREMENT) OR 18 (SEALED-BID PROCUREMENT) AS APPLICABLE

17. ☐CONTRACTOR' S NEGOTIATED AGREEMENT (*Contractor is required to sign this document and return_____copies to issuing office.)* Contractor agrees to furnish and deliver all items or perform all the services set forth or otherwise identified above and on any continuation sheets for the consideration stated herein. The rights and obligations of the parties to this contract shall be subject to and governed by the following documents: (a) this award/contract, (b) the solicitation, if any, and (c) such provisions, representations, certifications, and specifications, as are attached or incorporated by reference herein. *(Attachments are listed herein.)*

18. ☒ SEALED-BID AWARD (*Contractor is not required to sign this document.)* Your bid on Solicitation Number _____, including the additions or changes made by you which additions or changes are set forth in full above, is hereby accepted as to the items listed above and on any continuation sheets. This award consummates the contract which consists of the following documents: (a) the Government's solicitation and your bid, and (b) this award/contract. No further contractual document is necessary. (Block 18 should be checked only when awarding a sealed-bid contract.)

Confidential Treatment Requested by Mediwound Ltd.

19A. NAME AND TITLE OF SIGNER *(Type or print)*		20A. NAME OF CONTRACTING OFFICER JONATHAN F. GONZALEZ	
19B. NAME OF CONTRACTOR BY *(Signature of person authorized to sign)*	19C. DATE SIGNED	20B. UNITED STATES OF AMERICA BY *(Signature of the Contracting Officer)*	20C. DATE SIGNED

AUTHORIZED FOR LOCAL REPRODUCTION
Previous edition is NOT usable

STANDARD FORM 26 (Rev. 5/2011)
Prescribed by GSA - FAR (48 CFR) 53.214(a)

□ □

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

CONTRACT TABLE OF CONTENTS

PART I – THE SCHEDULE

SECTION B – SUPPLIES OR SERVICES AND PRICES/COSTS

B.1. BRIEF DESCRIPTION OF SUPPLIES OR SERVICES

The Pandemic and All Hazards Preparedness Act (PAHPA) of 2006 established the Biomedical Advanced Research and Development Authority (BARDA) and was reauthorized under the PAHPA of 2013 to support development and acquisition of medical countermeasure (MCMs) to prevent or treat the medical consequences of chemical, biological, radiological, and nuclear (CBRN) threats, pandemic influenza (PI), and emerging infectious diseases (EID). These MCMs include vaccines, therapeutics, diagnostics, and medical devices. Additionally, BARDA is entrusted to foster innovation of technologies that enable better manufacturing, testing, and utilization of these medical countermeasures.

This contract is for a potential 8-year product development plan to achieve the licensing of NexoBrid as a MCM for Sulfur Mustard (SM) injury. The existing BARDA MCM development program for NexoBrid for thermal burns has generated significant nonclinical and human clinical safety data. These data, as well as the manufacturing information for a currently approved human therapeutic commercial indication can be leveraged to obtain approval of the MCM indication for NexoBrid under the FDA Animal Rule.

MediWound considers NexoBrid as a proposed removal agent for tissue damaged by sulfur mustard which addresses unmet needs by being as effective as surgery, yet selective, non-invasive, and not pre-treatment diagnosis dependent. The use of NexoBrid resolves the first stage of wound bed preparation in the comprehensive wound care process. Additionally, NexoBrid facilitates the second stage of non-surgical or surgical wound closure by enabling earlier, direct visual assessment of the wound bed and by reducing surgical needs (e.g., extent of surgical excisional debridement) which is an integral, substantial, demanding part of the surgical wound closure process.

Work performed during the base period and during each option period constitutes an independent, non-severable discrete work segment that cannot be subdivided for separate performance and is necessary to support R&D tasks related to the development of the product/service. Each work segment constitutes an entire job (discrete requirement) which shall contain multiple R&D activities that when reviewed in total shall constitute a non-severable requirement. Each non-severable work segment will be fully funded from an appropriation source that is current at the time the work under such segment will begin.

The Government has determined a Bona Fide Need for each non-severable discrete work segment which will conclude upon the completion of a defined task or defined tasks that provide(s) independent merit and value to the Government. The Contractor's success in completing the required tasks under the work segments must be demonstrated through the Deliverables and Milestones specified under Article F of this contract. As set forth in the Contract WBS Milestones/Deliverables and Technical Deliverables chart under Article F of this contract, the GO/NO GO Contract Milestones and Decision Gates will constitute the basis for the Government's decision, at its sole discretion, to exercise any follow-on option period(s).

The base and option period segments under Contract Line Item (CLIN) 0001 are event driven work segments rather than time driven CLINs. The funds for each independent, non-severable discrete work segment (requirement), regardless of duration, shall only be used for the scope of work covered in each discrete work segment (i.e., the base period work segment and each option work segment). The periods of performance listed under each of the CLINs under Article B.2 and Article B.3 below are estimated time periods. Those individual time periods may be extended to complete the tasks required under each work segment. It is possible that more than one option period (requirement), may be awarded at one time and that individual CLINs may overlap and/or proceed concurrently.

B.2 BASE PERIOD

1. [***].

2. [***].

3. [***] $11,942,818. The Government will not be responsible for any contractor-incurred costs that exceed this amount unless a modification to the contract that expressly increases this amount is signed by the Contracting Officer.

4. The Contractor shall maintain records of all contract costs and such records shall be subject to FAR 52.215-2 (Oct 2010), Audit and Records – Negotiation, and Health and Human Services Acquisition Regulation (HHSAR) 352.242-74, Final Decisions on Audit Findings, incorporated by reference into the contract in SECTION I.

5. [***].

CLIN	Period of Performance	Supplies/Services	Estimated Cost	Fixed Fee	Estimated Total
0001	[***]	Select method of SM exposure for wound depth (mini-pig), Efficacy studies (mini-pig), and IND submission and regulatory support.	[***]	[***]	$11,942,818

6. The Government shall withhold payment of fee as necessary to protect the Government's interest as set forth in Federal Acquisition Regulation (FAR) 52.216-8 Fixed Fee (June 2011).

B.3. OPTION PERIODS

B.3.1 COST REIMBURSMENT OPTIONS

a. The contract includes optional, cost plus fixed-fee reimbursement CLINs 0002, 0003, 0004, and 0005. The Government may exercise Option Periods in accordance with FAR 52.217-9 Option to Extend the Term of the Contract (March 2000), as set forth in Section I of the contract.

b. Unless the government exercises its option pursuant to the option clause contained in ARTICLE I.2, the contract consists only of the Base Work segment specified in the Statement of Work as defined in SECTONS C and F, for the price set forth in ARTICLE B.2 of the contract.

c. The Government may modify the contract unilaterally and require the contractor to provide supplies and services for Option Periods listed below, in accordance with FAR 52.217-9.

d. If the Government decides to exercise an option(s), the Government will provide the Contractor a preliminary written notice of its intent as referenced in the clause. Specific information regarding the time frame for this notice is set forth in the OPTION CLAUSE Article in SECTION G of this contract. The estimated cost of the contract will be increased as set forth below:

Option	CLIN	Period of Performance	Supplies/Services	Estimated Cost	Fixed Fee	Estimated Total
1	0002	[***]	**Option 1 Period**: Mini-pig pivotal study and BLA Submission	[***]	[***]	[***]
2	0003	[***]	**Option 2 Period:** Hairless guinea pig POC Animal Study and regulatory support.	[***]	[***]	[***]
3	0004	[***]	**Option 3 Period:** Hairless Guinea Pig Pivotal Study and additional BLA update and regulatory support.	[***]	[***]	[***]
4	0005	[***]	**Option 4 Period:** [***]	[***]	[***]	[***]
		TOTALS	**Only option years**	[***]	[***]	[***]
		TOTALS	**Base + options**	[***]	[***]	[***]

B.4. LIMITATIONS APPLICABLE TO DIRECT COSTS

a. Items Unallowable Unless Otherwise Provided

Notwithstanding the clauses and unless authorized in writing by the Contracting Officer or set forth in the Statement of Work, the cost of the following items or activities shall be unallowable as direct costs:

1) Acquisition, by purchase or lease, of any interest in real property;

2) Special rearrangement or alteration of facilities;

3) Accountable Government Property (see the HHS Contracting Guide for Control for Government Property incorporated by Section G.10. of this contract);

   Note: this includes the lease or purchase of any item of general purpose office furniture or office equipment regardless of dollar value.

4) Purchase or lease of scientific instruments or equipment over $10,000 except for instruments and equipment specifically included in the Statement of Work;

5) Travel to attend general scientific meetings/conferences;

6) Printing Costs (as defined in the Government Printing and Binding Regulations);

7) Overtime (premium) compensation

8) Entering into certain types of subcontracting arrangements (See Section B.5(c) for specific obligations). Note that most consulting agreements require CO's written consent.

9) Foreign Travel (see Subparagraph b.3);

10) Patient care costs (see Section J-List of Attachments);

11) Light Refreshment and Meal Expenditures - Requests to use contract funds to provide light refreshments and/or meals to either federal or nonfederal employees must be submitted to the Contracting Officer's Representative (COR), with a copy to the Contracting Officer, at least six (6) weeks in advance of the event and are subject to "HHS Policy on Promoting Efficient Spending: Use of Appropriate Funding for Conferences and Meetings, Food and Promotional Items and Printing and Publications." The request shall contain the following information: (a) name, date, and location of the event at which the light refreshments and/or meals will be provide; (b) a brief description of the purpose of the event; (c) a cost breakdown of the estimated light refreshments and/or meals costs; (d) the number of nonfederal and federal attendees receiving light refreshments and/or meals; and (e) if the event will be held at a government facility.

b. Travel Costs

1) Total expenditures for travel (transportation, lodging, subsistence, and incidental expenses) incurred in direct performance of this contract during the Base Period (CLIN 0001) shall not exceed $39,995 without the prior written approval of the Contracting Officer. The Contractor shall notify the Contracting Officer in writing when travel expenditures have exceeded 80% of the base period travel expenses. Costs must be consistent with Federal Acquisition Regulations (FAR) 52.247-63 – Preference for U.S. Air Flag carriers.

2) Subject to the annual dollar limitation specified under B.4.b.1. above, the Contactor shall invoice and be reimbursed for all travel costs in accordance with Federal Acquisition Regulation (FAR) 31.2 – Contracts with Commercial Organizations, Sub-Section 31.205- 46, Travel Costs.

3) If foreign travel is necessary, a Contracting Officer Authorization (COA) will be required. Expenditures for foreign travel (transportation, lodging, subsistence, and incidental expenses) incurred in direct performance of this contract shall not exceed the amount specified in each approved COA, without the prior written approval of the Contracting Officer.

   Requests for foreign travel must be submitted at least four weeks in advance and shall contain the following:

   - Meeting(s) and place(s) to be visited, with costs and dates; name(s) and title(s) of Contractor personnel to travel and their functions in the contract project;
   - Contract purposes to be served by the travel;
   - How travel of Contractor personnel will benefit and contribute to accomplishing the contract project, or will otherwise justify the expenditure of BARDA contract funds;
   - How such advantages justify the costs for travel and absence from the project of more than one person if such are suggested; and
   - What additional functions may be performed by the travelers to accomplish other purposes of the contract and thus further benefit the project.

B.5. ADVANCE UNDERSTANDINGS

a. **Person-in-Plant**

With seven (7) days advance notice to the Contractor in writing from the Contracting Officer, the Government may place a man-in-plant in the Contractor's or Subcontractor's facility, who shall be subject to the Contractor's or Subcontractor's policies and procedures regarding security and facility access at all times while in the Contractor's or Subcontractor's facility. The Government's representative shall be provided reasonable access, during normal business hours, of the production areas being utilized in performance on the Contract. As determined by federal law, no Government representative shall publish, divulge, disclose, or make known in any manner, or to any extent not authorized by law, any information coming to him in the course of employment or official duties, while stationed in a contractor or subcontractor plant.

An article substantially similar to this Person-in-Plant article shall be incorporated into any subcontract for experimental or manufacturing work.

b. **Security**

No security plan is required at this point for this effort. It is anticipated that a security waiver will be approved.

c. **Subcontracts**

Prior written consent from the Contracting Officer in the form of Contracting Officer Authorization (COA) is required for any subcontract that:

- Is of the cost-reimbursement type and exceeds $150,000; or
- Is of the fixed price type and exceeds $150,000 or 5% of the contract, whichever is less.

The Contracting Officer shall request appropriate supporting documentation in order to review and determine authorization, pursuant with FAR Clause 52.244-2, Subcontracts. After receiving written consent of the subcontract by the Contracting Officer, the Contractor shall provide a copy of the signed, executed subcontract and consulting agreement to the Contracting Officer within ten (10) calendar days.

Note: Consulting services are treated as subcontracts and subject to the 'consent to subcontract' provisions set forth in this Section.

d. **Overtime Compensation**

No overtime (premium) compensation is authorized under the subject contract.

e. **Sharing of contract deliverables within United States Government (USG)**

In an effort to build a robust medical countermeasure pipeline through increased collaboration, the Government may share technical deliverables with Government entities responsible for Medical Countermeasure Development. In accordance with recommendations from the Public Health Emergency Medical Countermeasure Enterprise Review, agreements established in the Integrated Portfolio Advisory Committee (PAC) Charter, and agreements between BARDA and the Department of Defense, the National Institutes of Health, the Centers for Disease Control, and the Food and Drug Administration, BARDA may share technical deliverables and test results created in the performance of this Contract with colleagues within the Integrated Portfolio. This advance understanding does not authorize the Government to share financial information outside of the United States Government. The Contractor is advised to review the terms of FAR 52.227-14, Rights in Data – General, regarding the government's rights to deliverables submitted during performance as well as the government's rights to data contained within those deliverables.

f. **Approval of Human and Animal Protocols**

The Contractor shall submit all human and animal protocols and human informed consent documents as referenced under this Contract to the COR for review and approval **prior** to seeking other approvals (Institutional Review Board, Human Use Committee, Institutional Animal Care and Use Committee). The Government requires no fewer than eight (8) business days to perform a review. The Contractor shall take this review time into account and submit protocols as early as possible to avoid delays. The Government's comments and feedback shall be addressed prior to approval. The COR will review and provide approval of protocols. Human informed consents shall also be submitted and reviewed with any human protocol.

g. **Rights in Data**

The contract will incorporate the FAR Clause 52.227-14, Rights in Data—General. The Contractor is advised to review the terms of FAR 52.227-14, Rights in Data, regarding the government's rights to deliverables submitted during performance as well as the government's rights to data contained within those deliverables.

h. **Invoice Submission during end of Fiscal Year**

The government will not accept invoices for processing from Sep 6th through Oct 5th because of end of year fiscal requirements. Any invoices received from September 6th through October 5th will be canceled and returned to the Contractor for resubmission beginning on October 6th.

SECTION C - DESCRIPTION/SPECIFICATIONS/WORK STATEMENT

C.1. STATEMENT OF WORK

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 attached to this contract as Attachment 1 (Section J-List of Attachments).

C.2. REPORTING REQUIREMENTS

Refer to Section F.2 for specific instructions regarding Reporting Requirements.

C.3. PROJECT MEETING CONFERENCE CALLS

A conference call between the Contract Officer, the Contracting Officer's Representative (COR) and designees and the Contractor's Project Leader/delegate and designees shall occur bi-weekly or as otherwise mutually agreed upon by the Government and the Contractor or determined by the Contracting Officer. During this call the Contractor's Project Leader/delegate and designees will discuss the activities since the last call, any problems that have arisen and the activities planned until the next call takes place. The Contractor's Project Leader/delegate may choose to include other key personnel on the conference call to give detailed updates on specific projects or this may be requested by the Contracting Officer's Representative. Electronic copy of conference call meeting minutes/summaries shall be provided via e-mail to the CO, COR, and uploaded in eRoom by the Contractor within five (5) business days after the conference call is held.

C.4. PROJECT MEETINGS

The Contractor shall participate in Project Meetings to coordinate the performance of the contract, as requested by the COR. These meetings may include face-to-face meetings with BARDA and AMCG in Washington, D.C. and at work sites of the Contractor and its subcontractors. Such meetings may include, but are not limited to, meetings of the Contractor (and subcontractors invited by the Contractor) to discuss study designs, site visits to the Contractor's and subcontractor's facilities, and meetings with the Contractor and HHS officials to discuss the technical, regulatory, and ethical aspects of the program. The Contractor must provide data, reports, and presentations to groups of outside experts (subject to appropriate protections for Contractor confidential or proprietary data) and Government personnel as required by the COR in order to facilitate review of contract activities.

a. Kickoff Meeting

The Contractor and Government shall conduct a kickoff meeting within 45 calendar days after contract award to review HHS procedures, processes and expectations. Contractor shall provide an itinerary/agenda no later than 5 business days before meeting. Minutes from the kickoff meeting must be provided within 10 business days of the event.

b. Quarterly and Ad-Hoc Meetings

At the discretion of the CO or COR, the Contractor shall participate in Project Meetings to coordinate the performance of the contract, as requested by the Contracting Officer's Representative. These meetings may be conducted via teleconferences or face-to-face meetings in Washington, D.C. or at work sites of the Contractor and its subcontractors. Such meetings may include, but are not limited to, meetings of the Contractor (and subcontractors invited by the Contractor) to discuss study designs, site visits to the Contractor's and subcontractor's facilities, and meetings with the Contractor and HHS officials to discuss the technical, regulatory, and ethical aspects of the program. The Contractor must provide data, reports, and presentations to groups of outside experts (subject to appropriate protections for Contractor's confidential or proprietary data) and Government personnel as required by the Contracting Officer's Representative, giving reasonable prior notice of such requirement to Contractor, in order to facilitate review of contract activities.

Contractor shall provide itinerary/agenda at least 5 business days in advance of face-to-face meeting.

c. Face-to-Face Project Review Meetings

The Contractor shall, at a time to be determined later, present a comprehensive review of contract progress to date annually in a face-to-face meeting in Washington, DC. The Contractor will be responsible for updating the BARDA program on technical progress under the Statement of Work. Presentation must be delivered seven (7) business days prior to the scheduled meeting.

C.5 RISK MANAGEMENT

The Contractor shall establish and maintain an active, enterprise-wide risk management system as well as a specific risk management plan that includes the SOPs governing risk management, a description of the risk management activities required to oversee the project across its range of scope, and the processes for reviewing completed risk mitigations. The Contractor shall complete risk management documentation for the program as applicable, such as:

1. Preliminary hazard analyses as necessary for each product component
2. Design, user, and process FMEA plans
3. Risk control plans to verify the proposed mitigations

C.6 REGULATORY ACTIVITIES

The Contractor shall submit to the COR for review and acceptance, pre-submission documents and all proposed regulatory filing documents.

The Contractor shall provide the COR the opportunity to review and comment upon any draft documents, including draft pre-submission packages, and meeting requests, to be submitted to the FDA or other regulatory agency. The Contractor shall provide the COR with five (5) business days for review and comments. An acceptable version shall be provided to the COR prior to FDA submission.

The Contractor shall provide the COR initial draft minutes and final draft minutes of any - meeting with the FDA and other regulatory agencies.

The Contractor shall communicate the dates and times of any meeting with the FDA and other regulatory agencies to the COR and ensure participation for appropriate COR and BARDA SMEs staff to attend the meetings.

The Contractor shall forward Standard Operating Procedures (SOPs) upon request from Contracting Officer's Representative /Contracting Officer.

The Contractor shall support FDA audits. Within thirty (30) calendar days of an FDA audit of Contractor or subcontractor facilities, the Contractor shall provide copies of the audit findings, final report, and a plan for addressing areas of nonconformance to FDA regulations and guidance for GLP, GMP or GCP guidelines as identified in the final audit report.

C.7 QUALITY

The Contractor shall establish and maintain a Quality Management System with sufficient content to include but not limited to the elements contained in the Code of Federal Regulations Title 21 Part 820.

The Contractor shall establish routine internal reviews, documentation, and evidence of the ability to maintain, and adhere to the Code of Federal Regulations Title 21 Part 820.

The Contractor shall contract for an independent audit of its system quality system adherence, resolve any issues noted by the auditor, and provide the audit findings and resolutions to the Government.

SECTION D – PACKAGING, MARKING, AND SHIPPING

All deliverables required under this contract shall be packaged, marked and shipped in accordance with Government specifications and Section F. At a minimum, all deliverables shall be marked with the contract number and Contractor name. The Contractor shall guarantee that all required materials shall be delivered in immediate usable and acceptable condition

Unless otherwise specified by the CO, delivery of reports to be furnished to the Government under this contract (including invoices) shall be delivered to the CO and COR electronically along with a concurrent email notification to the CO and COR (as defined in Section F.3. Electronic Submission) summarizing the electronic delivery.

SECTION E – INSPECTION AND ACCEPTANCE

E.1. FAR 52.252-2, CLAUSES INCORPORATED BY REFERENCE (FEBRUARY 1998)

This contract incorporates the following clauses by reference, with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available. Also, the full text of a clause may be accessed electronically at these addresses: https://www.acquisition.gov/FAR/ . HHSAR Clauses at: http://www.hhs.gov/policies/hhsar/subpart352.html.

FAR Clause **Title and Date**

FAR 52.246-3, Inspection of Supplies – Cost-Reimbursement (May 2001)
FAR 52.246-5, Inspection of Services - Cost-Reimbursement (April 1984)
FAR 52.246-8, Inspection of Research and Development – Cost Reimbursement (May 2001)
FAR 52.246-9, Inspection of Research and Development (Short Form) (April 1984)
FAR 52.246-16, Responsibility for Supplies (April 1984)

E.2. DESIGNATION OF GOVERNMENT PERSONNEL

For the purpose of this Section E, the designated Contracting Officer's Representative (COR) is the authorized representative of the Contracting Officer. The COR will assist in resolving technical issues that arise during performance. The COR however is not authorized to change any contract terms or authorize any changes in the Statement of Work or modify or extend the period of performance, or authorize reimbursement of any costs incurred during performance.

E.3. INSPECTION, ACCEPTANCE AND CONTRACT MONITORING

Inspection and acceptance of the product, services, and documentation called for herein shall be accomplished by the Contracting Officer or a duly authorized representative. Delivery, technical inspection and acceptance will be take place at a location designated by the Contracting Officer or at:

Office of the Assistant Secretary for Preparedness and Response
Biomedical Advanced Research and Development Authority
O'Neill House Office Building
Washington, DC 20515

a. **Site Visits and Inspections**

At the discretion of the Government and independent of activities conducted by the Contractor, with 48 hours' notice to the Contractor, the Government reserves the right to conduct site visits and inspections related to this Contract on an as needed basis during normal business hours, including collection of product samples and intermediates held at the location of the Contractor, or its subcontractor. All costs reasonably incurred by the Contractor and subcontractor for such visit and/or inspection shall be allowable costs subject to the Allowable cost requirements in FAR Subpart 31.2. The Contractor shall coordinate these visits and shall have the opportunity to accompany the Government on any such visits. Under time-sensitive or critical situations, the Government reserves the right to suspend the 48 hour notice to the Contractor. The areas included under the site visit could include, but are not limited to: security, regulatory and quality systems, manufacturing processes and cGMP/GLP/GCP compliance related to activities funded under this Contract.

If the Government, Contractor, or other party identifies any issues during an audit, the Contractor shall capture the issues, identify potential solutions, and provide a report to the Government for review and acceptance:

- If issues are identified during the audit, the Contractor shall submit a report to the CO and COR within five (5) business days detailing the finding and corrective action(s) of the audit.
- COR and CO will review the report and provide a response to the Contractor within ten (10) business days.
- Once corrective action is completed, the Contractor will provide a final report to the CO and COR.

SECTION F – DELIVERIES OR PERFORMANCE

F.1. ESTIMATED PERIOD OF PERFORMANCE

The estimated period of performance for this contract shall be consistent with the dates set forth in the Base Period in Section B.2. If the Government exercises the Options Period(s) pursuant to the Option Clause in Section I.3 of the contract, the period of performance shall be increased as shown in the table in Section B.3.

F.2. DELIVERABLES

Successful performance of the final contract shall be deemed to occur upon completion of performance of the work set forth in the Statement of Work dated 02 September 2018, set forth in Section J - List of Attachments of this contract and upon delivery and acceptance, as required by the Statement of Work, by the COR, of each of the deliverables described in Section C, Section F, and Section J.

All deliverables and reporting documents listed within this Section shall be delivered electronically (as defined in Section F.3 Electronic Submission) to the CO, CS, and the COR unless otherwise specified by the CO.

Unless otherwise specified by the CO, the deliverables identified in this Section F shall also be delivered electronically to the designated eRoom along with a concurrent email notification sent to the CO, CS, COR, and Alternate COR stating delivery has been made.

All paper/hardcopy documents/reports submitted under this contract shall be printed or copied, double-sided, on at least 30 percent post-consumer fiber paper, whenever practicable, in accordance with FAR 4.302(b). Hard copies of deliverables and reports furnished to the Government under the resultant Contract (including invoices) shall be addressed as follows:

HHS/ASPR/AMCG:

ATTN: Jonathan Gonzalez (Contracting Officer)
U.S. Department of Health & Human Services
Office of the Assistant Secretary for Preparedness and Response
Office of Acquisition Management, Contracts, and Grants (AMCG)
O'Neill House Office Building
Room Number: 22J12
Washington, DC 20515
Email: Jonathan.Gonzalez@hhs.gov

HHS/ASPR/BARDA:

ATTN: Efrain E Garcia, Ph.D. (COR)
U.S. Department of Health & Human Services
Office of the Assistant Secretary for Preparedness and Response
Biomedical Advanced Research & Development Authority (BARDA)
O'Neill House Office Building
Room Number: 24E25
Washington, DC 20515
Email: Efrain,garcia@hhs.gov

Contract Data Requirements List (CDRLs)

CDRL#	Deliverable	Description	Reporting Procedures and Due Dates
01	Kickoff Meeting	The Contractor shall complete a Kickoff meeting after contract award	● Within 45 calendar days after contract award. ● Materials: Contractor shall provide itinerary and agenda to CO and COR at least 5 business days in advance of meeting. CO approves and the COR distributes itinerary and agenda within 3 business days. ● Due out: Contractor provides meeting minutes to CO and COR within 5 business days after the meeting. The CO and COR reviews, comments, and the CO approves minutes within 10 business days of the event.
02	Quarterly Meetings	At the discretion of the government the Contractor shall hold recurring teleconference or face-to-face Project Review Meetings up to four per year either in Washington D.C or at work sites of the Contractor or subcontractors. Face-to-face meetings shall alternate between Washington DC and Contractor, sub-contractor sites. The meetings will be used to discuss contract progress in relation to the Program Management deliverables described below as well as study designs, technical, regulatory, and ethical aspects of the program.	● Materials: Contractor shall provide itinerary and agenda to CO and COR at least 5 business days in advance of site visit. The COR approves and distributes itinerary and agenda within 3 business days. ● Due out: Contractor provides meeting minutes to the CO and the COR within 5 business days after the meeting. The CO and COR reviews, comments, and the CO approves minutes within 10 business days.
03	Biweekly Teleconference Meetings	The Contractor shall participate in teleconferences every two weeks with the CO and the COR to discuss the performance of the contract.	● Materials: Contractor provides agenda to the CO and COR no later than 2 business days in advance of meeting. The COR approves and distributes agenda prior to meeting. ● Due out: Contractor provides meeting minutes to the CO and COR within 5 business days following the meeting. The CO and COR reviews, comments, and the COR approves minutes within 10 business days following the meeting.

CDRL#	Deliverable	Description	Reporting Procedures and Due Dates
04 (Monthly) 05 (Annual)	Monthly & Annual Technical Progress Reports	The Monthly and Annual Technical Progress report shall address each of the below items and be cross-referenced to the Work Breakdown Structure (WBS), Statement of Work (SOW), Integrated Master Schedule (IMS), and Contract Performance Report (CPR). 1. An Executive Summary highlighting the progress, issues and relevant manufacturing, non-clinical, clinical and regulatory activities. The Executive Summary should highlight only critical issues for that reporting period and resolution approach; limited to 2-3 pages. 2. Progress in meeting contract milestones – broken out by subtasks within each milestone, overall project assessment, problems encountered and recommended solutions. The reports shall detail the planned and actual progress during the period covered, explaining occurrences of any differences between the two and the corrective steps. 3. The reports shall also include a three-month rolling forecast of the key planned activities, referencing the WBS/IMS. 4. A tracking log of progress on regulatory submissions with the FDA number, description of submission, date of submission, status of submission and next steps. 5. Estimated and Actual Expenses. 6. This report shall also contain a narrative or table detailing whether there is a significant discrepancy (>10%) at this time between the % of work completed and the cumulative costs incurred to date. Monthly and actual expenses should be broken down to the appropriate WBS level. This section of the report should also contain estimates for the Subcontractors' expenses from the previous month if the Subcontractor did not submit a bill in the previous month. If the subcontractor(s) was not working or did not incur any costs in the previous month, then a statement to this effect should be included in this report for those respective subcontractors.	● Due: Monthly Reports shall be submitted on the 25th day of the month after the end of each month with an Annual Report submitted on the 30th calendar day of the final month of each contract year for the previous twelve calendar months. ● When the 25th or 30th falls on a weekend or a US Holiday, the reports will be due the next business day. ● Monthly progress reports are not required for the periods when the Annual Report(s) and Final Report are due. The CO and the COR will review the monthly reports and provide feedback within 5 business days of receiving the report. The CO approves acceptance of monthly and annual reports.

CDRL#	Deliverable	Description	Reporting Procedures and Due Dates
06	Risk Management Plan	The Contractor shall provide a Risk Management Plan that outlines the impacts of each risk in relation to the cost, schedule, and performance objectives. The plan shall include risk mitigation strategies. Each risk mitigation strategy will capture how the corrective action will reduce impacts on cost, schedule and performance.	● Due: Within 90 days of contract award. ● Due out: Contractor provides updated Risk Management Plan in Monthly Progress Report. The COR shall provide Contractor with written comments in response submitted plan. Contractor must address, in writing, all commercially reasonable concerns raised by the COR within 20 business days of Contractor's receipt of COR's concerns for CO approval.
07	Deviation Notification and Mitigation Strategy	Process for changing IMS activities associated with cost and schedule as baselined at the PMBR. Contractor shall notify BARDA of significant changes the IMS defined as increases in cost above 5% or schedule slippage of more than 30 days, which would require a PoP extension. Contractor shall provide a high-level management strategy for risk mitigation.	● Due: As needed.
08	Go/No-Go Decision Gate Presentation	Contractor shall provide a presentation detailing technical progress made towards completion of Go/No-Go decision gate milestones following a prescribed template provided by BARDA prior to the In-Process Review (IPR).	● Materials: Contractor shall provide presentation materials to the CO and COR 10 business days prior to the IPR. Contractor shall submit written justification of progress towards satisfying Go/No-Go criteria. After reviewing, the CO and COR will provide a written response within 10 business days.
09	Incident Report	Contractor shall communicate and document all critical programmatic concerns, risks, or potential risks with the CO and COR.	● Due: Within 48 hours of activity or incident or within 24 hours for a security activity or incident via email or telephone, with written follow-up to the CO and COR. Additional updates due within 48 hours of additional developments. ● Due out: Contractor shall submit, within 5 business days, a Corrective Action Plan (if deemed necessary by either party) to address any potential issues. If corrective action is deemed necessary, Contractor must address in writing, its consideration of concerns raised by the CO, within 5 business days of receiving such concerns in writing.

CDRL#	Deliverable	Description	Reporting Procedures and Due Dates
10	Draft and Final Reports for Clinical,Non-Clinical, and Human Factors Studies (if applicable)	Contractor shall provide Draft and Final Clinical/Non-Clinical and Human Factors Study Reports to the CO and COR for review and comment.	● Draft - within 45 calendar days after completion of analysis and at least 15 business days prior to submission to FDA. Subcontractor prepared reports received by the Contractor shall be submitted to the CO and COR for review and comment no later than 5 business days after receipt by Contractor. The CO shall provide written comments to the Draft Final Report for Clinical and Non-Clinical Studies within 15 business days after the submission. ● Final - due 30 calendar days after receiving comments on the Draft Final Report for Clinical and Non-Clinical Studies. If corrective action is recommended, Contractor must address, in writing, all reasonable concerns raised by the CO in writing. Contractor shall consider revising reports to address CO's recommendations prior to FDA submission. ● Final FDA submissions shall be provided to the CO and COR concurrently or no later than 5 business days after submission to the FDA.
11	Standard Operating Procedures	The Contractor shall make internal and, to the extent possible, subcontractor Standard Operating Procedures (SOPs) available for review electronically.	Upon request from the CO.
12	FDA Correspondence	The Contractor shall memorialize any correspondence between Contractor and FDA and submit to the CO and COR. All documents shall be duly marked as either "Draft" or "Final".	● Due: Contractor shall provide written summary of any FDA correspondence within 5 business days of correspondence.

CDRL#	Deliverable	Description	Reporting Procedures and Due Dates
13	FDA Meetings	The Contractor shall forward the dates and times of any meeting with the FDA to the CO and COR and make arrangements for appropriate Government staff to attend the FDA meetings. Government staff shall include up to a maximum of four people (COR, CO and up to 2 subject matter experts).	● Contractor shall schedule upcoming FDA meetings, so at a minimum the CO, COR, and RQA persons from BARDA can attend. Additionally, a pre-meeting needs to be held with BARDA to review slides and discuss meeting strategies. ● Contractor shall notify the CO and COR of upcoming FDA meeting within 24 hours of scheduling. ● The Contractor shall forward initial Contractor and FDA-issued draft minutes and final minutes of any meeting with the FDA to the CO and COR within 5 business days of receipt. All documents shall be duly marked as either "Draft" or "Final".
14	FDA Submissions	The Contractor shall provide the CO and COR the opportunity to review and comment upon all draft submissions before submission to the FDA. Contractor shall provide the CO and COR with an electronic copy of the final FDA submission. All documents shall be duly marked as either "Draft" or "Final".	● Due: Contractor shall submit draft FDA submissions to the CO and COR at least 15 business days prior to FDA submission. The CO and COR will provide feedback to Contractor within 10 business days of receipt. ● Due out: If corrective action is recommended, the Contractor must address, in writing, its consideration of all concerns raised by the CO. ● The Contractor shall consider revising their documents to address CO's concerns and/or recommendations prior to FDA submission. ● Final FDA submissions shall be submitted to the CO and COR concurrently or no later than 5 calendar day of its submission to CDER.
15	FDA Audits	In the event of an FDA inspection which occurs as a result of this contract and for the product, or for any other FDA inspection that has the reasonable potential to impact the performance of this contract, the Contractor shall provide the Government with an exact copy (non-redacted) of the FDA Form 483 and the Establishment Inspection Report (EIR). The Contractor shall provide the COR and CO with copies of the plan for addressing areas of non-conformance to FDA regulations for GLP, GMP, or GCP guidelines as identified in the audit report, status updates during the plans execution and a copy of all final responses to the FDA. The Contractor shall also provide redacted copies of any FDA audits received from subcontractors that occur as a result of this contract or for this product. The Contractor shall make arrangements for BARDA representative(s) to be present during the final debrief by the regulatory inspector.	● Contractor shall notify the CO and COR within 10 business days of a scheduled FDA audit or within 24 hours of an ad hoc site visit/audit if the FDA does not provide advanced notice. ● Contractor shall provide copies of any FDA audit report received from subcontractors that occur as a result of this contract or for this product within 5 business days of receiving correspondence from the FDA or third party. ● Within 10 business days of audit report, Contractor shall provide CO with a plan for addressing areas of nonconformance, if any are identified.

CDRL#	Deliverable	Description	Reporting Procedures and Due Dates
16	QA Audit Reports	The COR reserves the right to participate in QA audits. Upon completion of the audit/site visit the Contractor shall provide a report capturing the findings, results and next steps in proceeding with the subcontractor. If action is requested of the subcontractor, detailed concerns for addressing areas of non-conformance to FDA regulations for GLP, GMP, or GCP guidelines, as identified in the audit report, must be provided to the CO and COR. The Contractor shall provide responses from the subcontractors to address these concerns and plans for corrective action execution.	● Contractor shall notify the CO and COR 10 days in advance of upcoming, ongoing, or recent audits/site visits of subcontractors as part of weekly communications. ● Contractor shall notify the CO and COR within 5 business days of report completion.
17	BARDA Audit	Contractor shall accommodate periodic or ad hoc site visits by the CO and COR. If the CO, COR, Contractor, or other parties identifies any issues during an audit, the Contractor shall capture the issues, identify potential solutions, and provide a report to the CO and COR.	● If issues are identified during the audit, Contractor shall submit a report to the CO and COR detailing the finding and corrective action(s) within 10 business days of the audit. ● Due out: The CO and COR will review the report and provide a response to the Contractor with 10 business days. Once corrective action is completed, the Contractor will provide a final report to the CO and COR.
18	Technical Documents	Upon request, Contractor shall provide CO and COR with deliverables from the following contract funded activities: process Development Reports, Assay Qualification Plan/Report, Assay Validation Plan/Report, Assay Technology Transfer Report, Batch Records, SOPs, Master Production Records, Certificate of Analysis, Clinical Studies Data or Reports. The CO and COR reserve the right to request within the PoP a non-proprietary technical document for distribution within the Government.	● Contractor shall provide technical document within 10 business days of COR's request. Contractor can request additional time on an as needed basis. ● If corrective action is recommended by the COR, the Contractor must address, in writing, concerns raised by the COR to the COR and CO in writing.

CDRL#	Deliverable	Description	Reporting Procedures and Due Dates
19	Raw Data or Data Analysis	Contractor shall provide raw data or data analysis to the CO and COR upon request.	● Contractor shall provide data or data analysis to the CO and COR within 20 business days of request.
20	Publications	Any manuscript or scientific meeting abstract containing data generated under this contract must be submitted to the CO and COR for review prior to submission.	● Contractor must submit all manuscript or scientific meeting abstract to the CO and COR within 30 days for manuscripts and 15 days for abstracts. ● Contractor must address in writing all concerns raised by the CO and COR in writing. ● Final submissions shall be submitted to the CO and COR concurrently or no later than five (5) calendar days after its submission.
21	Press Releases	Contractor agrees to accurately and factually represent the work conducted under this contract in all press releases.	● With the exception of ad-hoc press releases required by applicable law or regulations, Contractor shall ensure that the CO and COR has received and approved an advanced copy of any draft press release to this contract not less than 2 business days prior to the issuance of the press release. The CO shall reply with comments within 1 business day of receipt of the draft press release. Should no comments be forthcoming from the CO by end of the 1st business day, Contractor will be permitted to issue the press release ● If corrective action is required, the Contractor agrees to accurately and factually represent the work conducted under this contract in all press releases. ● Any final press releases shall be submitted to the CO and COR no later than 1 (one) calendar day prior to its release.
22	Integrated Master Schedule (IMS)	The Contractor shall provide an IMS including WBS, critical path milestones, and Earned Value Management Plan.	● Due: Contractor shall provide the draft IMS within 90 days of contract award with final due 8 months after award and updated monthly as part of the Monthly Progress Report. ● Contractor must address, in writing, all concerns raised by the COR in writing and provide response to the CO and COR.

CDRL#	Deliverable	Description	Reporting Procedures and Due Dates
23	Draft and Final Technical Progress Report	A Draft Final Technical Progress Report containing a summation of the work performed and the results obtained for the entire contract PoP. The draft report shall be duly marked as 'Draft'. The Final Technical Progress Report incorporating feedback received from the CO and COR and containing a summation of the work performed and the results obtained for the entire contract PoP. The final report shall document the results of the entire contract. This report shall be in sufficient detail to fully describe the progress achieved under all milestones. The final report shall be duly marked as 'Final'.	● Due: Contractor shall provide a draft Technical Progress Report 75 calendar days before the end of the PoP and the Final Technical Progress Report on or before the completion date of the PoP. ● Subcontractor prepared reports received by the Contractor shall be submitted to the CO and COR for review and comment no later than 5 business days after receipt by the Contractor. ● Due out: the CO shall provide feedback on draft report within 15 calendar days of receipt, which the Contractor shall consider incorporating into the Final Report. ● Contractor shall submit, with the Final Technical Progress Report, a summary (not to exceed 200 words) of salient results achieved during the performance of the contract.
24	Draft and Final Study Protocols	Contractor shall provide all Draft and Final Study Protocols to the COR for evaluation. (The CO and COR reserves the right to request within the period of performance a non-proprietary Study Protocol for distribution within the Government	● The Contractor will submit all proposed protocols to the CO and COR at least 10 business days prior to study start. If corrective action is required, the Contractor must address in writing all concerns raised by the CO and COR to the satisfaction of the COR before study execution and provide the CO and COR a revised draft protocol that addresses the CO's comments and requested changes. ● After receiving the revised Study Protocol that satisfies the COR, the CO will approve the revised Study Protocol and will provide a written approval to the Contractor that provides authorization to the Contractor to execute the specific study. ● Contractor shall not proceed with any study protocol until the COR gives its approval and the Contractor has provided the CO and COR with a final and approved Study Protocol.

CDRL#	Deliverable	Description	Reporting Procedures and Due Dates
25	Clinical Study Status Update (if applicable)	Contractor shall provide COR with a status update of clinical studies that are actively enrolling patients to include by study site: cumulative enrollment; new enrollments; screen failures; patients dropped from study; AE and SAEs; activation or inactivation of study sites; investigator appointments or changes; and status of IRB/IEC review/approval/renewal. Contractor will provide proposed format for the COR's review and approval.	● Update will be submitted by e-mail or other electronic format to be provided by the COR by the end of the 25th business day of each new month. ● When the 25th falls on a weekend or US Holiday, the update will be due the next business day. ● Updates, to the extent they are available, will be presented during biweekly teleconferences. ● If no changes have occurred since the prior update only a simple statement that there is no new data is required.

NOTE: Pursuant to the Trade Secrets Act, 18 U.S.C. § 1905, no Government personnel shall publish or, disclose to any non-Government entity any Contractor data marked according to FAR 52.227-14 that qualifies as trade secrets or other confidential information unless permitted to do so by law or regulation.

GO/NO GO Milestones and Technical Deliverables

Milestone	Go Criteria	No-Go Criteria	WBS #	Due Date
Initiate Option 1 CLIN 0002: (Pivotal efficacy studies in mini pigs and BLA submission)				
POC Efficacy Study: Mini-Pig (Gottingen)	Efficacy demonstrated in POC studies in minipigs.	Efficacy was not demonstrated in POC studies in minipigs.	1.3.2.4	[***]
End of Phase 2 Meeting with FDA	FDA accepts minipigs as valid model for Animal Rule approval.	FDA does not accept minipigs as valid model for Animal Rule approval.	1.5.1.4	[***]
Initiate Option 2 CLIN 0003: (Proof of Concept Studies in Hairless Guinea Pig Model (POC))				
POC Efficacy Study: Mini-Pig (Gottingen)	Efficacy demonstrated in POC studies in minipigs.	Efficacy was not demonstrated in POC studies in minipigs.	1.3.2.4	[***]
End of Phase 2 Meeting with FDA	FDA requires the hairless guinea pig model in addition to the minipig model.	FDA does not require an extra model.	1.5.1.4	[***]
Initiate Option 3 CLIN 0004: (Pivotal Efficacy Study in Hairless guinea pig, BLA Submission update).				
POC Efficacy Study: Hairless guinea pig	Efficacy demonstrated in hairless guinea pig model.	Failure to demonstrate efficacy in the hairless guinea pig model.	3.3.2.3	[***]
Initiate Option 4 CLIN 0005: ([***])				
[***]	[***]	Failure to demonstrate efficacy in minipigs	1.3.2.1	[***]
[***]	[***]	Failure to demonstrate efficacy in minipigs	1.3.2.2	[***]

CLIN / Deliverable	Deliverable	Due Date
CLIN 0001	**Base Period**	**[***]**
1	Integrated Product Development Plan (IPDP)	[***]
2	Base Period Subcontractor Management Plan	[***]
3	Risk mitigation plan	[***]
4	EVMS implementation plan and first monthly report	[***]
5	[***]	[***]
6	[***]	[***]
7	PIND and other RA Meetings/ requests for review at each development milestone.	[***]
8	Bioanalytical Methods Development: Mini-Pig (Gottingen)	[***]
9	IND preparation and submission	[***]
10	[***]	[***]
11	PK Studies: Mini-Pig (Gottingen)	[***]
12	[***]	[***]
13	[***]	[***]
14	[***]	[***]
15	POC Efficacy Study: Mini-Pig (Gottingen)	[***]
16	End of Phase 2 Meeting	[***]
CLIN 0002	**Option One**	**[***]**
1	Pre-BLA gap analysis by SMEs.	[***]
2	[***]	[***]
3	[***]	[***]
4	Pivotal Efficacy Studies: Mini-Pig (Gottingen)	[***]
5	Pre-BLA meeting	[***]
6	Plan for MCI Support	[***]
7	Preparation and Submission of BLA	[***]
CLIN 0003	**Option Two**	**[***]**
1	[***]	[***]
2	[***]	[***]
3	Bioanalytical Methods Development: Hairless guinea pig	[***]
4	PK Studies: Hairless guinea pig	[***]
5	[***]	[***]
6	POC Efficacy Study: Hairless guinea pig	[***]
7	End of Phase 2 Meeting	[***]
CLIN 0004	**Option Three**	**[***]**
1	Pivotal Efficacy Study: Hairless guinea pig	[***]
2	Regulatory - Gap Analysis	[***]
3	Pre-BLA Meeting	[***]
4	[***]	[***]
5	Submit BLA. Respond to FDA feedback and update BLA as needed (additional updates for second animal model)	[***]
CLIN 0005	**Option Four**	**[***]**
1	[***]	[***]
2	[***]	[***]
3	[***]	[***]

Detailed Description of Select Contract Deliverables

A. Monthly and Annual Progress Reports

In addition to those reports required by the other terms of this contract, the Contractor shall prepare and submit the following reports in the manner stated below and in accordance with this Section F of this contract, and in the Statement of Work, attached to this contract (see Section J-List of Attachments).

i. **Monthly Progress Report**

This report shall include a description of the activities during the reporting period, and the activities planned for the ensuing reporting period. The first reporting period consists of the first full month of performance plus any fractional part of the initial month. Thereafter, the reporting period shall consist of each calendar month.

The Contractor shall submit a Monthly Progress Report according to the dates set forth in the summary table ("Summary of Contract Deliverables") under this Section. The progress report shall conform to the requirements set forth in the Deliverables Chart in Section F of this contract.

The format should include:

- A cover page that includes the contract number and title; the type of report and period that it covers; the Contractor's name, address, telephone number, fax number, and e-mail address; and the date of submission;
- SECTION I – EXECUTIVE SUMMARY
- SECTION II - PROGRESS
- SECTION II Part A: OVERALL PROGRESS - A description of overall progress.
- SECTION II Part B: MANAGEMENT AND ADMINISTRATIVE UPDATE - A description of all meetings, conference calls, etc. that have taken place during the reporting period. Include progress on administration and management issues (e.g., evaluating, and managing subcontractor performance, and personnel changes).
- SECTION II Part C: TECHNICAL PROGRESS - For each activity related to Gantt chart, document the results of work completed and cost incurred during the period covered in relation to proposed progress, effort and budget. The report shall be in sufficient detail to explain comprehensively the results achieved. The description shall include pertinent data and/or graphs in sufficient detail to explain any significant results achieved and preliminary conclusions resulting from analysis and scientific evaluation of data accumulated to date under the contract. The report shall include a description of problems encountered and proposed corrective action; differences between planned and actual progress, why the differences have occurred and what corrective actions are planned; preliminary conclusions resulting from analysis and scientific evaluation of data accumulated to date under the project.
- SECTION II Part D: PROPOSED WORK - A summary of work proposed related to Gantt chart for the next reporting period and preprints/reprints of papers and abstracts.
- SECTION III: Estimated and Actual Expenses.
  a. This Section of the report shall contain a narrative or table detailing whether there is a significant discrepancy (>10%) at this time between the % of work completed and the cumulative costs incurred to date. Monthly and actual expenses should be broken down to the appropriate WBS level.
  b. This Section of the report should also contain estimates for the Subcontractors' expenses from the previous month if the Subcontractor did not submit a bill in the previous month. If the subcontractor(s) was not working or did not incur any costs in the previous month, then a statement to this effect should be included in this report for those respective subcontractors.

A Monthly Progress Report will not be required in the same month that the Annual Progress Report is submitted.

ii. **Annual Progress Report**

This report shall include a summation of the results of the entire contract work for the period covered. Monthly Progress Reports shall not be submitted in the same month when an Annual Progress Report is due. Furthermore, an Annual Progress Report will not be required for the period when the Final Report is due. The first Annual Progress Report shall be submitted in accordance with the date set forth in the table ("Summary of Contract Deliverables") under Section F.2. of this contract. The progress report shall conform to the requirements set forth in the Deliverables Chart in Section F of this contract.

Each Annual Progress Report shall include:

- A Cover page that includes the contract number and title; the type of report and period that it covers; the Contractor's name, address, telephone number, fax number, and email address; and the date of submission;
- SECTION I: EXECUTIVE SUMMARY - A brief overview of the work completed, and the major accomplishments achieved during the reporting period.
- SECTION II: PROGRESS
- SECTION II Part A: OVERALL PROGRESS - A description of overall progress.
- SECTION II Part B: MANAGEMENT AND ADMINISTRATIVE UPDATE -
  A high level summary of critical meetings, etc. that have taken place during the reporting period. Include progress on administration and management to critical factors of the project (e.g. regulatory compliance audits and key personnel changes).
- SECTION II Part C: TECHNICAL PROGRESS - A detailed description of the work performed structured to follow the activities and decision gates outlined at the Integrated Baseline Review and as described in the Integrated Master Schedule. The Report should include a description of any problems (technical or financial) that occurred or were identified during the reporting period, and how these problems were resolved.
- SECTION II Part D: PROPOSED WORK - A summary of work proposed for the next year period to include an updated Gantt Chart.

Contractor also should include the following in the Annual Progress Report:

1. Copies of manuscripts (published and unpublished), abstracts, and any protocols or methods developed specifically under the contract during the reporting period; and
2. A summary of any Subject Inventions per the requirements under FAR Clause 52.227-11.

iii. **Draft Final Report and Final Report**

These reports are to include a summation of the work performed and results obtained for the entire contract period of performance. This report shall be in sufficient detail to describe comprehensively the results achieved. The Draft Final Report and Final Report shall be submitted in accordance with the Deliverables Chart in Section F of the contract. An Annual Progress Report will not be required for the period when the Final Report is due. The Draft Final Report and the Final Report shall be submitted in accordance with the dates set forth in the table ("Summary of Contract Deliverables") under SECTION F.2. of this contract. The report shall conform to the following format:

1. Cover page to include the contract number, contract title, performance period covered, Contractor's name and address, telephone number, fax number, email address and submission date.
2. SECTION I: EXECUTIVE SUMMARY - Summarize the purpose and scope of the contract effort including a summary of the major accomplishments relative to the specific activities set forth in the Statement of Work.
3. SECTION II: RESULTS - A detailed description of the work performed related to WBS and Gantt chart, the results obtained, and the impact of the results on the scientific and/or public health community including a listing of all manuscripts (published and in preparation) and abstracts presented during the entire period of performance and a summary of all inventions.

Draft Final Report: The Contractor is required to submit the Draft Final Report to the Contracting Officer's Representative and Contracting Officer. The Contracting Officer's Representative and Contracting Officer will review the Draft Final Report and provide the Contractor with comments in accordance with the dates set forth in Section F.2. of the contract.

Final Report: The Contractor will deliver the final version of the Final Report on or before the completion date of the contract. The final version shall include or address the COR's and CO's written comments on the draft report. Final Report shall be submitted on or before the completion date of the contract.

iv. **Summary of Salient Results**

The Contractor shall submit, with the Final Report, a summary of salient results achieved during the performance of the contract.

v. **Audit Reports**

Within thirty (30) calendar days of an audit related to conformance to FDA regulations and guidance, including adherence to GLP, GMP, GCP guidelines, the Contractor shall provide copies of the audit report (so long as received from the FDA) and a plan for addressing areas of nonconformance to FDA regulations and guidelines for GLP, GMP, or GCP guidelines as identified in the final audit report and as related to activities funded under this contract.

vi. **Periodic Document Review**

Upon request, Contractor shall provide CO and COR with the following contract funded documents as specified below but not limited to: Process Development Reports; Assay Qualification Plan/Report, Assay Validation Plan/Report, Assay Technology Transfer Report, Batch Records, Contractor/Subcontractor Standard Operating Procedures (SOP's), Master Production Records, Certificate of Analysis, Clinical Studies Data or Reports. The CO and COR reserve the right to request within the Period of Performance a non-proprietary technical document for distribution within the Government. Contractor shall provide technical document within 10 business days of CO or COR request. Contractor can request additional time on an as needed basis. If edits are recommended, the Contractor must address, in writing, concerns raised by BARDA in writing.

vii. **Risk Management Plan**

The Contractor shall provide a Risk Management Plan that outlines the impacts of each risk in relation to the cost, schedule, and performance objectives. The plan shall include risk mitigation strategies. Each risk mitigation strategy will capture how the corrective action will reduce impacts on cost, schedule and performance.

- Due within 180 days of contract award
- Contractor provides updated Risk Management Plan in Monthly Progress Report
- The COR shall provide Contractor with a written list of concerns in response plan submitted

Contractor must address, in writing, all concerns raised by COR within 20 business days of Contractor's receipt of COR's concerns.

B. Deliverables Arising from FDA Correspondence

i. **FDA Meetings**

The Contractor shall forward the dates and times of any meeting with the FDA to BARDA and make arrangements for appropriate BARDA staff to attend the FDA meetings. BARDA staff shall include up to a maximum of four people (COR, CO and up to 2 subject matter experts).

- Contractor shall notify BARDA of upcoming FDA meeting within 24 hours of scheduling.
- The Contractor shall forward initial Contractor and FDA-issued draft minutes and final minutes of any meeting with the FDA to the CO and COR within 5 business days of receipt. All documents shall be duly marked as either "Draft" or "Final."

ii. **FDA Submissions**

The Contractor shall provide the COR all documents submitted to the FDA.
Contractor shall provide the COR with an electronic copy of the final FDA submission. All documents shall be duly marked as either "Draft" or "Final."

- If draft documents are submitted to the COR for review, the COR will provide feedback to Contractor within 10 business days of receipt.
- If BARDA reviews draft documents, the Contractor shall revise their documents to address BARDA's written concerns and/or recommendations prior to FDA submission.
- Final FDA submissions shall be submitted to the CO and COR concurrently or no later than 5 calendar days of their submission to FDA.

iii. **FDA Audits**

In the event of an FDA inspection which occurs as a result of this contract and for the product, or for any other FDA inspection that has the reasonable potential to impact the performance of this contract, the Contractor shall provide the CO and COR with an exact copy (non-redacted) of the FDA Form 483 and the Establishment Inspection Report (EIR) within five (5) business days after the Contractors receipt of those documents. The Contractor shall provide the COR and CO with copies of the plan for addressing areas of non-conformance to FDA regulations for GLP, GMP, or GCP guidelines as identified in the audit report, status updates during the plans execution and a copy of all final responses to the FDA. The Contractor shall also provide redacted copies of any FDA audits received from subcontractors that occur as a result of this contract or for this product. The Contractor shall make arrangements for BARDA representative(s) to be present during the final debrief by the regulatory inspector.

- Contractor shall notify CO and COR within 10 business days of a scheduled FDA audit or within 24 hours of an ad hoc site visit/audit if the FDA does not provide advanced notice.
- Contractor shall provide copies of any FDA audit report received from subcontractors that occur as a result of this contract or for this product within 5 business days of receiving correspondence from the FDA, Subcontractor, or third party.
- Within 15 business days of audit report, Contractor shall provide CO with a plan for addressing areas of nonconformance, if any are identified.

iv. **Other FDA Correspondence**

The Contractor shall memorialize any correspondence between Contractor and FDA as related to activities funded under this contract and submit to BARDA. All documents shall be duly marked as either "Draft" or "Final." Contractor shall provide written summary of any FDA correspondence within 5 business days of correspondence.

F.3. ELECTRONIC SUBMISSION

For electronic delivery, the Contractor shall upload documents to the appropriate folder on https://eroom.bardatools.hhs.gov/eRoom ("eRoom") which is the designated Government file sharing system. The Government shall provide two contractor representatives authorized log in access to the file share program. Each representative must complete a mandatory training provided by the Government prior to gaining user access. A notification email should be sent to the CO and COR upon electronic delivery of any documents.

F.4. SUBJECT INVENTION REPORTING REQUIREMENT

All reports and documentation required by FAR Clause 52.227-11, Patent Rights-Ownership by the Contractor, including, but not limited to, the invention disclosure report, the confirmatory license, and the Government support certification, one copy of an annual utilization report, and a copy of the final invention statement, shall be submitted to the Contracting Officer. A final invention statement (see FAR 27.303 (b)(2)(ii)) shall be submitted to the Contracting Officer on the expiration date of the contract.

Reports and documentation submitted to the Contracting Officer shall be sent to the address set forth in Section G – Contract Administration Data.

If no invention is disclosed or no activity has occurred on a previously disclosed invention during the applicable reporting period, a negative report shall be submitted to the Contracting Officer at the address listed above.

F.5. FEDERAL ACQUISITION REGULATION CLAUSES INCORPORATED BY REFERENCE

This contract incorporates the following clause(s) by reference, with the same force and effect as if it were given in full text. Upon request, the Contracting Officer will make its full text available. The full text of each clause may be accessed electronically at this address: http://www.acquisition.gov/comp/far/index.html.

FAR 52.242-15, Stop Work Order (August 1989), Alternate 1 (April 1984)

SECTION G - CONTRACT ADMINISTRATION DATA

G.1. CONTRACTING OFFICER

The following Contracting Officers (CO) will represent the Government for the purpose of this contract:

Jonathan Gonzalez (Contracting Officer)
U.S. Department of Health & Human Services
Office of the Assistant Secretary for Preparedness and Response
Office of Acquisition Management, Contracts, and Grants (AMCG)
O'Neill House Office Building
Room Number: 22J12
Washington, DC 20515
202-401-4685 (Office)
Jonathan.Gonzalez@hhs.gov

1) The Contracting Officer is the only individual who can legally commit the Government to the expenditure of public funds. No person other than the Contracting Officer can make any changes to the terms, conditions, general provisions, or other stipulations of this contract.
2) The Contracting Officer is the only person with the authority to act as agent of the Government under this contract. Only the Contracting Officer 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 reimburse to the Contractor of any costs incurred during the performance of this contract; (5) otherwise change any terms and conditions of this contract.
3) No information other than that which may be contained in an authorized modification to this contract, duly issued by the Contracting Officer, which may be received from any person employed by the US Government, other otherwise, shall be considered grounds for deviation from any stipulation of this contract.
4) The Government may unilaterally change its CO designation, after which it will notify the Contractor in writing of such change.

G.2. CONTRACTING OFFICER'S REPRESENTATIVE (COR)

The following Contracting Officer's Representative (COR) will represent the Government for the purpose of this contract:

ATTN: Efrain Garcia (COR)
U.S. Department of Health & Human Services
Office of the Assistant Secretary for Preparedness and Response
Biomedical Advanced Research & Development Authority (BARDA)
O'Neill House Office Building
Room Number:
Washington, DC 20515
Email: Efrain.Garcia@hhs.gov

The COR is responsible for:

1) Monitoring the Contractor's technical progress, including the surveillance and assessment of performance and recommending to the Contracting Officer changes in requirements;
2) Assisting the Contracting Officer in interpreting the statement of work and any other technical performance requirements;
3) Performing technical evaluation as required;
4) Performing technical inspections and acceptances required by this contract; and
5) Assisting in the resolution of technical problems encountered during performance. The Government may unilaterally change it's COR designation, after which it will notify Contractor in writing of such change.

G.3. KEY PERSONNEL

Pursuant to the Key Personnel clause incorporated in Section I of this contract, the following individuals are considered to be essential to the work being performed hereunder:

Name	Title
Gal Cohen	President and CEO
Sharon Malka	Chief Financial & Operation Officer
Lior Rosenberg	Chief Medical Officer
Ety Klinger	Chief R&D Officer
Andrey Kon	Plant Manager
Eilon Asculai	VP R&D
Smadar Nestor	Director Regulatory Affairs
Nimrod Leuw	Director of QA/QC
Elanite Caspi	R&D Project Manager

The key personnel specified in this contract are considered to be essential to work performance. At least 30 days prior to diverting any of the specified individuals to other programs or contracts (or as soon as possible, if an individual must be replaced, for example, as a result of leaving the employ of the Contractor), the Contractor shall notify the Contracting Officer and shall submit comprehensive justification for the diversion or replacement request (including proposed substitutions for key personnel) and qualifications of the individual proposed as a substitute to permit evaluation by the Government of the impact on performance under this contract. The Contractor shall not divert or otherwise replace any key personnel without the written consent of the Contracting Officer. The Government may modify the contract to add or delete key personnel at the request of the contractor or Government. At a minimum, the key personnel should include the project manager, principal investigator, radiation biologist, quality control manager, quality assurance director, regulatory lead, and manufacturing lead.

G.4. CONTRACT FINANCIAL REPORT

a. Financial reports on the attached Financial Report of Individual Project/Contract shall be submitted by the Contractor to the CO with a copy to the COR in accordance with the instructions for completing this form, which accompany the form, in an original and one electronic copy, not later than the 30th business day after the close of the reporting period. The line entries for subdivisions of work and elements of cost (expenditure categories), which shall be reported within the total contract, are discussed in paragraph e., below. Subsequent changes and/or additions in the line entries shall be made in writing.

b. Unless otherwise stated in the instructions for completing this form, all columns A through J, shall be completed for each report submitted.

c. The first financial report shall cover the period consisting of the first full three calendar months following the date of the contract, in addition to any fractional part of the initial month. Thereafter, reports will be on a quarterly basis.

d. The Contracting Officer may require the Contractor to submit detailed support for costs contained in one or more interim financial reports. This clause does not supersede the record retention requirements in FAR Part 4.7.

e. The listing of expenditure categories to be reported is incorporated as a part of this contract and can be found under Section J entitled, “Financial Report of Individual Project/Contract,”.

f. Monthly invoices must include the cumulative total expenses to date, adjusted (as applicable) to show any amounts suspended by the Government.

g. Contractor invoices/financial reports shall conform to the form, format, and content requirements of the instructions for Invoice/Financing requests and Contract Financial Reporting, and be sent to the following points of contact:

CO	COR	PSC
Jonathan Gonzalez (Contracting Officer) HHS/ASPR/BARDA/CMA O'Neill House Office Building Room Number: 22J12 Washington, DC 20515 Email: Jonathan.Gonzalez@hhs.gov	Efrain Garcia COR HHS/ASPR/BARDA O'Neill House Office Building Room Number: Washington, DC 20515 202-205-3817 (Office) Efrain.Garcia@hhs.gov	PSC_Invoices@psc.hhs.gov & "e-Room"

The Contractor agrees to immediately notify the CO in writing if there is an anticipated overrun (any amount) or unexpended balance (greater than 10%) of the estimated costs for the base period or any option period(s) (See estimated costs under Section B) and the reasons for the variance. These requirements are in addition to the specified requirements of FAR Clause 52.232-20, Limitation of Cost that is incorporated by reference under Section I.1 which states;

Limitation of Cost (Apr 1984)

- The parties estimate that performance of this contract, exclusive of any fee, will not cost the Government more than (1) the estimated cost specified in the Schedule or, (2) if this is a cost-sharing contract, the Government's share of the estimated cost specified in the Schedule. The Contractor agrees to use its best efforts to perform the work specified in the Schedule and all obligations under this contract within the estimated cost, which, if this is a cost-sharing contract, includes both the Government's and the Contractor's share of the cost.

- The Contractor shall notify the Contracting Officer in writing whenever it has reason to believe that—

- The costs the Contractor expects to incur under this contract in the next 60 days, when added to all costs previously incurred, will exceed 75 percent of the estimated cost specified in the Schedule; or

- The total cost for the performance of this contract, exclusive of any fee, will be either greater or substantially less than had been previously estimated.

- As part of the notification, the Contractor shall provide the Contracting Officer a revised estimate of the total cost of performing this contract.

- Except as required by other provisions of this contract, specifically citing and stated to be an exception to this clause—

- The Government is not obligated to reimburse the Contractor for costs incurred in excess of (i) the estimated cost specified in the Schedule or, (ii) if this is a cost-sharing contract, the estimated cost to the Government specified in the Schedule; and

- The Contractor is not obligated to continue performance under this contract (including actions under the Termination clause of this contract) or otherwise incur costs in excess of the estimated cost specified in the Schedule, until the Contracting Officer (i) notifies the Contractor in writing that the estimated cost has been increased and (ii) provides a revised estimated total cost of performing this contract. If this is a cost-sharing contract, the increase shall be allocated in accordance with the formula specified in the Schedule.

- No notice, communication, or representation in any form other than that specified in paragraph (d)(2) of this clause, or from any person other than the Contracting Officer, shall affect this contract's estimated cost to the Government. In the absence of the specified notice, the Government is not obligated to reimburse the Contractor for any costs in excess of the estimated cost or, if this is a cost-sharing contract, for any costs in excess of the estimated cost to the Government specified in the Schedule, whether those excess costs were incurred during the course of the contract or as a result of termination.

- If the estimated cost specified in the Schedule is increased, any costs the Contractor incurs before the increase that are in excess of the previously estimated cost shall be allowable to the same extent as if incurred afterward, unless the Contracting Officer issues a termination or other notice directing that the increase is solely to cover termination or other specified expenses.

- Change orders shall not be considered an authorization to exceed the estimated cost to the Government specified in the Schedule, unless they contain a statement increasing the estimated cost.

- If this contract is terminated or the estimated cost is not increased, the Government and the Contractor shall negotiate an equitable distribution of all property produced or purchased under the contract, based upon the share of costs incurred by each.

h. The Contractor shall submit an electronic copy of the payment request to the approving official instead of a paper copy. The payment request shall be transmitted as an attachment via e-mail to the address listed above in one of the following formats: MSWord, MS Excel, or Adobe Portable Document Format (PDF). Only one payment request shall be submitted per e-mail and the subject line of the e-mail shall include the Contractor's name, contract number, and unique invoice number.

i. An electronic copy of the payment request shall be uploaded into the designated eRoom (as defined in Section F.3 ELECTRONIC SUBMISSION) and an e-mail notification of the upload will be provided to the CO and COR.

j. All invoice submissions shall be in accordance with FAR Clause 52.232-25, Prompt Payment (Jan 2017).

k. Invoices - Cost and Personnel Reporting, and Variances from the Negotiated Budget.

The Contractor agrees to provide a detailed breakdown on invoices of the following cost categories:

1. Direct Labor - List individuals by name, title/position, hourly/annual rate, level of effort (actual hours or % of effort), and amount claimed.
2. Fringe Benefits - Cite rate and amount
3. Overhead - Cite rate and amount

4. Materials & Supplies - Include detailed breakdown when total amount is over $10,000.
5. Travel - Identify travelers, dates, destination, purpose of trip, and total breaking out amounts for transportation (plane, car etc), lodging, M&IE. Cite COA, if appropriate. List separately, domestic travel, general scientific meeting travel, and foreign travel.
6. Consultant Fees - Identify individuals, amounts and activities. Cite appropriate COA
7. Subcontracts - Attach subcontractor invoice(s). Cite appropriate COA
8. Equipment - Cite authorization and amount. Cite appropriate COA
9. Other Direct Costs - Include detailed breakdown when total amount is over $10,000.
10. G&A - Cite rate and amount.
11. Total Cost (and applicable cost-shared ratio)
12. Fixed Fee (if applicable)
13. Total Cost Plus Fixed Fee

Additional instructions and an invoice template are provided in Section J-List of Attachments, Invoice/Financing Request Instructions and Contract Financial Reporting Instructions for Cost- Reimbursement Contracts. All invoices must be signed by a representative of the contractor authorized to certify listed charges are accurate and comply with government regulations. Invoices shall be signed and submitted electronically (in accordance with Section F.3 Electronic Submission).

If applicable, the Contractor shall convert any foreign currency amount(s) in the monthly invoice to U.S. dollars each month, on the 1st of the month, using the foreign exchange rate index published on www.federalreserve.gov. Payment of invoices is subject to the U.S. dollar limits within the Total Costs of CLIN 0001 in Section B of the contract.

The Government shall use electronic funds transfer to the maximum extent possible when making payments under this contract. FAR 52.232-33, Payment by Electronic Funds Transfer–System for Award Management, in Section I requires the Contractor to designate in writing a financial institution for receipt of electronic funds transfer payments.

G.5. REIMBURSEMENT OF COST

The Government shall reimburse the Contractor the cost determined by the Contracting Officer to be allowable (hereinafter referred to as allowable cost) in accordance with FAR Clause 52.216-7, Allowable Cost and Payment incorporated by reference in Section I, Contract Clauses, of this contract, and FAR Subpart 31.2. Examples of allowable costs include, but are not limited to, the following:

a) All direct materials and supplies that are used in performing the work provided for under the contract, including those purchased for subcontracts and purchase orders.

b) All direct labor, including supervisory, that is properly chargeable directly to the contract, plus fringe benefits.

c) All other items of cost budgeted for and accepted in the negotiation of this basic contract or modifications thereto.

d) Travel costs including per diem or actual subsistence for personnel while in an actual travel status in direct performance of the work and services required under this contract subject to the following:

(i) Air travel shall be by the most direct route using "air coach" or "air tourist" (less than first class) unless it is clearly unreasonable or impractical (e.g., not available for reasons other than avoidable delay in making reservations, would require circuitous routing or entail additional expense offsetting the savings on fare, or would not make necessary connections).

(ii) Rail travel shall be by the most direct route, first class with lower berth or nearest equivalent.

(iii) Costs incurred for lodging, meals, and incidental expenses shall be considered reasonable and allowable to the extent that they do not exceed on a daily basis the per diem rates set forth in the Federal Travel Regulation (FTR).

(iv) Travel via privately owned automobile shall be reimbursed at not more than the current General Services Administration (GSA) FTR established mileage rate.

G.6. INDIRECT COST RATES

The following Contractor established provisional billing rates are incorporated into the contract, and will be utilized for billing purposes during the Base Period (CLIN 0001) and total estimated cost plus fixed fee Option Periods (CLINs 0002, 0003, 0004, and 0005) ONLY if exercised by the CO pending the establishment of final indirect cost rates for each fiscal year or until revised by the CO in accordance with the provisions of FAR 42.705-1. FAR clause 52.216-7 will be utilized for billing purposes during both the Base Period (CLIN 0001) and total estimated cost plus fixed fee Option Periods (CLINs 0002, 0003, 0004, and 0005) ONLY if exercised by the CO.

MediWound Ltd.			
Rate Type	**Rate**	**Ceiling Rate**	**Allocation Base**
[***]	[***]	[***]	[***]
[***]	[***]	[***]	[***]

The Indirect Cost Ceilings are established for the Base Period (CLIN 0001) and total estimated cost plus fixed fee Option Periods (CLINs 0002, 0003, 0004, and 0005) ONLY if exercised by the CO. The Contractor cannot seek reimbursement in excess of the Indirect Cost Ceilings.

Use of the above provisional rates does not change any cost ceilings, contract obligations, or specific allowance or disallowance provided for in the contract.

Final rate proposals must be sent to the CO, within 6 months subsequent to the fiscal year end. (See also FAR Clause 52.216-7 incorporated herein).

G.7. POST AWARD EVALUATION OF CONTRACTOR PERFORMANCE

Contractor Performance Evaluations

Interim and final evaluations of Contractor performance will be prepared on this contract in accordance with FAR Subpart 42.15. The final performance evaluation will be prepared at the time of completion of work. In addition to the final evaluation, an interim evaluation shall be submitted annually.

Interim and final evaluations will be provided to the Contractor as soon as practicable after completion of the evaluation. The Contractor will be permitted thirty days to review the document and to submit additional information or a rebutting statement. If agreement cannot be reached between the parties, the matter will be referred to an individual one level above the Contracting Officer whose decision will be final.

Copies of the evaluations, Contractor responses, and review comments, if any, will be retained as part of the contract file, and may be used to support future award decisions.

Electronic Access to Contractor Performance Evaluations

Contractors that have Internet capability may access evaluations through a secure Web site for review and comment by completing the registration form that can be obtained at the following address:

http://www.cpars.csd.disa.mil/cparsmain.htm

The registration process requires the Contractor to identify an individual that will serve as a primary contact and who will be authorized access to the evaluation for review and comment. In addition, the Contractor will be required to identify an alternate contact that will be responsible for notifying the cognizant contracting official in the event the primary contact is unavailable to process the evaluation within the required 30-day time frame.

G.8. CONTRACT COMMUNICATIONS/CORRESPONDENCE (JULY 1999)

The Contractor shall identify all correspondence, reports, and other data pertinent to this contract by imprinting the contract number from Page 1 of the contract.

G.9. GOVERNMENT PROPERTY

In addition to the requirements of the Government Property clause incorporated in Section I of this contract, the Contractor shall comply with the provisions of HHS Publication, "HHS Contracting Guide for Control of Government Property," which is incorporated into this contract by reference. This document can be accessed at:

http://www.hhs.gov/hhsmanuals/ (HHS Logistics Management Manual)

Among other issues, this publication provides a summary of the Contractor's responsibilities regarding purchasing authorizations and inventory and reporting requirements under the contract.

Notwithstanding the provisions outlined in the HHS Publication, "HHS Contracting Guide for Control of Government Property," which is incorporated in this contract in paragraph 1. above, the Contractor shall use the form entitled, "Report of Government Owned, Contractor Held Property" for submitting summary reports required under this contract, as directed by the Contracting Officer or his/her designee. This form is attached to this contract (see Section J-List of Attachments). Title will vest in the Government for equipment purchased as a direct cost.

SECTION H - SPECIAL CONTRACT REQUIREMENTS

The Contractor, depending upon the nature of the work, is responsible for following the provisions below in conducting its own work under this contract. The Contractor also is responsible for incorporating these provisions into any subcontract awarded, if applicable to the specific nature of the work in the subcontract. Accordingly, those provisions shall be flowed-down as applicable.

H.1 CLINICAL AND NON-CLINICAL TERMS OF AWARD

BARDA has a responsibility to obtain documentation concerning mechanisms and procedures that are in place to protect the safety of participants and animals in BARDA funded clinical trials and non-clinical studies. Therefore, the Contractor shall develop a protocol for each clinical trial *and* non-clinical study funded under this contract and submit all such protocols and protocol amendments to the Contracting Officer's Representative (COR) for evaluation and comment.

Approval by the COR is required before work under a protocol may begin. The COR comments will be forwarded to the Contractor at least (10) business days prior to the start of any study under the protocol. The Contractor must address, in writing, all concerns (*e.g.* study design, safety, regulatory, ethical, and conflict of interest) noted by the COR.

If the draft protocols are to be submitted to the FDA, the COR review shall occur before submission, pursuant to the terms set forth by Section F.2 of this contract. The Contractor shall revise their protocols to address BARDA's concerns and recommendations prior to FDA submission. The Contractor must provide BARDA with a copy of FDA submissions, within the time frame set forth by Section F.2 of this contract.

Execution of clinical and non-clinical studies requires written authorization from the Government. The Government will provide written authorization to the Contractor upon either 1) receiving documentation in which all COR comments have been satisfactorily addressed; or 2) receiving documentation that the FDA has reviewed and commented on the protocol.

The Government shall have unlimited rights to all protocols, data resulting from execution of these protocols, and final reports funded by BARDA under this contract, as set forth in the FAR clauses referenced in PART II of this contract. The Government reserves the right to request that the Contractor provide any contract deliverable in a non-proprietary form to ensure the Government has the ability to review and distribute the deliverables as the Government deems necessary. Important information regarding performing human subject research is available at http://www3.niaid.nih.gov/healthscience/clinicalstudies/.

Any updates to technical reports are to be addressed in the Monthly and Annual Progress Reports. The Contractor shall advise the Contracting Officer's Representative or designee in writing and via electronic communication in a timely manner of any issues potentially affecting contract performance.

1. Non-Clinical Terms of Award

These Non-Clinical Terms of Award detail an agreement between the Biomedical Advanced Research and Development Authority (BARDA) and the Contractor; they apply to all grants and contracts that involve non-clinical research.

a. Safety and Monitoring Issues

i. PHS Policy on Humane Care and use of Laboratory Animals

Within 30 days of award and then with the annual progress report, the Contractor must submit to BARDA a copy of the current Institutional Animal Care and Use Committees (IACUC) documentation of continuing review and approval and the Office of Laboratory Animal Welfare (OLAW) federal wide assurance number for the institution or site.

If other institutions are involved in the research (e.g., a multicenter trial or study), each institution's IACUC must review and approve the protocol. They must also provide BARDA initial and annual documentation of continuing review and approval and federal wide assurance number.

The Contractor must ensure that the application, as well as all protocols, is reviewed by the performing institution's IACUC.

To help ensure the safety of animals used in BARDA-funded studies, the Contractor must provide BARDA copies of documents related to all major changes in the status of ongoing protocols, including the following:

- All amendments or changes to the protocol, identified by protocol version number, date, or both and date it is valid.
- All material changes in IACUC policies and procedures, identified by version number, date, and all required signatories (if applicable).
- Termination or temporary suspension of the study(ies) for regulatory issues.
- Termination or temporary suspension of the protocol.
- Any change that is made in the specific IACUC approval for the indicated study(ies).
- Any other problems or issues that could affect the scientific integrity of the study(ies), i.e., fraud, misrepresentation, misappropriation of funds, etc.

Contractor must notify BARDA of any of the above changes within five (5) working days from the time the Contractor becomes aware of such changes by email or fax, followed by a letter signed by the institutional business official, detailing notification of the change of status to the local IACUC and a copy of any responses from the IACUC.

If a non-clinical protocol has been reviewed by an institutional biosafety committee (IBC) or the NIH Recombinant DNA Advisory Committee (RAC), the Contractor must provide information about the initial and ongoing review and approval, if any. See the NIH Guidelines for Research Involving Recombinant DNA Molecules.

ii. Non-Clinical Data and Safety Monitoring Requirements

BARDA strongly recommends continued safety monitoring for all non-clinical studies of investigational drugs, devices, or biologics. FDA expects non- clinical studies to include safety in addition to efficacy. The Contractor should consider evaluation of clinical relevant safety markers in the pivotal and non- pivotal, non-clinical studies. In preparation for clinical trials of licensed or not yet licensed products, it is imperative that BARDA- sponsored studies of any type measure the risk and safety parameters that are elicited and provide a safety profile from the studies for future human risk assessment.

A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For example, the risk of drawing a small amount of blood from a healthy subject for research purposes is no greater than the risk of doing so as part of a routine physical examination (45 CFR 46.102(i)).

The COR will work with the Contractor on decisions regarding the type and extent of safety data accrual to be employed before the start of efficacy or safety studies.

The Contractor shall inform the CO and COR of any upcoming site visits and/or audits of CRO facilities funded under this effort. BARDA reserves the right to accompany the Contractor on site visits and/or audits of CRO's as BARDA deems necessary, provided reasonable prior notice is given to the Contractor.

b. BARDA Review Process before Non-Clinical study Execution Begins

BARDA is under the same policy-driven assurances as NIH in that it has a responsibility to ensure that mechanisms and procedures are in place to protect the safety and welfare of animals used in BARDA-funded non-clinical trials. Therefore, before study execution, the Contractor must provide the following (as applicable) for review and comment by the COR:

- IACUC approved (signed) non-clinical research protocol identified by version number, date, or both, including details of study design, euthanasia criteria, proposed interventions, and exclusion criteria.
- For non-pivotal mouse studies, the Contractor will provide an annual animal care and use protocol.
- Documentation of IACUC approval, including OLAW federal wide number, IACUC registration number, and IACUC name.
- Contractor should reduce the number of animals required for a study using power of statistics.
- Plans for the management of side effects, rules for interventions and euthanasia criteria.
- Procedures for assessing and collecting safety data were appropriate.
- If a study is contracted through Contract Research Organizations (CROs), work orders and service agreements the Contractor shall assure an integrated safety documentation plan is in place for the study site, pharmacy service records on the dosing material to be used and excipients, and laboratory services (including histopathology).
- Documentation that the Contractor and all required staff responsible for the conduct of the research have received training in the protection and handling of animals, or that the CRO has the required documentation.
- Purchasing of animals and/or other supplies for non-clinical studies funded in part or in whole by BARDA requires written approval by the Contracting Officer in accordance with the contract. The Contractor must have the ability to return/re-sell animals, at purchase price, to distributor or a third party, in the event that the Contracting Officer Authorization is not granted.

- Provide justification for whether studies require good laboratory practice (GLP) conditions.
- Provide justification for whether studies will be classified as non-pivotal or pivotal studies.

Documentation of each of the above items shall be submitted to the COR for evaluation and comment in conjunction with the protocol. Execution of non-clinical studies requires written authorization from the Contracting Officer in accordance with this Section of the contract.

c. References

Public Health Service Policy on Humane Care and Use of Laboratory Animals:
http://grants.nih.gov/grants/olaw/InvestigatorsNeed2Know.pdf

USDA Animal Welfare Act:
http://awic.nal.usda.gov/nal_display/index.php?info_center=3&tax_level=3&tax_subject=182&topic_id=1118&level3_id=6735&level4_id=0&level5_id=0&placement_default=0

2. Clinical Terms of Award

These Clinical Terms of Award detail an agreement between the Government and the Contractor; they apply to all grants and contracts that involve clinical research.

BARDA shall have unlimited rights to all protocols, data generated from the execution of these protocols, and final reports, funded by BARDA under this contract, as defined in Rights in Data Clause in FAR 52.227-14. BARDA reserves the right to request that the Contractor provide any contract deliverable that is produced in the performance of this contract without any restrictive legends to ensure BARDA has the ability to review and distribute the deliverables, as BARDA deems necessary.

a. Safety and Monitoring Issues

i. Institutional Review Board or Independent Ethics Committee Approval

Within 30 days of award and then with the annual progress report, the Contractor must submit to the COR a copy of the current IRB-or IEC-approved informed consent document, documentation of continuing review and approval and the OHRP federal wide assurance number for the institution or site.

If other institutions are involved in the research (e.g., a multicenter clinical trial or study), each institution's IRB or IEC must review and approve the protocol. They must also provide BARDA initial and annual documentation of continuing review and approval, including the current approved informed consent document and federal wide number.

The Contractor must ensure that the application as well as all protocols is reviewed by their IRB or IEC.

To help ensure the safety of participants enrolled in BARDA-funded studies, the Contractor must provide the COR copies of documents related to all major changes in the status of ongoing protocols, including the following:

- All amendments or changes to the protocol, identified by protocol version number, date, or both and dates it is valid.
- All changes in informed consent documents, identified by version number, dates, or both and dates it is valid.
- Termination or temporary suspension of patient accrual.
- Termination or temporary suspension of the protocol.
- Any change in IRB approval.
- Any other problems or issues that could affect the participants in the studies.

The Contractor must notify the COR and CO of any of the above changes within five (5) working days by email or fax, followed by a letter signed by the institutional business official, detailing notification of the change of status to the local IRB and a copy of any responses from the IRB or IEC.

If a clinical protocol has been reviewed by an institutional biosafety committee (IBC) or the NIH Recombinant DNA Advisory Committee (RAC), the Contractor must provide information about the initial and ongoing review and approval, if any. See the NIH Guidelines for Research Involving Recombinant DNA Molecules.

ii. Data and Safety Monitoring Requirements

BARDA strongly recommends independent safety monitoring for clinical trials of investigational drugs, devices, or biologics; clinical trial of licensed products; and clinical research of any type involving more than minimal risk to volunteers. Independent monitoring can take a variety of forms. Phase III clinical trials must be reviewed by an independent data and safety monitoring board (DSMB); other trials may require DSMB oversight as well. The Contractor shall inform BARDA of any upcoming site visits and/or audits of CRO facilities funded under this effort. BARDA reserves the right to accompany the Contractor on site visits and/or audits of CROs as BARDA deems necessary.

A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research and not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For examples, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of a routine physical examination (45 CFR 46.102I).

Final decisions regarding the type of monitoring to be used must be made jointly by BARDA and the Contractor before enrollment starts. Discussions with the responsible BARDA Project Officer regarding appropriate safety monitoring and approval of the final monitoring plan by BARDA must occur before patient enrollment begins and may include discussions about the appointment of one of the following.

- **Independent Safety Monitor** – a physician or other appropriate expert who is independent of the study and available in real time to review and recommend appropriate action regarding adverse events and other safety issues.

- **Independent Monitoring Committee (IMC) or Safety Monitoring Committee (SMC)** – a small group of independent investigators and biostatisticians who review data from a particular study.

- **Data and Safety Monitoring Board** – an independent committee charged with reviewing safety and trial progress and providing advice with respect to study continuation, modification, and termination. The Contractor may be required to use an established BARDA DSMB or to organize an independent DSMB. All phase III clinical trials must be reviewed by a DSMB; other trials may require DSMB oversight as well. Please refer to: NIAID Principles for Use of a Data and Safety Monitoring Board (DSMB) For Oversight of Clinical Trials Policy

When a monitor or monitoring board is organized, a description of it, its charter or operating procedures (including a proposed meeting schedule and plan for review of adverse events), and roster and *curriculum vitae* from all members must be submitted to and approved by the COR before enrollment starts. The Contractor will also ensure that the monitors and board members report any conflicts of interest and the Contractor will maintain a record of this. The Contractor will share conflict of interest reports with the CO and COR.

Additionally, the Contractor must submit written summaries of all reviews conducted by the monitoring group to the BARDA within thirty (30) days of reviews or meetings.

iii. BARDA Protocol Review Process Before Patient Enrollment Begins The COR has a responsibility to ensure that mechanisms and procedures are in place to protect the safety of participants in BARDA-supported clinical trials. Therefore, before patient accrual or participant enrollment, the Contractor must ensure the following (as applicable) are in place at each participating institution, prior to patient accrual or enrollment:

- IRB- or IEC-approved clinical research protocol identified by version number, date, or both, including details of study design, proposed interventions, patient eligibility, and exclusion criteria.
- Documentation of IRB or IEC approval, including OHRP federal wide number, IRB or IEC registration number, and IRB and IEC name.
- IRB- or IEC- approved informed consent document, identified by version number, date, or both and dates it is valid.
- Plans for the management of side effects.
- Procedures for assessing and reporting adverse events.
- Plans for data and safety monitoring (see above) and monitoring of the clinical study site, pharmacy, and laboratory.
- Documentation that the Contractor and all study staff responsible for the design or conduct of the research have received training in the protection of human subjects.

Documentation to demonstrate that each of the above items are in place shall be submitted to the COR) for evaluation and comment in conjunction with the protocol. Execution of clinical studies requires written authorization from the COR in accordance with this Section of this contract.

iv. Investigational New drug or Investigational Device Exemption Requirements

Consistent with federal regulations, clinical research projects involving the use of investigational therapeutics, vaccines, or other medical interventions (including licensed products and devices for a purpose other than that for which they were licensed) in humans under a research protocol must be performed under a Food and Drug Administration (FDA) investigational new drug (IND) or investigational device exemption (IDE).

Exceptions must be granted in writing by FDA. If the proposed clinical trial will be performed under an IND or IDE, the Contractor must provide BARDA with the name and institution of the IND or IDE sponsor, the date the IND or IDE was filed with FDA, the FDA IND or IDE number, any written comments from FDA, and the written responses to those comments.

Unless FDA notifies Contractor otherwise, The Contractor must wait thirty (30) calendar days from FDA receipt of an initial IND or IDE application before initiating a clinical trial.

The Contractor must notify BARDA if the FDA places the study on clinical hold and provide BARDA any written comments from FDA, written responses to the comments, and documentation in writing that the hold has been lifted. The Contractor must not use grant or contract funds during a clinical hold to fund clinical studies that are on hold. The Contractor must not enter into any new financial obligations related to clinical activities for the clinical trial on clinical hold.

v. Required Time-Sensitive Notification

Under an IND or IDE, the sponsor must provide FDA safety reports of serious adverse events. Under these Clinical Terms of Award, the Contractor must submit copies to the responsible Contracting Officer's Representative (COR) as follows:

i. Expedited safety report of unexpected or life-threatening experience or death:
A copy of any report of unexpected or life-threatening experience or death associated with the use of an IND drug, which must be reported to FDA by telephone or fax as soon as possible but no later than seven (7) days after the IND sponsor's receipt of the information, must be submitted to the COR within 24 hours of FDA notification.

ii. Expedited safety reports of serious and unexpected adverse experiences: A copy of any report of unexpected and serious adverse experience associated with use of an IND drug or any finding from tests in laboratory animals that suggests a significant risk for human subjects, which must be reported in writing to FDA as soon as possible but no later than 15 days after the IND sponsor's receipt of the information, must be submitted to the COR within 24 hours of FDA notification. For medical devices, adverse events should be reported under the MedWatch (MDR) program with reporting timelines of 5 days for serious adverse events or 30 days for reportable events.

iii. IDE reports of unanticipated adverse device effect:

A copy of any reports of unanticipated adverse device effect submitted to FDA must be submitted to the COR within 24 hours of FDA notification.

iv. Expedited safety reports: Sent to the COR concurrently with the report to FDA.

v. Other adverse events documented during the course of the trial should be included in the annual IND or IDE report and reported to BARDA annually.

In case of problems or issues, the Contracting Officer's Representative will contact the Contractor within ten (10) business days by email or fax, followed within thirty (30) calendar days by an official letter to the Contractor's Project Manager, with a copy to the institutions' office of sponsored programs, listing issues and appropriate actions to be discussed.

vi. Safety reporting for research not performed under an IND or IDE.

Final decisions regarding ongoing safety reporting requirements for research not performed under an IND or IDE must be made jointly by the Contracting Officer's Representative and the Contractor.

H.2. PROTECTION OF HUMAN SUBJECTS, HHSAR 352.270-4(b) (December 2015)

a. The Contractor agrees that the rights and welfare of human subjects involved in research under this contract shall be protected in accordance with 45 CFR Part 46 and with the Contractor's current federal wide Assurance of Compliance on file with the Office for Human Research Protections (OHRP), Department of Health and Human Services. The Contractor further agrees to provide certification at least annually that the Institutional Review Board has reviewed and approved the procedures, which involve human subjects in accordance with 45 CFR Part 46 and the Assurance of Compliance.

b. The Contractor shall bear full responsibility for the performance of all work and services involving the use of human subjects under this contract and shall ensure that work is conducted in a proper manner and as safely as is feasible. The parties hereto agree that the Contractor retains the right to control and direct the performance of all work under this contract. The Contractor shall not deem anything in this contract to constitute the Contractor or any subcontractor, agent or employee of the Contractor, or any other person, organization, institution, or group of any kind whatsoever, as the agent or employee of the Government. The Contractor agrees that it has entered into this contract and will discharge its obligations, duties, and undertakings and the work pursuant thereto, whether requiring professional judgment or otherwise, as an independent contractor without imputing liability on the part of the Government for the acts of the Contractor or its employees.

c. Contractors involving other agencies or institutions in activities considered to be engaged in research involving human subjects must ensure that such other agencies or institutions obtain their own FWA if they are routinely engaged in research involving human subjects or ensure that such agencies or institutions are covered by the Contractors' FW' via designation as agents of the institution of via individual investigator agreements (see OHRP website at: http//:www.hhs.gov/ohrp/policy/guidanceonalternativeofwa.pdf).

d. If at any time during the performance of this contract, the Contractor is not in compliance with any of the requirements and/or standards stated in paragraphs (a) and (b) above, the Contracting Officer may immediately suspend, in whole or in part, work and further payments under this contract until the Contractor corrects the noncompliance. The Contracting Officer may communicate the notice of suspension by telephone with confirmation in writing. If the Contractor fails to complete corrective action within the period of time designated in the Contracting Officer's written notice of suspension, the Contracting Officer may, after consultation with OHRP, terminate this contract in whole or in part.

H.3. HUMAN MATERIALS (ASSURANCE OF OHRP COMPLIANCE)

The acquisition and supply of all human specimen material (including fetal material) used under this contract shall be obtained by the Contractor in full compliance with applicable Federal, State and Local laws and the provisions of the Uniform Anatomical Gift Act in the United States, and no undue inducements, monetary or otherwise, will be offered to any person to influence their donation of human material.

The Contractor shall provide written documentation that all human materials obtained as a result of research involving human subjects conducted under this contract, by collaborating sites, or by subcontractors identified under this contract, were obtained with prior approval by the Office for Human Research Protections (OHRP) of an Assurance to comply with the requirements of 45 CFR 46 to protect human research subjects. This restriction applies to all collaborating sites without OHRP- approved Assurances, whether domestic or foreign, and compliance must be ensured by the Contractor.

Provision by the Contractor to the Contracting Officer of a properly completed "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263(formerly Optional Form 310), certifying IRB review and approval of the protocol from which the human materials were obtained constitutes the written documentation required. The human subject certification can be met by submission of a self-designated form provided that it contains the information required by the "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263 (formerly Optional Form 310).

H.4. RESEARCH INVOLVING HUMAN FETAL TISSUE

All research involving human fetal tissue shall be conducted in accordance with the Public Health Service Act, 42 U.S.C. 289g-1 and 289g-2. Implementing regulations and guidance for conducting research on human fetal tissue may be found at 45 CFR 46, Subpart B and http://grants1.nih.gov/grants/guide/notice-files/not93-235.html and any subsequent revisions to this NIH Guide to Grants and Contracts ("Guide") Notice.

The Contractor shall make available, for audit by the Secretary, HHS, the physician statements and informed consents required by 42 USC 289g-1(b) and (c), or ensure HHS access to those records, if maintained by an entity other than the Contractor.

H.5. CARE OF LIVE VERTEBRATE ANIMALS, HHSAR 352.270-5 (Dec 2015)

a. Before undertaking performance of any contract involving animal-related activities where the species is regulated by USDA, the Contractor shall register with the Secretary of Agriculture of the United States in accordance with 7 U.S.C. 2136 and 9 CFR Sections 2.25 through 2.28. The Contractor shall furnish evidence of the registration to the Contracting Officer.

b. The Contractor shall acquire vertebrate animals used in research from a dealer licensed by the Secretary of Agriculture under 7 U.S.C. 2133 and 9 CFR Sections 2.1-2.11, or from a source that is exempt from licensing under those Sections.

c. The Contractor agrees that the care, use and intended use of any live vertebrate animals in the performance of this contract shall conform with the Public Health Service (PHS) Policy on Humane Care of Use of Laboratory Animals (PHS Policy), the current Animal Welfare Assurance, the Guide for the Care and Use of Laboratory Animals (National Academy Press, Washington, DC) and the pertinent laws and regulations of the United States Department of Agriculture (see 7 U.S.C. 2131 et seq. and 9 CFR Subchapter A, Parts 1-4). In case of conflict between standards, the more stringent standard shall govern.

d. If at any time during performance of this contract, the Contracting Officer determines, in consultation with the Office of Laboratory Animal Welfare (OLAW), National Institutes of Health (NIH), that the Contractor is not in compliance with any of the requirements and standards stated in paragraphs (a) through (c) above, the Contracting Officer may immediately suspend, in whole or in part, work and further payments under this contract until the Contractor corrects the noncompliance. Notice of the suspension may be communicated by telephone and confirmed in writing. If the Contractor fails to complete corrective action within the period of time designated in the Contracting Officer's written notice of suspension, the Contracting Officer may, in consultation with OLAW, NIH, terminate this contract in whole or in part, and the Contractor's name may be removed from the list of those contractors with approved Assurances.

Note: The Contractor may request registration of its facility and a current listing of licensed dealers from the Regional Office of the Animal and Plant Health Inspection Service (APHIS), USDA, for the region in which its research facility is located. The location of the appropriate APHIS Regional Office, as well as information concerning this program may be obtained by contacting the Animal Care Staff, USDA/APHIS, 4700 River Road, Riverdale, Maryland 20737 (E- mail: ace@aphis.usda.gov; W eb site: (http://www.aphis.usda.gov/animal_welfare).

H.6. ANIMAL WELFARE

All research involving live, vertebrate animals shall be conducted in accordance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals. This policy may be accessed at: http://grants1.nih.gov/grants/olaw/references/phspol.htm

H.7. INFORMATION ON COMPLIANCE WITH ANIMAL CARE REQUIREMENTS

Registration with the U. S. Dept. of Agriculture (USDA) is required to use regulated species of animals for biomedical purposes. USDA is responsible for the enforcement of the Animal Welfare Act (7 U.S.C. 2131 et. seq.), http://www.nal.usda.gov/awic/legislat/awa.htm.

The Public Health Service (PHS) Policy is administered by the Office of Laboratory Animal Welfare (OLAW) http://grants2.nih.gov/grants/olaw/olaw.htm. An essential requirement of the PHS Policy http://grants2.nih.gov/grants/olaw/references/phspol.htm is that every institution using live vertebrate animals must obtain an approved assurance from OLAW before they can receive funding from any component of the U. S. Public Health Service.

The PHS Policy requires that Assured institutions base their programs of animal care and use on the Guide for the Care and Use of Laboratory Animals http://www.nap.edu/readingroom/books/labrats/ and that they comply with the regulations (9 CFR, Subchapter A)http://www.nal.usda.gov/awic/legislat/usdaleg1.htm issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act. The Guide may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of this Policy.

The Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) http://www.aaalac.org is a professional organization that inspects and evaluates programs of animal care for institutions at their request. Those that meet the high standards are given the accredited status. As of the 2002 revision of the PHS Policy, the only accrediting body recognized by PHS is the AAALAC. While AAALAC Accreditation is not required to conduct biomedical research, it is highly desirable. AAALAC uses the Guide as their primary evaluation tool. They also use the Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching. It is published by the Federated of Animal Science Societies http://www.fass.org.

H.8. REQUIREMENTS FOR ADEQUATE ASSURANCE OF PROTECTION OF VERTEBRATE ANIMAL SUBJECTS

The PHS Policy on Humane Care and Use of Laboratory Animals requires that applicant organizations proposing to use vertebrate animals file a written Animal Welfare Assurance with the Office for Laboratory Animal Welfare (OLAW), establishing appropriate policies and procedures to ensure the humane care and use of live vertebrate animals involved in research activities supported by the PHS. The PHS Policy stipulates that an applicant organization, whether domestic or foreign, bears responsibility for the humane care and use of animals in PHS- supported research activities. Also, the PHS policy defines "animal" as "any live, vertebrate animal used, or intended for use, in research, research training, experimentation, biological testing or for related purposes." This Policy implements and supplements the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training, and requires that institutions use the Guide for the Care and Use of Laboratory Animals as a basis for developing and implementing an institutional animal care and use program. This Policy does not affect applicable State or local laws or regulations that impose more stringent standards for the care and use of laboratory animals. All institutions are required to comply, as applicable, with the Animal Welfare Act as amended (7 USC 2131 et. seq.) and other Federal statutes and regulations relating to animals. These documents are available from the Office of Laboratory Animal Welfare, National Institutes of Health, Bethesda, MD 20892, (301) 496-7163. See: http://grants.nih.gov/grants/OLAW/olaw.htm

No PHS supported work for research involving vertebrate animals will be conducted by an organization, unless that organization is operating in accordance with an approved Animal Welfare Assurance and provides verification that the Institutional Animal Care and Use Committee (IACUC) has reviewed and approved the proposed activity in accordance with the PHS policy. Applications may be referred by the PHS back to the institution for further review in the case of apparent or potential violations of the PHS Policy. No award to an individual will be made unless that individual is affiliated with an assured organization that accepts responsibility for compliance with the PHS Policy. Foreign applicant organizations applying for PHS awards for activities involving vertebrate animals are required to comply with PHS Policy or provide evidence that acceptable standards for the humane care and use of animals will be met. Foreign applicant organizations are not required to submit IACUC approval, but should provide information that is satisfactory to the Government to provide assurances for the humane care of such animals.

H.9. APPROVAL OF REQUIRED ASSURANCE BY OLAW

Under governing regulations, federal funds which are administered by the Department of Health and Human Services, Office of Biomedical Advanced Research and Development Authority (BARDA) shall not be expended by the Contractor for research involving live vertebrate animals, nor shall live vertebrate animals be involved in research activities by the Contractor under this award unless a satisfactory assurance of compliance with 7 U.S.C. 2316 and 9 CFR Sections 2.25-2.28 is submitted within 30 days of the date of this award and approved by the Office of Laboratory Animal Welfare (OLAW). Each performance site (if any) must also assure compliance with 7 U.S.C. 2316 and 9 CFR Sections 2.25-2.28 with the following restriction: Only activities which do not directly involve live vertebrate animals (i.e. are clearly severable and independent from those activities that do involve live vertebrate animals) may be conducted by the Contractor or individual performance sites pending OLAW approval of their respective assurance of compliance with 7 U.S.C. 2316 and 9 CFR Sections 2.25-2.28. Additional information regarding OLAW may be obtained via the Internet at http://grants2.nih.gov/grants/olaw/references/phspol.htm

H.10. REPORTING MATTERS INVOLVING FRAUD, WASTE AND ABUSE

Anyone who becomes aware of the existence or apparent existence of fraud, waste and abuse in BARDA funded programs should report such matters to the HHS Inspector General's Office in writing or on the Inspector General's Hotline. The toll free number is 1-800-HHS-TIPS (1-800- 447-8477). All telephone calls will be handled confidentially. The e-mail address is Htips@os.dhhs.gov and the mailing address is:

Office of Inspector General
Department of Health and Human Services TIPS HOTLINE
P.O. Box 23489 Washington, D.C. 20026

H.11. PROHIBITION ON CONTRACTOR INVOLVEMENT WITH TERRORIST ACTIVITIES

The Contractor acknowledges that U.S. Executive Orders and Laws, including but not limited to 13224 and P.L. 107-56, prohibit transactions with, and the provision of resources and support to, individuals and organizations associated with terrorism. It is the legal responsibility of the Contractor to ensure compliance with these Executive Orders and Laws. This clause must be included in all subcontracts issued under this contract.

H.12. IDENTIFICATION AND DISPOSITION OF DATA

The Contractor will be required to provide certain data generated under this contract to the Department of Health and Human Services (DHHS). DHHS reserves the right to review any other data determined by DHHS to be relevant to this contract. The Contractor shall keep copies of all data required by the Food and Drug Administration (FDA) relevant to this contract for the time specified by the FDA.

H.13. EXPORT CONTROL NOTIFICATION

Contractors are responsible for ensuring compliance with all export control laws and regulations that may be applicable to the export of and foreign access to their proposed technologies. Contractors may consult with the Department of State with any questions regarding the International Traffic in Arms Regulation (ITAR) (22 CRF Parts 120-130) and /or the Department of Commerce regarding the Export Administration Regulations (15 CRF Parts 730-774).

H.14. CONFLICT OF INTEREST

The Contractor represents and warrants that, to the best of the Contractor's knowledge and belief, there are no relevant facts or circumstances which could give rise to an organizational conflict of interest, as defined in FAR 2.101 and Subpart 9.5, and that the Contractor has disclosed all such relevant information. Prior to commencement of any work, the Contractor agrees to notify the Contracting Officer promptly that, to the best of its knowledge and belief, no actual or potential conflict of interest exists or to identify to the Contracting Officer any actual or potential conflict of interest the firm may have. In emergency situations, however, work may begin but notification shall be made within five (5) working days. The Contractor agrees that if an actual or potential organizational conflict of interest is identified during performance, the Contractor shall promptly make a full disclosure in writing to the Contracting Officer. This disclosure shall include a description of actions which the Contractor has taken or proposes to take, after consultation with the Contracting Officer, to avoid, mitigate, or neutralize the actual or potential conflict of interest. The Contractor shall continue performance until notified by the Contracting Officer of any contrary action to be taken. Remedies include termination of this contract for convenience, in whole or in part, if the Contracting Officer deems such termination necessary to avoid an organizational conflict of interest. If the Contractor was aware of a potential organizational conflict of interest prior to award or discovered an actual or potential conflict after award and did not disclose it or misrepresented relevant information to the Contracting Officer, the Government may terminate the contract for default, debar the Contractor from Government contracting, or pursue such other remedies as may be permitted by law or this contract.

H.15. INSTITUTIONAL RESPONSIBILITY REGARDING INVESTIGATOR FINANCIAL CONFLICTS OF INTEREST

The Contractor shall comply with the requirements of 45 CFR Part 94, Responsible Prospective Contractors, which promotes objectivity in research by establishing standards to ensure that Investigators (defined as the project director or principal Investigator and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded under BARDA contracts, or proposed for such funding, which may include, for example, collaborators or consultants) will not be biased by any Investigator financial conflicts of interest.

If the failure of an Investigator to comply with an Institution's financial conflicts of interest policy or a financial conflict of interest management plan appears to have biased the design, conduct, or reporting of the BARDA-funded research, the Contractor must promptly notify the Contracting Officer of the corrective action taken or to be taken. The Contracting Officer will consider the situation and, as necessary, take appropriate action or refer the matter to the Contractor for further action, which may include directions to the Contractor on how to maintain appropriate objectivity in the BARDA-funded research project.

The Contracting Officer and/or HHS may inquire at any time before, during, or after award into any Investigator disclosure of financial interests, and the Contractor's review of, and response to, such disclosure, regardless of whether the disclosure resulted in the Contractor's determination of a financial conflict of interests. The Contracting Officer may require submission of the records or review them on site. On the basis of this review of records or other information that may be available, the Contracting Officer may decide that a particular financial conflict of interest will bias the objectivity of the BARDA-funded research to such an extent that further corrective action is needed or that the Institution has not managed the financial conflict of interest in accordance with 45 CFR Part 94. The issuance of a Stop Work Order by the Contracting Officer may be necessary until the matter is resolved.

If the Contracting Officer determines that BARDA-funded clinical research, whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment, has been designed, conducted, or reported by an Investigator with a financial conflict of interest that was not disclosed managed or reported the Contractor shall require the Investigator involved to disclose the financial conflict of interest in each public presentation of the results of the research and to request an addendum to previously published presentations.

The Contractor shall comply with the requirements of 45 CFR Part 94, Responsible Prospective

Contractors, which promotes objectivity in research by establishing standards to ensure that investigators (defined as the principal investigator and any other person who is responsible for the design, conduct, or reporting of research funded under BARDA contracts) will not be biased by any conflicting financial interest. 45 CFR Part 94 is available at the following Web site: http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=cc7504e541bc62939c52389e9afc27d5&rgn=div5&view=text&node=45:1.0.1.1.51&idno=45

As required by 45 CFR Part 94, the Contractor shall, at a minimum:

52. Maintain a written, enforceable policy on conflict of interest that complies with 45 CFR Part 94 and inform each investigator of the policy, the investigator's reporting responsibilities, and the applicable regulations. The Contractor must take reasonable steps to ensure that investigators working as collaborators or subcontractors comply with the regulations.

52. Designate an official(s) to solicit and review financial disclosure statements from each investigator participating in BARDA-funded research. Based on established guidelines consistent with the regulations, the designated official(s) must determine whether a conflict of interest exists, and if so, determine what actions should be taken to manage, reduce, or eliminate such conflict. A conflict of interest exists when the designated official(s) reasonably determines that a *Significant Financial Interest* could directly and significantly affect the design, conduct, or reporting of the BARDA-funded research. The Contractor may require the management of other conflicting financial interests in addition to those described in this paragraph, as it deems appropriate. Examples of conditions or restrictions that might be imposed to manage actual or potential conflicts of interests are included in 45 CFR Part 94, under Management of Conflicting Interests.

52. Require all financial disclosures to be updated during the period of the award, either on an annual basis or as new reportable Significant Financial Interests are obtained.

52. Maintain records, identifiable to each award, of all financial disclosures and all actions taken by the Contractor with respect to each conflicting interest 3 years after final payment or, where applicable, for the other time periods specified in 48 CFR Part 4, subpart 4.7, Contract Records Retention.

52. Establish adequate enforcement mechanisms and provide for sanctions where appropriate.

If a conflict of interest is identified, the Contractor shall report to the Contracting Officer, the existence of the conflicting interest found. This report shall be made and the conflicting interest managed, reduced, or eliminated, at least on a temporary basis, within sixty (60) days of that identification.

If the failure of an investigator to comply with the conflict of interest policy has biased the design, conduct, or reporting of the BARDA-funded research, the Contractor must promptly notify the Contracting Officer of the corrective action taken or to be taken. The Contracting Officer will take appropriate action or refer the matter to the Contractor for further action, which may include directions to the Contractor on how to maintain appropriate objectivity in the funded research.

The Contracting Officer may at any time inquire into the Contractor's procedures and actions regarding conflicts of interests in BARDA-funded research, including a review of all records pertinent to compliance with 45 CFR Part 94. The Contracting Officer may require submission of the records or review them on site. On the basis of this review, the Contracting Officer may decide that a particular conflict of interest will bias the objectivity of the BARDA-funded research to such an extent that further corrective action is needed or that the Contractor has not managed, reduced, or eliminated the conflict of interest. The issuance of a Stop Work Order by the Contracting Officer may be necessary until the matter is resolved.

If the Contracting Officer determines that BARDA-funded clinical research, whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment, has been designed, conducted, or reported by an investigator with a conflict of interest that was not disclosed or managed, the Contractor must require disclosure of the conflict of interest in each public presentation of the results of the research.

H.16. NEEDLE DISTRIBUTION

The Contractor shall not use contract funds to carry out any program of distributing sterile needles or syringes for the hypodermic injection of any illegal drug.

H.17. RESTRICTION ON ABORTIONS

The Contractor shall not use contract funds for any abortion.

H.18. CONTINUED BAN ON FUNDING OF HUMAN EMBRYO RESEARCH

The Contractor shall not use contract funds for (1) the creation of a human embryo or embryos for research purposes; or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR 46.204(b) and Section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)). The term "human embryo or embryos" includes any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells.

Additionally, in accordance with a March 4, 1997 Presidential Memorandum, Federal funds may not be used for cloning of human beings.

H.19. DISSEMINATION OF FALSE OR DELIBERATELY MISLEADING INFORMATION

The Contractor shall not use contract funds to disseminate information that is deliberately false or misleading.

H.20. CONFIDENTIALITY OF INFORMATION

[Reserved]

H.21. ACCESS TO DOCUMENTATION/DATA

The Government shall have physical and electronic access to all documentation and data generated under this contract, including: all data documenting Contractor performance; all data generated; all communications and correspondence with regulatory agencies and bodies to include all audit observations, inspection reports, milestone completion documents, and all Offeror commitments and responses. Contractor shall provide the Government with an electronic copy of all correspondence and submissions to the FDA within 5 business days of receipt. The Government shall acquire unlimited rights to all data funded or furnished without proprietary restrictions under this contract in accordance with FAR Subpart 27.4 and FAR Clause 52.227-14.

H.22. EPA ENERGY STAR REQUIREMENTS

In compliance with Executive Order 12845 (requiring Agencies to purchase energy efficient computer equipment), all microcomputers, including personal computers, monitors, and printers that are purchased using Government funds in performance of a contract shall be equipped with or meet the energy efficient low-power standby feature as defined by the EPA Energy Star program unless the equipment always meets EPA Energy Star efficiency levels. The microcomputer, as configured with all components, must be Energy Star compliant.

This low-power feature must already be activated when the computer equipment is delivered to the agency and be of equivalent functionality of similar power managed models. If the equipment will be used on a local area network, the vendor must provide equipment that is fully compatible with the network environment. In addition, the equipment will run commercial off-the-shelf software both before and after recovery from its energy conservation mode.

H.23. ACKNOWLEDGMENT OF FEDERAL FUNDING

Section 507 of P.L. 104-208 mandates that Contractors funded with Federal dollars, in whole or in part, acknowledge Federal funding when issuing statements, press releases, requests for proposals, bid solicitations and other documents. This requirement is in addition to the continuing requirement to provide an acknowledgment of support and disclaimer on any publication reporting the results of a contract funded activity.

Publication and Publicity

No information related to data obtained under this contract shall be released or publicized without providing BARDA with at least thirty (30) days advanced notice and an opportunity to review the proposed release or publication.

In addition to the requirements set forth in HHSAR Clause 352.227-70, Publications and Publicity incorporated by reference in Section I of this contract, Section 507 of P.L. 104-208 mandates that Contractors funded with Federal dollars, in whole or in part, acknowledge Federal funding when issuing statements, press releases, requests for proposals, bid solicitations and other documents. Contractors are required to state:

(1) The percentage and dollar amounts of the total program or project costs financed with Federal money and;

(2) The percentage and dollar amount of the total costs financed by non-governmental sources. For purposes of this contract "publication" is defined as an issue of printed material offered for distribution or any communication or oral presentation of information, including any manuscript or scientific meeting abstract. Any publication containing data generated under this contract must be submitted for BARDA review no less than thirty (30) calendar days for manuscripts and fifteen (15) calendar days for abstracts

before submission for public presentation or publication. Contract support shall be acknowledged in all such publications substantially as follows:

"This project has been funded in whole or in part with Federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, under Contract No. HHSO100201800023C."

Press Releases

Misrepresenting contract results or releasing information that is injurious to the integrity of BARDA may be construed as improper conduct. Press releases shall be considered to include the public release of information to any medium, excluding peer-reviewed scientific publications. With the exception of ad-hoc press releases required by applicable law or regulations, the Contractor shall ensure that the COR has received an advance copy of any press release related to the contract not less than two (2) business days prior to the issuance of the press release.

The Contractor shall acknowledge the support of the Department of Health and Human Service, Office of the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority, whenever publicizing the work under this contract in any media by including an acknowledgment substantially as follows:

"This project has been funded in whole or in part with Federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, under Contract No. HHSO100201800023C."

H.24. PROHIBITION ON THE USE OF APPROPRIATED FUNDS FOR LOBBYING ACTIVITIES AND HHSAR 352.203-70 ANTI-LOBBYING (December 2015)

Pursuant to the HHS annual appropriations acts, except for normal and recognized executive- legislative relationships, the Contractor shall not use any HHS contract funds for:

(a) Publicity or propaganda purposes;

(b) The preparation, distribution, or use of any kit, pamphlet, booklet, publication, electronic communication, radio, television, or video presentation designed to support or defeat the enactment of legislation before the Congress or any State or local legislature or legislative body, except in presentation to the Congress or any state or local legislature itself; or designed to support or defeat any proposed or pending regulation, administrative action, or order issued by the executive branch of any state or local government, except in presentation to the executive branch of any state or local government itself; or

(c) Payment of salary or expenses of the Contractor, or any agent acting for the Contractor, related to any activity designed to influence the enactment of legislation, appropriations, regulation, administrative action, or Executive order proposed or pending before the Congress or any state government, state legislature or local legislature or legislative body, other than for normal and recognized executive-legislative relationships or participation by an agency or officer of a state, local, or tribal government in policymaking and administrative processes within the executive branch of that government.

(d) The prohibitions in subSections (a), (b), and (c) above shall include any activity to advocate or promote any proposed, pending, or future federal, state, or local tax increase, or any proposed, pending, or future requirement for, or restriction on, any legal consumer product, including its sale or marketing, including, but not limited to, the advocacy or promotion of gun control.

H.25. PRIVACY ACT APPLICABILITY

Notification is hereby given that the Contractor and its employees are subject to criminal penalties for violation of the Privacy Act to the same extent as employees of the Government. The Contractor shall assure that each of its employees knows the prescribed rules of conduct and that each is aware that he or she can be subjected to criminal penalty for violation of the Act. A copy of 45 CFR Part 5b, Privacy Act Regulations, may be obtained at https://www.gpo.gov/fdsys/granule/CFR-2007- title45-vol1/CFR-2007-title45-vol1-part5b

The Project Officer is hereby designated as the official who is responsible for monitoring contractor compliance with the Privacy Act.

The Contractor shall follow the Privacy Act guidance as contained in the Privacy Act System of Records number 09-25-0200. This document may be obtained at the following link: http://oma.od.nih.gov/ms/privacy/pa-files/0200.htm

H.26. LABORATORY LICENSE REQUIREMENTS

The Contractor shall comply with all applicable requirements of Section 353 of the Public Health Service Act (Clinical Laboratory Improvement Act as amended) (42 U.S.C. 263a and 42 CFR Part 493). This requirement shall also be included in any subcontract for services under the contract.

H.27. QUALITY ASSURANCE (QA) AUDIT REPORTS

BARDA reserves the right to participate in QA audits as related to activities funded under this contract. Upon completion of the audit/site visit the Contractor shall provide a report capturing the findings, results and next steps in proceeding with the subcontractor. If action is requested of the subcontractor, detailed concerns for addressing areas of non-conformance to FDA regulations for GLP, GMP, or GCP guidelines, as identified in the audit report, must be provided to BARDA. The Contractor shall provide responses from the subcontractors to address these concerns and plans for corrective action execution.

- Contractor shall notify CO and COR of upcoming, ongoing, or recent audits/site visits of subcontractors as part of weekly communications.
- Contractor shall notify the COR and CO within five (5) business days of report completion.

H.28. BARDA AUDITS

Contractor shall accommodate periodic or reasonable ad hoc site visits during normal business hours by the Government with forty-eight (48) hours advance notice. If the Government, the Contractor, or other parties identifies any issues during an audit, the Contractor shall capture the issues, identify potential solutions, and provide a report to the Government.

- If issues are identified during the audit, Contractor shall submit a report to the CO and COR detailing the finding and corrective action(s) within 10 business days of the audit.
- COR and CO will review the report and provide a response to the Contractor with ten (10) business days.
- Once corrective action is completed, the Contractor will provide a final report to the CO and COR.

H.29. RESTRICTION ON EMPLOYMENT OF UNAUTHORIZED ALIEN WORKERS

The Contractor shall not use contract funds to employ workers described in Section 274A (h)(3) of the Immigration and National Act, which reads as follows:

"(3) Definition of unauthorized alien – As used in this Section, the term 'unauthorized alien' with respect to the employment of an alien at a particular time, that the alien is not at that time either an alien lawfully admitted for permanent residence, or (B) authorized to be so employed by this Act or by the Attorney General."

H.30. NOTIFICATION OF CRITICAL PROGRAMMATIC CONCERNS, RISKS, OR POTENTIAL RISKS

If any action occurs that creates a cause for critical programmatic concern, risk, or potential risk to BARDA or the Contractor and Incident Report shall be delivered to BARDA.

- Within 48 hours of activity or incident or within 24 hours for a security related activity or incident, Contractor must notify BARDA.
- Additional updates due to COR and CO within 48 hours of additional developments.
- Contractor shall submit within 5 business days a Corrective Action Plan (if deemed necessary by either party) to address any potential issues.

If corrective action is deemed necessary, Contractor must address in writing, its consideration of concerns raised by BARDA within 5 business days.

H.31. PROTECTION OF PERSONNEL WHO WORK WITH NONHUMAN PRIMATES

All Contractor personnel who work with nonhuman primates or enter rooms or areas containing nonhuman primates shall comply with the procedures set forth in NIH Policy Manual 3044-2, entitled, "Protection of NIH Personnel Who Work with Nonhuman Primates," located at the following URL: http://www1.od.nih.gov/oma/manualchapters/intramural/3044-2/

H.32. DISSEMINATION OF INFORMATION (May 2004)

Other than scientific and technical Sections for which the contractor can assert a copyright under FAR Clause 52.227-14 I no information related to data obtained under this contract shall be released or publicized without the prior written consent of the Contracting Officer. In the event that the contractor seeks to publicize data through a scientific or technical Section, the contractor shall provide BARDA, through the COR, with a minimum of thirty (30) business days to review the Section prior to publication.

H.33. REGISTRATION WITH THE SELECT AGENT PROGRAM FOR WORK INVOLVING THE POSSESSION, USE, AND/OR TRANSFER OF SELECT BIOLOGICAL AGENTS OR TOXINS

Work involving select biological agents or toxins shall not be conducted under this contract until the Contractor and any affected subcontractor(s) are granted a certificate of registration or are authorized to work with the applicable select agents.

For prime or subcontract awards to domestic institutions who possess, use, and/or transfer Select Agents under this contract, the institution must complete registration with the Centers for Disease Control and Prevention (CDC), Department of Health and Human Services (DHHS) or the Animal and Plant Health Inspection Services (APHIS), U.S. Department of Agriculture (USDA), as applicable, before performing work involving Select Agents, in accordance with 42 CFR 73. No Government funds can be used for work involving Select Agents, as defined in 42 CFR 73, if the final registration certificate is denied.

For prime or subcontract awards to foreign institutions who possess, use, and/or transfer Select Agents under this contract, the institution must provide information satisfactory to the Government that a process equivalent to that described in 42 CFR 73 (http://www.cdc.gov/od/sap/docs/42cfr73.pdf) for U.S. institutions is in place and will be administered on behalf of all Select Agent work sponsored by these funds before using these funds for any work directly involving the Select Agents. The Contractor must provide information addressing the following key elements appropriate for the foreign institution: safety, security, training, procedures for ensuring that only approved/appropriate individuals have access to the Select Agents, and any applicable laws, regulations and policies equivalent to 42 CFR 73. The Government will assess the policies and procedures for comparability to the U.S. requirements described in 42 CFR Part 73. When requested by the contracting officer, the Contractor shall provide key information delineating any laws, regulations, policies, and procedures applicable to the foreign institution for the safe and secure possession, use, and transfer of Select Agents. This includes summaries of safety, security, and training plans, and applicable laws, regulations, and policies. For the purpose of security risk assessments, the Contractor must provide the names of all individuals at the foreign institution who will have access to the Select Agents and procedures for ensuring that only approved and appropriate individuals have access to Select Agents under the contract.

Listings of HHS select agents and toxins, biologic agents and toxins, and overlap agents or toxins as well as information about the registration process, can be obtained on the Select Agent Program Web site at http://selectagents.gov

H.34. MANUFACTURING STANDARDS

The Good Manufacturing Practice Regulations (GMP)(21 CFR Parts 820) will be the standard to be applied for manufacturing, processing, packaging, storage and delivery of this product.

If at any time during the life of the contract, the Contractor fails to comply with GMP in the manufacturing, processing, packaging, storage, stability and other testing of the manufactured drug substance or product and delivery of this product and such failure results in a material adverse effect on the safety, purity or potency of the product (a material failure) as identified by the FDA, the Contractor shall have thirty (30) calendar days from the time such material failure is identified to cure such material failure. If, within the thirty (30) calendar day period, the Contractor fails to take such an action to the satisfaction of the Government Project Officer, or fails to provide a remediation plan that is acceptable to the COR, then the contract may be terminated.

H.35. IN-PROCESS REVIEW

In Process Reviews (IPR) will be conducted at the discretion of the Government to discuss the progression of the milestones. The Government reserves the right to revise the milestones and budget pending the development of the project. Deliverables such as an overall project summary report and/or slides will be required when the IPRs are conducted. The Contractor's success in completing the required tasks under each work segment must be demonstrated through the Deliverables and Milestones specified under Section F. Those deliverables will constitute the basis for the Government's decision, at its sole discretion, to proceed with the work segment, or institute changes to the work segment, or terminate the work segment.

IPRs may be scheduled at the discretion of the Government to discuss progression of the contract. The Contractor shall provide a presentation following a prescribed template which will be provided by the Government at least 30 business days prior to the IPR. Subsequently, the contractor will be requested to provide a revised/final presentation to the Contracting Officer at least 10 business days prior to the IPR.

H.36. LABORATORY LICENSE REQUIREMENTS

The contractor shall comply with all applicable requirements of the Code of Federal Regulations Title 21, Part 58 and FDA Medical Device GMP Guidance. This requirement shall also be included in any subcontract for services under the contract.

H.37. CARE OF LABORATORY ANIMALS

(a) Notice to Offerors of Requirement for Compliance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals (January 2006)

The Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (PHS Policy) establishes a number of requirements for research activities involving animals. Before award may be made to an applicant organization, the organization shall file, with the Office of Laboratory Animal Welfare (OLAW), National Institutes of Health (NIH), a written Animal Welfare Assurance (Assurance) which commits the organization to comply with the provisions of the PHS Policy, the Animal Welfare Act, and the Guide for the Care and Use of Laboratory Animals (National Academy Press, Washington, DC). In accordance with the PHS Policy, applicant organizations must establish an Institutional Animal Care & Use Committee (IACUC), qualified through the experience and expertise of its members, to oversee the institution's animal program, facilities and procedures. Applicant organizations are required to provide verification of IACUC approval prior to release of an award involving live vertebrate animals. No award involving the use of animals shall be made unless OLAW approves the Assurance and verification of IACUC approval for the proposed animal activities has been provided to the Contracting Officer. Prior to award, the Contracting Officer will notify Contractor(s) selected for projects that involve live vertebrate animals that an Assurance and verification of IACUC approval are required. The Contracting Officer will request that OLAW negotiate an acceptable Assurance with those Contractor(s) and request verification of IACUC approval. For further information, contact OLAW at NIH, 6705 Rockledge Drive, RKL1, Suite 360, MSC 7982 Bethesda, Maryland 20892–7982 (E-mail: *olaw@od.nih.gov* ; Phone: 301–496–7163).

H.38. HUMAN SUBJECTS

The Contractor shall submit all human clinical protocols and informed consent documents to BARDA for review and comment prior to submission to another entity.

Research involving human subjects shall not be conducted under this contract until the study protocol has been approved by the Department of Health and Human Services, written notice of such approval has been provided by the CO, and the Contractor has provided to the CO a properly completed "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263 (formerly Optional Form 310) certifying IRB review and approval of the protocol. The human subject certification can be met by submission of the Contractor's self-designated form, provided that it contains the information required by the "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263 (formerly Optional Form 310).

When research involving Human Subjects will take place at collaborating sites or other performance sites, the Contractor shall obtain, and keep on file, a properly completed "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263 (formerly Optional Form 310) certifying IRB review and approval of the research.

H.39. SHARING RESEARCH DATA

The Contractor's data sharing plan, due date to be determined at contract award, is hereby incorporated by reference. The Contractor agrees to adhere to its plan and shall request prior approval of the Contracting Officer for any changes in its plan.

BARDA endorses the sharing of final research data to serve health. This contract is expected to generate research data that must be shared with the public and other researchers.

BARDA recognizes that data sharing may be complicated or limited, in some cases, by institutional policies, local IRB rules, as well as local, state and Federal laws and regulations, including the Privacy Rule (see HHS-published documentation on the Health Information Privacy at http://www.hhs.gov/ocr/privacy/index.html). The rights and privacy of people who participate in BARDA-funded research must be protected at all times; thus, data intended for broader use should be free of identifiers that would permit linkages to individual research participants and variables that could lead to deductive disclosure of the identity of individual subjects.

H.40 CONTINUED BAN ON FUNDING ABORTION AND CONTINUED BAN ON FUNDING OF HUMAN EMBRYO RESEARCH, HHSAR 352.270-13 (December 2015)

52. The Contractor shall not use any funds obligated under this contract for any abortion.

b. The Contractor shall not use any funds obligated under this contract for the following:
(1) The creation of a human embryo or embryos for research purposes; or
(2) Research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury of death greater than that allowed for research on fetuses in utero under 45 CFR part 46 and Section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)).

52. The term "human embryo or embryos" includes any organism, not protected as a human subject under 45 CFR part 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes of human diploid cells.

52. The Contractor shall not use any Federal funds for the cloning of human beings.

(End of clause)

H.41 PUBLIC ACCESS TO ARCHIVED PUBLICATIONS RESULTING FROM ASPR FUNDED RESEARCH

All ASPR-funded investigators shall submit to the NIH National Library of Medicine's (NLM) PubMed Central (PMC) an electronic version of the author's final manuscript, upon acceptance for publication, of any peer-reviewed scientific publications resulting from research supported in whole or in part with Federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response. ASPR defines the author's final manuscript as the final version accepted for journal publication, and includes all modifications from the publishing peer review process. The PMC archive will preserve permanently these manuscripts for use by the public, health care providers, educators, scientists, and ASPR. The Policy directs electronic submissions to the NIH/NLM/PMC: http://www.pubmedcentral.nih.gov.

H.42 BARDA SECURITY REQUIREMENTS FOR FACILITIES

Security plan must be provided within 60 days if required and security remediation plan (if needed) must be required within 120 days. All security requirements must be met prior to commencing manufacturing of any product. See Section C for a detailed list of security requirements.

PART II – CONTRACT CLAUSES

SECTION I – CONTRACT CLAUSES

I.1. FAR 52.252-2, CLAUSES INCORPORATED BY REFERENCE (FEBRUARY 1998)

This contract incorporates the following clauses by reference, with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available. Also, the full text of a clause may be accessed electronically at: http://www.acquisition.gov/far. HHSAR clauses at http://www.hhs.gov/policies/hhsar/subpart352.html

General Clauses for Cost-Reimbursement Research and Development Contract

a. FEDERAL ACQUISITION REGULATION (FAR) (48 CFR CHAPTER 1) CLAUSES:

Reg	Clause	Date	Clause Title
FAR	52.202-1	Nov 2013	Definitions
FAR	52.203-3	Apr 1984	Gratuities
FAR	52.203-5	May 2014	Covenant Against Contingent Fees
FAR	52.203-6	Sep 2006	Restrictions on Subcontractor Sales to the Government
FAR	52.203-7	May 2014	Anti-Kickback Procedures
FAR	52.203-8	May 2014	Cancellation, Rescission, and Recovery of Funds for Illegal or Improper Activity
FAR	52.203-10	May 2014	Price or Fee Adjustment for Illegal or Improper Activity
FAR	52.203-11	Sept 2007	Certification and Disclosure Regarding Payments to Influence Certain Federal Transactions
FAR	52.203-12	Oct 2010	Limitation on Payments to Influence Certain Federal Transactions
FAR	52.203-13	Oct 2015	Contractor Code of Business Ethics and Conduct
FAR	52.203-14	Oct 2015	Display of Hotline Poster(s)
FAR	52.203-17	Apr 2014	Contractor Employee Whistleblower Rights and Requirement To Inform Employees of Whistleblower Rights
FAR	52.204-1	Dec 1989	Administrative Matters Provisions and Clauses
FAR	52.204-4	May 2011	Printed or Copied Double-Sided on Postconsumer Fiber Content Paper
FAR	52.204-5	Oct 2014	Women-Owned Business (Other Than Small Business)
FAR	52.204-7	Oct 2016	System for Award Management
FAR	52.204-10	Oct 2016	Reporting Executive Compensation and First-Tier Subcontract Awards
FAR	52.204-13	Oct 2016	System for Award Management Maintenance
FAR	52.204-16	Jul 2016	Commercial and Government Entity Code Reporting
FAR	52.204-17	Jul 2016	Ownership of Control or Offeror
FAR	52.204-18	Jul 2015	Commercial and Government Entity Code Maintenance
FAR	52.207-1	May 2006	Notice of Standard Competition
FAR	52.209-5	Oct 2015	Certification Regarding Responsibility Matters
FAR	52.209-6	Oct 2015	Protecting the Government's Interests When Subcontracting With Contractors Debarred, Suspended, or Proposed for Debarment
FAR	52.209-9	Jul 2013	Updates of Publicly Available Information Regarding Responsibility Matters

FAR	52.209-10	Nov 2015	Prohibition on Contracting with Inverted Domestic Corporations
FAR	52.210-1	Apr 2011	Market Research
FAR	52.211-5	Aug 2000	Material Requirements
FAR	52.215-2	Oct 2010	Audit and Records – Negotiation
FAR	52.215-8	Oct 1997	Order of Precedence – Uniform Contract Format
FAR	52.215-10	Aug 2011	Price Reduction for Defective Cost or Pricing Data
FAR	52.215-11	Aug 2011	Price Reduction for Defective Certified Cost or Pricing Data —Modifications.
FAR	52.215-12	Oct 2010	Subcontractor Certified Cost or Pricing Data
FAR	52.215-13	Oct 2010	Subcontractor Certified Cost or Pricing Data—Modifications
FAR	52.215-14	Oct 2010	Integrity of Unit Prices (Over the Simplified Acquisition Threshold
FAR	52.215-15	Oct 2010	Pension Adjustments and Asset Reversions
FAR	52.215-16	June 2003	Facilities Capital Cost of Money
FAR	52.215-17	Oct 1997	Waiver of Facilities Capital Cost of Money
FAR	52.215-18	Jul 2005	Reversion or Adjustment of Plans for Postretirement Benefits (PRB) other than Pensions
FAR	52.215-19	Oct 1997	Notification of Ownership Changes
FAR	52.215-20	Oct 2010	Requirements for Certified Cost or Pricing Data and Data Other Than Certified Cost or Pricing Data
FAR	52.215-21	Oct 2010	Requirements for Certified Cost or Pricing Data and Data Other Than Certified Cost or Pricing Data – Modifications
FAR	52.215-22	Oct 2009	Limitations on Pass-Through Charges—Identification of Subcontract Effort
FAR	52.215-23	Oct 2009	Limitations on Pass-Through Charges
FAR	52.216-7	Aug 2018	Allowable Cost and Payment
FAR	52.216-8	Jun 2011	Fixed Fee
FAR	52.219-8	Nov 2016	Utilization of Small Business Concerns
FAR	52.219-9	Aug 2018	Small Business Subcontracting Plan
FAR	52.219-10	Oct 2014	Incentive Subcontracting Program
FAR	52.219-16	Jan 1999	Liquidated Damages – Subcontracting Plan
FAR	52.219-28	Jul 2013	Post-Award Small Business Program Representation
FAR	52.222-3	Jun 2003	Convict Labor
FAR	52.222-21	Apr 2015	Prohibition of Segregated Facilities
FAR	52.222-24	Feb 1999	Pre-award On-Site Equal Opportunity Compliance Evaluation
FAR	52.222-25	Apr 1984	Affirmative Action Compliance
FAR	52.222-26	Sept 2016	Equal Opportunity
FAR	52.222-35	Oct 2015	Equal Opportunity for Veterans ($150,000 or more)
FAR	52.222-36	Jul 2014	Equal Opportunity for Workers with Disabilities
FAR	52.222-37	Feb 2016	Employment Reports on Veterans
FAR	52.222-38	Feb 2016	Compliance with Veterans' Employment Reporting Requirements
FAR	52.222-40	Dec 2010	Notification of Employee Rights Under the National Labor Relations Act
FAR	52.222-50	Mar 2015	Combating Trafficking in Persons
FAR	52.222-54	Oct 2015	Employment Eligibility Verification
FAR	52.222-59	Dec 2016	Compliance With Labor Laws (Executive Order 13673)

FAR	52.222-60	Oct 2016	Paycheck Transparency (Executive Order 13673)
FAR	52.222-61	Dec 2016	Arbitration of Contractor Employee Claims (Executive Order 13673)
FAR	52.222-62	Jan 2017	Paid Sick Leave Under Executive Order 13706
FAR	52.223-6	May 2001	Drug-Free Workplace
FAR	52.223-18	Aug 2011	Encouraging Contractor Policy to Ban Text Messaging While Driving
FAR	52.225-13	Jun 2008	Restrictions on Certain Foreign Purchases
FAR	52.225-25	Oct 2015	Prohibition on Contracting with Entities Engaging in Certain Activities or Transactions Relating to Iran—Representation and Certifications
FAR	52.226-1	Jun 2000	Utilization of Indian Organizations and Indian-Owned Economic Enterprises.
FAR	52.227-1	Dec 2007	Authorization and Consent, Alternate 1 (APR 1984)
FAR	52.227-2	Dec 2007	Notice and Assistance Regarding Patent and Copyright Infringement
FAR	52.227-3	Apr 1984	Patent Indemnity
FAR	52.227-11	May 2014	Patent Rights – Ownership by the Contractor
FAR	52.227-14	May 2014	Rights in Data – General
FAR	52.227-14 Alt. II	Dec 2007	Rights in Data – General – Limited Rights Notice
FAR	52.227-15	Dec 2007	Representation of Limited Rights Data and Restricted Computer Software
FAR	52.227-16	June 1987	Additional Data Requirements
FAR	52.228-7	Mar 1996	Insurance – Liability to Third Persons
FAR	52.230-2	Oct 2015	Cost Accounting Standards
FAR	52.230-3	Oct 2015	Disclosure and Consistency of Cost Accounting Practices
FAR	52.230-6	Jun 2010	Administration of Cost Accounting Standards
FAR	52.230-7	Apr 2005	Proposal Disclosure—Cost Accounting Practice Changes
FAR	52.232-9	Apr 1984	Limitation on Withholding of Payments
FAR	52.232-17	May 2014	Interest
FAR	52.232-20	Apr 1984	Limitation of Cost
FAR	52.232-23	May 2014	Assignment of Claims
FAR	52.232-25	Jan 2017	Prompt Payment
FAR	52.232-33	Jul 2013	Payment by Electronic Funds Transfer–System for Award Management
FAR	52.232.39	Jun 2013	Unenforceability of Unauthorized Obligations
FAR	52.232-40	Dec 2013	Providing Accelerated Payments to Small Business Subcontractors
FAR	52.233-1	May 2014	Disputes
FAR	52.233-3	Aug 1996	Protest After Award, Alternate 1 (Jun 1985)
FAR	52.233-4	Oct 2004	Applicable Law for Breach of Contract Claim
FAR	52.242-1	Apr 1984	Notice of Intent to Disallow Costs
FAR	52.242-3	May 2014	Penalties for Unallowable Costs
FAR	52.242-4	Jan 1997	Certification of Final Indirect Costs
FAR	52.242-13	Jul 1995	Bankruptcy
FAR	52.243-2	Aug 1987	Changes – Cost-Reimbursement Alternate V (Apr 1984)

FAR	52.244-2	Oct 2010	Subcontracts, Alternate 1 (Jun 2007)
FAR	52.244-5	Dec 1996	Competition in Subcontracting
FAR	52.244-6	Aug 2018	Subcontracts for Commercial Items
FAR	52.245-1	Apr 2012	Government Property
FAR	52.245-9	Apr 2012	Use and Charges
FAR	52.246-23	Feb 1997	Limitation of Liability
FAR	52.249-6	May 2004	Termination (Cost-Reimbursement)
FAR	52.249-14	Apr 1984	Excusable Delays
FAR	52.253-1	Jan 1991	Computer Generated Forms

b. DEPARTMENT OF HEALTH AND HUMAN SERVICES ACQUISITION REGULATION (HHSAR) (48 CFR CHAPTER 3) CLAUSES:

HHSAR	352.203-70	Dec 2015	Anti-Lobbying
HHSAR	352.208-70	Dec 2015	Printing and Duplication
HHSAR	352.211-3	Dec 2015	Paperwork Reduction Act
HHSAR	352.219-70	Dec 2015	Mentor-Protégé Program
HHSAR	352.219-71	Dec 2015	Mentor-Protégé Program Reporting Requirements
HHSAR	352.222-70	Dec 2015	Contractor Cooperation in Equal Employment Opportunity Investigations
HHSAR	352.223-70	Dec 2015	Safety and Health
HHSAR	352.224-70	Dec 2015	Privacy Act
HHSAR	352.224-71	Dec 2016	Confidential Information
HHSAR	352.227-70	Dec 2015	Publications and Publicity
HHSAR	352.231-70	Dec 2015	Salary Rate Limitation
HHSAR	352.233-71	Dec 2015	Litigation and Claims
HHSAR	352.237-75	Dec 2015	Key Personnel
HHSAR	352.239-74	Dec 2015	Electronic and Information Technology Accessibility
HHSAR	352.270-9	Dec 2015	Non-discrimination for Conscience

I.2. ADDITIONAL FAR CONTRACT CLAUSES INCLUDED IN FULL TEXT

This contract incorporates the following clauses in full text. FEDERAL ACQUISITION REGULATION (FAR) (48 CFR CHAPTER 1) CLAUSES:

FAR Clause 52.217-8 Option to Extend Services (Nov 1999)

The Government may require continued performance of any services within the limits and at the rates specified in the contract. These rates may be adjusted only as a result of revisions to prevailing labor rates provided by the Secretary of Labor. The option provision may be exercised more than once, but the total extension of performance hereunder shall not exceed 6 months. The Contracting Officer may exercise the option by written notice to the Contractor within 30 days of end of period of performance.

FAR Clause 52.217-9, Option to Extend the Term of the Contract (Mar 2000)

The Government may extend the term of this contract by written notice to the Contractor within 15 days provided that the Government gives the Contractor a preliminary written notice of its intent to extend at least 30 days before the contract expires. The preliminary notice does not commit the Government to an extension.

- If the Government exercises this option, the extended contract shall be considered to include this option clause.

- The total duration of this contract, including the exercise of any options under this clause, shall not exceed 10 years.

FAR Clause 52.219-28, Post-Award Small Business Program Representation (July 2013)

a. *Definitions*. As used in this clause--

Long-term contract means a contract of more than five years in duration, including options. However, the term does not include contracts that exceed five years in duration because the period of performance has been extended for a cumulative period not to exceed six months under the clause at 52.217-8, Option to Extend services, or other appropriate authority.

Small business concern means a concern, including its affiliates, that is independently owned and operated, not dominant in the field of operation in which it is bidding on Government contracts, and qualified as a small business under the criteria in 13 CFR part 121 and the size standard in paragraph (c) of this clause. Such a concern is "not dominant in its field of operation" when it does not exercise a controlling or major influence on a national basis in a kind of business activity in which a number of business concerns are primarily engaged. In determining whether dominance exists, consideration shall be given to all appropriate factors, including volume of business, number of employees, financial resources, competitive status or position, ownership or control of materials, processes, patents, license agreements, facilities, sales territory, and nature of business activity.

b. If the Contractor represented that it was a small business concern prior to award of this contract, the Contractor shall re-represent its size status according to paragraph (e) of this clause or, if applicable, paragraph (g) of this clause, upon the occurrence of any of the following:

(1) Within 30 days after execution of a novation agreement or within 30 days after modification of the contract to include this clause, if the novation agreement was executed prior to inclusion of this clause in the contract.

(2) Within 30 days after a merger or acquisition that does not require a novation or within 30 days after modification of the contract to include this clause, if the merger or acquisition occurred prior to inclusion of this clause in the contract.

(3) For long-term contracts--

(i) Within 60 to 120 days prior to the end of the fifth year of the contract; and
(ii) Within 60 to 120 days prior to the date specified in the contract for exercising any option thereafter.

c. The Contractor shall represent its size status in accordance with the size standard in effect at the time of this re-representation that corresponds to the North American Industry Classification System (NAICS) code assigned to this contract. The small business size standard corresponding to this NAICS code can be found at http://www.sba.gov/content/table-small-business-size-standards

d. The small business size standard for a Contractor providing a product which it does not manufacture itself, for a contract other than a construction or service contract, is 500 employees.

e. Except as provided in paragraph (g) of this clause, the Contractor shall make the representation required by paragraph (b) of this clause by validating or updating all its representations in the Representations and Certifications Section of the System for Award Management (SAM) and its other data in SAM, as necessary, to ensure that they reflect the Contractor's current status. The Contractor shall notify the contracting office in writing within the timeframes specified in paragraph (b) of this clause that the data have been validated or updated, and provide the date of the validation or update.

f. If the Contractor represented that it was other than a small business concern prior to award of this contract, the Contractor may, but is not required to, take the actions required by paragraphs (e) or (g) of this clause.

g. If the Contractor does not have representations and certifications in SAM, or does not have a representation in SAM for the NAICS code applicable to this contract, the Contractor is required to complete the following representation and submit it to the contracting office, along with the contract number and the date on which the representation was completed:

The Contractor represents that it [X] is, [ ] is not a small business concern under NAICS Code 541714 assigned to contract number HHSO100201800023C.

FAR 52.204-21 Basic Safeguarding of Covered Contractor Information Systems (Jun 2016)

(a) *Definitions*. As used in this clause--

"Covered contractor information system" means an information system that is owned or operated by a contractor that processes, stores, or transmits Federal contract information.

"Federal contract information" means information, not intended for public release, that is provided by or generated for the Government under a contract to develop or deliver a product or service to the Government, but not including information provided by the Government to the public (such as on public Web sites) or simple transactional information, such as necessary to process payments.

"Information" means any communication or representation of knowledge such as facts, data, or opinions, in any medium or form, including textual, numerical, graphic, cartographic, narrative, or audiovisual (Committee on National Security Systems Instruction (CNSSI) 4009).

"Information system" means a discrete set of information resources organized for the collection, processing, maintenance, use, sharing, dissemination, or disposition of information (44 U.S.C. 3502).

"Safeguarding" means measures or controls that are prescribed to protect information systems.

(b) Safeguarding requirements and procedures.

(1) The Contractor shall apply the following basic safeguarding requirements and procedures to protect covered contractor information systems. Requirements and procedures for basic safeguarding of covered contractor information systems shall include, at a minimum, the following security controls:

(i) Limit information system access to authorized users, processes acting on behalf of authorized users, or devices (including other information systems).

(ii) Limit information system access to the types of transactions and functions that authorized users are permitted to execute.

(iii) Verify and control/limit connections to and use of external information systems.

(iv) Control information posted or processed on publicly accessible information systems.

(v) Identify information system users, processes acting on behalf of users, or devices.

(vi) Authenticate (or verify) the identities of those users, processes, or devices, as a prerequisite to allowing access to organizational information systems.

(vii) Sanitize or destroy information system media containing Federal Contract Information before disposal or release for reuse.

(viii) Limit physical access to organizational information systems, equipment, and the respective operating environments to authorized individuals.

(ix) Escort visitors and monitor visitor activity; maintain audit logs of physical access; and control and manage physical access devices.

(x) Monitor, control, and protect organizational communications (i.e., information transmitted or received by organizational information systems) at the external boundaries and key internal boundaries of the information systems.

(xi) Implement subnetworks for publicly accessible system components that are physically or logically separated from internal networks.

(xii) Identify, report, and correct information and information system flaws in a timely manner.

(xiii) Provide protection from malicious code at appropriate locations within organizational information systems.

(xiv) Update malicious code protection mechanisms when new releases are available.

(xv) Perform periodic scans of the information system and real-time scans of files from external sources as files are downloaded, opened, or executed.

(2) *Other requirements*. This clause does not relieve the Contractor of any other specific safeguarding requirements specified by Federal agencies and departments relating to covered contractor information systems generally or other Federal safeguarding requirements for controlled unclassified information (CUI) as established by Executive Order 13556.

(c) *Subcontracts*. The Contractor shall include the substance of this clause, including this paragraph (c), in subcontracts under this contract (including subcontracts for the acquisition of commercial items, other than commercially available off-the-shelf items), in which the subcontractor may have Federal contract information residing in or transiting through its information system.

(End of clause)

PART III - LIST OF DOCUMENTS, EXHIBITS AND OTHER ATTACHMENTS

SECTION J - LIST OF ATTACHMENTS

The following documents are attached and incorporated in this contract:

1. Statement of Work

Statement of Work, dated 09/02/2018 11 pages

2. Invoice/Financing Request Instructions for AMCG Cost-Reimbursement Type Contracts,

Invoice/Financing Request Instructions and Contract Financial Reporting Instructions for AMCG Cost-Reimbursement Type Contracts, 2 pages.

3. Sample Invoice, 1 page

4. Financial Report of Individual Project/Contract, 1 page

5. Instructions for Completing Financial Report of Individual Project/Contract, 2 pages

6. Inclusion Enrollment Report

Inclusion Enrollment Report, 5/01 (Modified OAMP: 10/01), 1 page.

7. Research Patient Care Costs

Research Patient Care Costs, 1 page.

8. Report of Government Owned, Contractor Held Property

Report of Government Owned, Contractor Held Property,1 page. Located at: http://rcb.cancer.gov/rcb-internet/forms/Govt-Owned-Prop.pdf

Attachment #1

BARDA Broad Agency Announcement (BAA)

(Solicitation BAA-16-100-SOL-0001 (CBRN)

Advanced Research and Development of Chemical, Biological, Radiological, and Nuclear Medical Countermeasures

NEXOBRID
Topic Area of Interest No. (5) – 5.2, "Vesicants"

Contractual Statement of Work
September 2, 2018 (r04)

PREAMBLE

Independently, and not as an agent of the Government, the Contractor shall furnish all necessary services, qualified professional, technical, and administrative personnel, material, equipment and facilities, not otherwise provided by the Government under the terms of this contract, as needed to perform the tasks set forth below according to BAA-16-100-SOL-0001 (CBRN).

Overall Objectives and Scope

The overall objective of this contract is to advance the development of "NexoBrid" as a proposed removal agent for tissue damaged by Sulfur-Mustard. The Research and Development (R&D) effort for the **NexoBrid** will progress in specific stages that cover the base performance (I) segment and 4 option segments as specified in this contract.

SOW Table 1: Contract Option Summary

Option	Description
CLIN 0001 (base period)	Development of NexoBrid as an MCM with the Gottingen Mini-Pig Model (POC)
CLIN 0002 (option)	Pivotal Trials in Gottingen Mini-Pigs and BLA Submission
CLIN 0003 (option)	Proof of Concept Studies Hairless Guinea Pig Model (POC)
CLIN 0004 (option)	Pivotal Trial in Hairless Guinea Pig
CLIN 0005 (option)	[***]

SOW Table 2: SOW Summary Table

WBS	Title	Description	Milestone	Deliverables	Cost	Delivery Date (est)	CLIN
1	**Base Period**	**NexoBrid for the Treatment of SM Cutaneous Injury (POC)**					**0001**
1.1	Program Management	Program Management					0001
1.1.1	Technical and Project Management						0001
1.1.1.1	Project Management and Reporting	The overall management, integration and coordination of all contract activities. Staffing, review meetings and monthly and annual reports.	PM designated. Monthly technical progress reports. Annual technical progress report. Biweekly meeting minutes.	PM designated. Reports submitted to BARDA PO/CO.	[***]	[***]	0001
1.1.1.2	Integrated Product Development Plan (IPDP)	Prepare IPDP including IMS, GO/NO-GO and TLCC for BARDA PO/CO approval.	IPDP draft completed within 14 days of contract award.	IPDP completed within 14 days of contract award. IMS completed.	[***]	[***]	0001
1.1.2	Subcontractor Management						0001
1.1.2.1	Base Period Subcontractor Management Plan	Directing and overseeing subcontractors and consultants to assure successful performance of planned activities within the cost and schedule constraints of the contract.	Completion of subcontractor management plan.	Completion of subcontractor management plan.	[***]	[***]	0001
1.1.3	Risk Management						0001
1.1.3.1	Risk Management	Risk mitigation plan, PMBR, deviation requests as needed.	Complete risk mitigation plan. PMBR	Develop Risk Mitigation Plan (timeline TBD) PMBR within 90 days of award, deviation requests as required.	[***]	[***]	0001
1.1.4	EVMS						0001
1.1.4.1	EVMS System Implementation	Elements of EVMS shall be applied to all CLINs as part of the IPDP, the Contractor shall submit a written summary of the management procedures that it will establish, maintain and use to comply with EVMS requirements	Complete EVMS plan and report.	Develop EVMS Plan. Complete EVMS Plan Implementation.	[***]	[***]	0001
1.1.4.2	EVMS Monthly Reports Begin	Prepare EVMS monthly reports after first report.	Complete monthly reports.	Complete monthly reports and submit to BARDA CO/PO.	[***]	[***]	0001
1.2	Non-Clinical Toxicology	Non-Clinical PK/PD and Safety studies.					0001
1.2.1	PK/PD	Pharmacokinetic (PK) and Pharmacodynamic (PD) studies.					
1.2.1.1	Bioanalytical Methods Development: Mini-Pig (Gottingen)	Adapt existing bioanalytical methods for NXB PK and immunogenicity to models. Develop/transfer and validate methods for GLP use per ICH method validation guidance.	Complete method development and validation.	Reports submitted to BARDA.	[***]	[***]	0001
1.2.1.2	PK Studies: Mini-Pig (Gottingen)	Conduct pilot PK study for this model prior to POC.. *[***]*	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0001
1.3	Non-Clinical Pharmacology	Non-Clinical animal model development and proof of concept efficacy studies					0001
1.3.1	Animal Model Development	Animal Model Development studies					0001

WBS	Title	Description	Milestone	Deliverables	Cost	Delivery Date (est)	CLIN
1.3.1.1	SM Exposure [***] Wound Depth: Mini-Pig (Gottingen)	[***]	Complete study.	Study protocol / report submitted to BARDA. [***]	[***]	[***]	0001
1.3.1.2	[***]	[***]	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0001
1.3.1.3	Statistical Analysis: Mini-Pig (Gottingen)	Provide statistical support including pharmacometric analysis for this model from PK and nonclinical data.	Provide support	Analysis submitted to BARDA as required	[***]	[***]	0001
1.3.2	POC Studies	Proof of Concept (POC) studies to enable pivotal studies.					0001
1.3.2.1	[***]	[***]	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0001
1.3.2.2	[***]	[***]	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0001
1.3.2.3	[***]	[***]	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0001
1.3.2.4	POC Efficacy Study: Mini-Pig (Gottingen)	Using the exposure and treatment scenarios as determined in earlier studies, this study will aim at determining the efficacy of NexoBrid in a non-GLP study. *[***]*	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0001
1.5	Regulatory	Regulatory activities.					0001
1.5.1	IND	For IND / EOP2					0001
1.5.1.1	FDA Meetings and Requests for Review	PIND and other RA Meetings/ requests for review at each development milestone.	Conduct meetings.	Meeting minutes to BARDA PO/CO	[***]	[***]	0001
1.5.1.2	[***]	[***]	[***]	[***]	[***]	[***]	0001
1.5.1.3	IND Submission	IND preparation and submission	Prepare IND.	Submit to FDA.	[***]	[***]	0001
1.5.1.4	End of P2 Meeting	End of Phase 2 Meeting	Conduct meeting.	Meeting minutes to BARDA PO/CO	[***]	[***]	0001

WBS	Title	Description	Milestone	Deliverables	Cost	Delivery Date (est.)	CLIN
2	**CLIN 0002**	**Pivotal Trials in Gottingen Mini-Pigs and BLA Submission**					**0002**
2.1	Program Management	Program Management					0002
2.1.1	Technical and Project Management						0002
2.1.1.1	Project Management and Reporting	Option project management.	Option project management.	Reports submitted to BARDA PO/CO.	[***]	[***]	0002
2.1.1.2	EVMS Monthly Reports Begin	Prepare EVMS monthly reports	Complete monthly reports.	Complete monthly reports and submit to BARDA CO/PO.	[***]	[***]	0002
2.3	Non-Clinical Pharmacology	Non-Clinical animal model pivotal studies					0002
2.3.3	Efficacy Studies	Pivotal Efficacy Studies					0002
2.3.3.1	Two Pivotal Efficacy Studies: Mini-Pig (Gottingen)	Show efficacy under the Animal Rule[***]	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0002
2.5	Regulatory	Regulatory activities.					0002
2.5.2	BLA	BLA submission					0002

WBS	Title	Description	Milestone	Deliverables	Cost	Delivery Date (est.)	CLIN
2.5.2.1	Regulatory - Gap Analysis	Pre-BLA gap analysis by SMEs.	Prepare gap analysis.	Submit to BARDA PO/CO.	$150,000	Q4 2021	0002
2.5.2.2	Pre-BLA Meeting	Pre-BLA meeting	Conduct pre-BLA meeting.	Meeting minutes to BARDA PO/CO	$150,000	Q4 2022	0002
2.5.2.3	[***]	[***]	[***]	[***]	[***]	[***]	0002
2.5.2.4	[***]	[***]	[***]	[***]	[***]	[***]	0002
2.5.2.5	Preparation and Submission of BLA	Submit BLA. Respond to FDA feedback and update BLA as needed.	Prepare BLA.	Submit to FDA	[***]	[***]	0002
2.5.3	Post-Approval	Post-approval					0002
2.5.3.1	MCI Support Under Animal Rule – Data Collection and Reporting	Create plan for this contingency.	Prepare plan.	Submit to BARDA PO/CO.	[***]	[***]	0002

WBS	Title	Description	Milestone	Deliverables	Cost	Delivery Date (est.)	CLIN
3	**Contract Option**	**CLIN 0003 Option – Proof of Concept Studies Hairless Guinea Pig Model (POC)**					**0003**
3.1	Program Management	Program Management					0003
3.1.1	Technical and Project Management						0003
3.1.1.1	Project Management and Reporting	Option project management.	Option project management.	Reports submitted to BARDA PO/CO.	[***]	[***]	0003
3.1.1.2	EVMS Monthly Reports	Prepare EVMS monthly reports	Complete monthly reports.	Complete monthly reports and submit to BARDA CO/PO.	[***]	[***]	0003
3.2	Non-Clinical Toxicology		Non-Clinical PK/PD and Safety studies.				0003
3.2.1	PK/PD	Pharmacokinetic (PK) and Pharmacodynamic (PD) studies.					0003
3.2.1.1	Bioanalytical Methods Development: Hairless guinea pig	Adapt existing development bioanalytical methods for NXB to model. Method development and Validate methods for GLP use per ICH method validation guidance.	Complete method development and validation.	Reports submitted to BARDA.	[***]	[***]	0003
3.2.1.2	PK Studies: Hairless guinea pig	Conduct pilot PK study for this model. [***]	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0003
3.3	Non-Clinical Pharmacology	Non-Clinical animal model development, proof of concept efficacy studies					0003
3.3.1	Animal Model Development	Animal Model Development studies					0003
3.3.1.1	SM Exposure [***] Wound Depth: Hairless guinea pig	[***]	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0003
3.3.1.2	Statistical Analysis: Hairless Guinea Pig	Provide statistical support including pharmacometric analysis for this model from PK and nonclinical data.	Provide support	Analysis submitted to BARDA as required	[***]	[***]	0003
3.3.2	POC Studies	Proof of Concept (POC) studies to enable pivotal studies.					0003
3.3.2.1	[***]	[***]	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0003
3.3.2.2	[***]	[***]	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0003
3.3.2.3	POC Efficacy Study: Hairless guinea pig	Using the exposure and treatment scenarios as determined in earlier studies, this study will aim at determining the efficacy of NexoBrid in a non-GLP study. *[***]*	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0003
3.5	Regulatory	Regulatory activities.					0003
3.5.1	IND	For IND / EOP2					0003
3.5.1.4	End of P2 Meeting	End of Phase 2 Meeting	Conduct meeting.	Meeting minutes to BARDA PO/CO	[***]	[***]	0003

WBS	Title	Description	Milestone	Deliverables	Cost	Delivery Date (est.)	CLIN
4	**Contract Option**	**CLIN 0004 Option – Pivotal Trials in Hairless Guinea Pig**					**0004**
4.1	Program Management	Program Management					0004
4.1.1	Technical and Project Management	Technical and Project Management					0004

WBS	Title	Description	Milestone	Deliverables	Cost	Delivery Date (est.)	CLIN
4.1.1.1	Project Management and Reporting	Option project management.	Option project management.	Reports submitted to BARDA PO/CO.	[***]	[***]	0004
4.1.1.2	EVMS Monthly Reports	Prepare EVMS monthly reports	Complete monthly reports.	Complete monthly reports and submit to BARDA CO/PO.	[***]	[***]	0004
4.3	Non-Clinical Pharmacology	Non-Clinical animal studies, pivotal trial					0004
4.3.3	Efficacy Studies	Efficacy Studies					0004
4.3.3.1	Pivotal Efficacy Study: Hairless guinea pig	Show efficacy under the Animal Rule, [***] test for efficacy of NXB under GLP conditions in accordance with the Animal Rule. *[***]*	Complete study.	Study protocol / report submitted to BARDA.	[***]	[***]	0004
4.5	Regulatory	Regulatory activities.					0004
4.5.2	BLA	BLA submission					0004
4.5.2.1	Regulatory - Gap Analysis	Pre-BLA gap analysis by SMEs.	Prepare gap analysis.	Submit to BARDA PO/CO.	[***]	[***]	0004
4.5.2.2	Pre-BLA Meeting	Pre-BLA meeting	Conduct pre-BLA meeting.	Meeting minutes to BARDA PO/CO	[***]	[***]	0004
4.5.2.3	Preparation and Submission of BLA	Submit BLA. Respond to FDA feedback and update BLA as needed (additional updates for second animal model)	Prepare BLA.	Submit to FDA	[***]	[***]	0004
4.5.2.5	[***]	[***]	[***]	Submit to FDA	[***]	[***]	0004

WBS	Title	Description	Milestone	Deliverables	Cost	Delivery Date (est.)	CLIN
5	**Contract Option**	**Option – Dual-Chamber Frangible Pouch Development (CLIN 0005)**					**0005**
5.1	Program Management	Program Management				Q	0005
5.1.1	Technical and Project Management						0005
5.1.1.1	Project Management and Reporting	Option project management.	Option project management.	Reports submitted to BARDA PO/CO.	[***]	[***]	0005
5.6	CMC	CMC development					0005
5.6.3	Packaging Development						0005
5.6.3.1	Feasibility for container/closure system for efficient & ease of use in MCI	Conduct feasibility study [***]	Feasibility studies	Submit report to BARDA PO/CO.	[***]	[***]	0005
5.6.3.2	Develop new container/closure system for efficient & ease of use in MCI	[***]	Development, batch manufacturing and stability.	Submit report to BARDA PO/CO.	[***]	[***]	0005
5.6.5	Analytical / Validation						0005
5.6.5.1	RT Stability	[***] ICH stability study in current configuration.	Complete study.	Report to BARDA PO/CO	[***]	[***]	0005

WBS 1 BASE PERIOD CONTRACT

The Contractor shall provide for the following as outlined below and in the contract deliverables list (Article F.2):

WBS 1.1 Program Management

Objective / Description of Work:

a. Identification of and management to, distinct stages of the product development pathway that are gates for Go/No Go decisions for advancing to the next stage of the Integrated Product Development Plan.
b. Establishment of and tracking of milestones and timelines for the initiation conduct, and completion of product development activities for each stage with a budget (in direct costs) linked to each stage.
c. Ongoing evaluation of qualitative and quantitative criteria and accompanying data used to assess the scientific merit and technical feasibility of proceeding to the next stage of product development.
d. Maintaining and managing staff (in-house and contracted) to assure the necessary expertise and dedicated effort to perform the work.
e. Directing and overseeing subcontractors and consultants to assure successful performance of planned activities within the cost and schedule constraints of the contract.
f. Conducting performance measurement that shall include establishing an initial plan; defining measurable parameters; defining how these parameters relate to cost and schedule impacts; their approach in providing a detailed schedule that generates a critical path for the project; and a description of the cost- accounting system used or intended to be used based on budget estimates to monitor all costs related to the contract award for both prime- and sub-contractors on a real time basis.
g. Perform assessments of technical approaches to reduce the Total Life Cycle Cost (TLCC) for the proposed countermeasure throughout the products life cycle and identify strategic approaches to ensure the product has a sustainable commercial value to ensure long term access to the medical countermeasure.

Milestones/Deliverables:

Described in individual WBS items below (1.1.1. – 1.1.4)

WBS 1.1.1 Technical and Project Management

WBS 1.1.1.1 Project Management and Reporting

Objective / Description of Work:

The overall management, integration and coordination of all contract activities.

Staffing: A Project Manager (PM) will be designated by MediWound who is responsible for project management, communication, tracking, monitoring and reporting on status and progress, costs incurred and responsibility for effective communication with the BARDA Project Officer and Contracting Officer.

Contract Review Meetings: The Contractor shall participate in regular meetings to coordinate and oversee the contract effort as directed by the Contracting and Project Officers. The Contractor shall participate in teleconferences every two weeks or as required with BARDA to review technical progress.

Monthly and Annual Reports: The Contractor shall deliver Project Status Reports monthly, referencing the WBS, SOW, IMS, and EVM.

Milestones/ Deliverables:

PM designated.

Monthly technical progress reports. Annual technical progress report.

Biweekly meeting minutes.

WBS 1.1.1.2 Integrated Product Development Plan (IPDP)

Objective / Description of Work:

MediWound shall prepare an IPDP including:

Integrated Master Schedule: The Integrated Master Schedule shall be incorporated into the contract and will be used to monitor performance of the contract. Contractor shall include the key milestones and Go/No Go decisions.

GO/ NO-GO Decisions: The Integrated Master Plan outlines key milestones with "Go/No Go" decision criteria (entrance and exit criteria for each phase of the project). The project plan should include, but not be limited to, milestones in manufacturing, non-clinical and clinical studies, and regulatory submissions.

TLCC: Perform assessments of technical approaches to reduce the Total Life Cycle Cost (TLCC) for the proposed countermeasure throughout the products life cycle and identify strategic approaches to ensure the product has a sustainable commercial value to ensure long term access to the medical countermeasure.

Milestones/ Deliverables:

IPDP completed within 14 days of contract award.

IMS completed.

WBS 1.1.2 Subcontractor Management

WBS 1.1.2.1 Base Period Subcontractor Management

Objective/Description of Work:

Contractor will direct and oversee subcontractors and consultants to assure successful performance of planned activities within the cost and schedule constraints of the contract.

Milestones/Deliverables:

Completion of subcontractor management activities for the base period. Documentation of completed work in the Technical Progress Reports.

WBS 1.1.3 Risk Management

WBS 1.1.3.1 Base Period Risk Management

Objective/Description of Work: MediWound will prepare a Risk Mitigation Plan and Matrix and submit to BARDA. MediWound will maintain and update the plan as necessary throughout the term of the contract and provide updates as requested by the COR. A report on these activities will be included as part of regular quarterly project status updates to the BARDA PO/CO.

Performance Measurement Baseline Review (PMBR): The Contractor shall submit a plan for a PMBR to occur within 90 days of contract award.

Deviation Request: During contract performance, in response to a need to change IMS activities as baselined at the PMBR, the Contractor shall submit a Deviation Report. This report shall request a change in the agreed-upon IMS and timelines.

Milestones/Deliverables:

Develop Risk Mitigation Plan (timeline TBD)
PMBR within 90 days of award
Deviation requests as required.

WBS 1.1.4 EVMS

WBS 1.1.4.1 EVMS System Implementation

Objective/Description of Work: Subject to the requirements under HHSAR Clause 352.234-4, the Contractor shall use principles of Earned Value Management System (EVMS) in the management of this contract.

Elements of EVMS shall be applied to all CLINs as part of the Integrated Master Project Plan, the Contractor shall submit a written summary of the management procedures that it will establish, maintain and use to comply with EVMS requirements.

Milestones/Deliverables:

Develop EVMS Plan.
Complete EVMS Plan Implementation.

WBS 1.1.4.2 EVMS Monthly Reports

Objective/Description of Work:

Prepare EVMS reports monthly.

Milestones/Deliverables:

Prepare EVMS reports monthly after first report.

WBS 1.2 Non-Clinical Toxicology

WBS 1.2.1 PK/PD

WBS 1.2.1.1 Bioanalytical Methods Technology Transfer Development& Validation: Mini-Pig (Gottingen)

Objective/Description of Work:

Adapt existing bioanalytical methods for NXB to model. Technology transfer & Validate methods for GLP use per ICH method validation guidance.

Milestones/Deliverables:

Complete method development transfer and validation and submit protocol and report to BARDA.

WBS 1.2.1.2 PK Studies: Mini-Pig (Gottingen)

Objective/Description of Work:

Validation of the bioanalytical method in mini pig serum. Conduct PK study for this model. [***]

Milestones/Deliverables:

Complete study and submit report to BARDA.

WBS 1.3 Non-Clinical Pharmacology

WBS 1.3.1 Animal Model Development

WBS 1.3.1.1 SM Exposure [***] Wound Depth: Mini-Pig (Gottingen)

Objective/Description of Work:

[***]

Milestones/Deliverables:

Complete study and submit protocol and report to BARDA

[***]

WBS 1.3.1.2 [***]

Milestones/Deliverables:

Complete study and submit protocol and report to BARDA.

WBS 1.3.1.3 Statistical Support

Provide statistical analysis support as needed for nonclinical studies.

WBS 1.3.2 Proof of Concept Studies

WBS 1.3.2.1 [***]

Objective/Description of Work:

[***]

Milestones/Deliverables:

Complete study and submit protocol and report to BARDA

WBS 1.3.2.2 [***]

Objective/Description of Work:

[***]

Milestones/Deliverables:

Complete study and submit protocol and report to BARDA

WBS 1.3.2.3 [***]

Objective/Description of Work:

[***]

Milestones/Deliverables:

Complete study and submit protocol and report to BARDA

WBS 1.3.2.4 POC Efficacy Study: Mini-Pig (Gottingen)

Objective/Description of Work:

[***], this study will aim at determining the efficacy of NexoBrid in a non-GLP study.

Milestones/Deliverables:

Complete study and submit protocol and report to BARDA

WBS 1.4 Clinical (Reserved)

WBS 1.5 Regulatory

WBS 1.5.1 IND

WBS 1.5.1.1 FDA Meetings and Requests for Review

Objective/Description of Work:

Under the Animal Rule, FDA will grant review requests for study protocols and reports, as well as at significant milestones.

Milestones/Deliverables:

PIND and other RA Meetings/ requests for review at each development milestone. Submit meeting minutes to BARDA PO/CO.

WBS 1.5.1.2 [***]

Objective/Description of Work:

[***]

Milestones/Deliverables:

Submit application to FDA.

WBS 1.5.1.3 Submit IND

Objective/Description of Work:

MediWound will submit an IND when required by FDA for further development under the Animal Rule.

the Securities and Exchange Commission.

Milestones/Deliverables:

Submit IND to FDA.

WBS 1.5.1.4 End of Phase 2 Meeting

Objective/Description of Work:

Conduct EOP2 meeting with FDA.

Milestones/Deliverables:

Conduct meeting, submit minutes to BARDA PO/CO.

WBS 2 OPTION PERIOD STATEMENT OF WORK – PIVOTAL TRIALS IN GOTTINGEN MINI-PIGS (CLIN 0002)

WBS 2.1 Program Management

WBS 2.1.1 Technical and Project Management

WBS 2.1.1.1 Option Project Management

WBS 2.2 Reserved

WBS 2.3 Non-Clinical Studies

WBS 2.3.1 Reserved

WBS 2.3.2 Reserved

WBS 2.3.3 Efficacy Studies

WBS 2.3.3.1 Two Pivotal Efficacy Studies: Mini-Pig (Gottingen)

Objective/Description of Work:

Show efficacy under the Animal Rule, [***], test for efficacy of NXB under GLP conditions in accordance with the Animal Rule.

Note; The size of the pivotal trials is subject to sample size calculations that will be done based on the efficacy studies results in CLIN 1.

Milestones/Deliverables:

Complete study and submit protocol and report to BARDA

WBS 2.4 Reserved

WBS 2.5 Regulatory

WBS 2.5.1 Reserved

WBS 2.5.2 BLA

WBS 2.5.2.1 Regulatory Gap Analysis

Objective/Description of Work:

As part of the BLA preparation, a gap analysis will be prepared to ensure that the data available are adequate, complete and meet FDA requirements, MediWound will perform a gap analysis by subject matter experts.

Milestones/Deliverables:

Submit gap analysis to BARDA PO/CO.

WBS 2.5.2.2 Pre-BLA Meeting

Objective/Description of Work:

Prior to BLA submission, MediWound plans a pre-BLA meeting with the FDA.

Milestones/Deliverables:

Submit meeting minutes to BARDA PO/CO.

WBS 2.5.2.3 [***]

Objective/Description of Work:

[***]

Milestones/Deliverables:

Submit request to FDA.

WBS 2.5.2.4 [***]

Objective/Description of Work:

[***]

Milestones/Deliverables:

Submit application to FDA.

WBS 2.5.2.5 Preparation and Submission of BLA

Objective/Description of Work:

MediWound plans on submitting BLA for NexoBrid approval when development is complete. MediWound will work closely with regulatory consultants to prepare CTD modules, file compilation and submission of electronic CTD. Following BLA submission MediWound will prepare responses to FDA comments as applicable.

Milestones/Deliverables:

Submission of BLA to FDA.

WBS 2.5.3 Post-Approval

WBS 2.5.3.1 MCI Support Under Animal Rule – Data Collection and Reporting Plan

Objective/Description of Work:

Under the Animal Rule, "some safety concerns may not become apparent until the drug is used in the general population during an actual event. Examples include the potential for drug-drug interactions and adverse interactions between the drug and a disease (preexisting or agent-induced). Such adverse interactions reinforce the critical need for post-marketing studies."

In accordance with this guidance, MediWound will prepare a plan to determine what data could be feasibly collected under an MCI.

Milestones/Deliverables:

Submission of plan to BARDA.

WBS 3 OPTION PERIOD STATEMENT OF WORK - PROOF OF CONCEPT STUDIES - HAIRLESS GUINEA PIG MODEL (CLIN 0003)

WBS 3.1 Program Management

Option project management.

WBS 3.2 Non-Clinical Toxicology

WBS 3.2.1 PK/PD

WBS 3.2.1.1 Bioanalytical Methods Development: Hairless guinea pig

Objective/Description of Work:

Adapt existing bioanalytical methods for NXB to model. Validate methods for GLP use per ICH method validation guidance.

Milestones/Deliverables:

Complete method development and validation and submit protocol and report to BARDA.

WBS 3.2.1.2 PK Studies: Hairless guinea pig

Objective/Description of Work:

Conduct PK study for this model. [***]

Milestones/Deliverables:

Complete study and submit report to BARDA.

WBS 3.3 Non-Clinical Pharmacology

WBS 3.3.1 Animal Model Development

WBS 3.3.1.1 SM Exposure [***] Wound Depth: Hairless guinea pig

Objective/Description of Work:

[***]

Milestones/Deliverables:

Complete study and submit protocol and report to BARDA

WBS 3.3.1.2 Statistical Support

Provide statistical analysis support as needed for nonclinical studies.

WBS 3.3.2 Proof of Concept Studies

WBS 3.3.2.1 [***]

Objective/Description of Work:

[***]

Milestones/Deliverables:

Complete study and submit protocol and report to BARDA.

WBS 3.3.2.2 [***]

Objective/Description of Work:

[***]

Milestones/Deliverables:

Complete study and submit protocol and report to BARDA

WBS 3.3.2.3 POC Efficacy Study: Hairless guinea pig

Objective/Description of Work:

Using the exposure and treatment scenarios as determined in earlier studies, this study will aim at determining the efficacy of NexoBrid in a non-GLP study.

Milestones/Deliverables:

Complete study and submit protocol and report to BARDA.

WBS 3.4 Reserved

WBS 3.5 Regulatory

WBS 3.5.1 IND

WBS 3.5.1.1 Reserved

WBS 3.5.1.2 Reserved

WBS 3.5.1.3 Reserved

WBS 3.5.1.4 End of Phase 2 Meeting

Objective/Description of Work:

Conduct EOP2 meeting with FDA.

Milestones/Deliverables:

Conduct meeting, submit minutes to BARDA PO/CO.

WBS 4 OPTION PERIOD STATEMENT OF WORK - PIVOTAL TRIAL IN HAIRLESS GUINEA PIG (CLIN 0004)

WBS 4.1 Program Management

Option project management.

WBS 4.2 Reserved

WBS 4.3 Non-Clinical Pharmacology

WBS 4.3.1 Reserved

WBS 4.3.2 Reserved

WBS 4.3.3 Efficacy Studies

WBS 4.3.3.1 Pivotal Efficacy Study: Hairless guinea pig

Objective/Description of Work:

Show efficacy under the Animal Rule, [***] of NXB under GLP conditions in accordance with the Animal Rule.

Note; The size of the pivotal trials is subject to sample size calculations that will be done based on the efficacy studies results in CLIN 3.

Milestones/Deliverables:

Complete study and submit protocol and report to BARDA

WBS 4.4 Reserved

WBS 4.5 Regulatory

WBS 4.5.1 Reserved

WBS 4.5.2 BLA

WBS 4.5.2.1 Regulatory Gap Analysis

Objective/Description of Work:

As part of the BLA preparation, a gap analysis will be prepared to ensure that the data available are adequate, complete and meet FDA requirements, MediWound will perform a gap analysis by subject matter experts.

Milestones/Deliverables:

Submit gap analysis to BARDA PO/CO.

WBS 4.5.2.2 Pre-BLA Meeting

Objective/Description of Work:

Prior to BLA submission, MediWound plans a pre-BLA meeting with the FDA.

Milestones/Deliverables:

Submit meeting minutes to BARDA PO/CO.

WBS 4.5.2.3 Preparation and Submission of BLA

Objective/Description of Work:

MediWound plans on submitting BLA for NexoBrid approval when development is complete. MediWound will work closely with regulatory consultants to prepare CTD modules, file compilation and submission of electronic CTD. Following BLA submission MediWound will prepare responses to FDA comments as applicable. This task is to include the additional data generated for the hairless guinea pig animal model.

Milestones/Deliverables:

Submission of BLA to FDA.

WBS 4.5.2.4 Reserved

WBS 4.5.2.5 [***]

Objective/Description of Work:

[***]

Milestones/Deliverables:

Submit request to FDA.

WBS 5 OPTION PERIOD STATEMENT OF WORK – [***] (CLIN0004)

WBS 5.1 Technical and Project Management

Option Management

WBS 5.2 Reserved

WBS 5.3 Reserved

WBS 5.4 Reserved

WBS 5.5 Reserved

WBS 5.6 CMC

WBS 5.6.1 Reserved

WBS 5.6.2 Reserved

WBS 5.6.3 Packaging Development

WBS 5.6.3.1 Feasibility for new container/closure system for efficient & ease of use in MCI

Objective/Description of Work:

Conduct feasibility [***] for finished product container/closure packaging.

Milestones/Deliverables:

Complete study and submit feasibility study report to BARDA.

WBS 5.6.3.2 Develop new container/closure system for efficient & ease of use in MCI

Objective/Description of Work:

Develop new dual-chamber container/closure system frangible pouch for finished product container/closure packaging.

Milestones/Deliverables:

Complete development, batch manufacturing and stability and submit report to BARDA.

WBS 5.6.4 Reserved

WBS 5.6.5 Analytical / Validation

WBS 5.6.5.1 RT Stability

Objective/Description of Work:

[***] ICH stability study in current configuration.

Milestones/Deliverables:

Submit report to BARDA.

ATTACHMENT #2
INVOICE/FINANCING REQUEST INSTRUCTIONS - FOR COST-REIMBURSEMENT TYPE CONTRACTS

Format: Payment requests shall be submitted on the Contractor's self-generated form in the manner and format prescribed herein and as illustrated in the Sample Invoice/Financing Request. Standard Form 1034, Public Voucher for Purchases and Services Other Than Personal, may be used in lieu of the Contractor's self-generated form provided it contains all of the information shown on the Sample Invoice/Financing Request. DO NOT include a cover letter with the payment request.

Number of Copies: Payment requests shall be submitted in the quantity specified in the Invoice Submission Instructions in SECTION G of the Contract Schedule.
Frequency: Payment requests shall not be submitted more frequently than once every two weeks in accordance with the Allowable Cost and Payment Clause incorporated into this contract. Small business concerns may submit invoices/financing requests more frequently than every two weeks when authorized by the Contracting Officer.
Cost Incurrence Period: Costs incurred must be within the contract performance period or covered by pre-contract cost provisions.
Billing of Costs Incurred: If billed costs include (1) costs of a prior billing period, but not previously billed, or (2) costs incurred during the contract period and claimed after the contract period has expired, the Contractor shall site the amount(s) and month(s) in which it incurred such costs.
Contractor's Fiscal Year: Payment requests shall be prepared in such a manner that the Government can identify costs claimed with the Contractor's fiscal year.
Currency: All government contracts are expressed in United States dollars. When the Government pays in a currency other than United States dollars, billings shall be expressed, and payment by the Government shall be made, in that other currency at amounts coincident with actual costs incurred. Currency fluctuations may not be a basis of gain or loss to the Contractor. Notwithstanding the above, the total of all invoices paid under this contract may not exceed the United States dollars authorized.
Costs Requiring Prior Approval: Costs requiring the Contracting Officer's approval, including those set forth in an Advance Understanding in the contract, shall be identified and reference the Contracting Officer's Authorization (COA) Number. In addition, the Contractor shall show any cost set forth in an Advance Understanding as a separate line item on the payment request.
Invoice/Financing Request Identification: Each payment request shall be identified as either:
(a) **Interim Invoice/Contract Financing Request:** These are interim payment requests submitted during the contract performance period.
(b) **Completion Invoice:** The completion invoice shall be submitted promptly upon completion of the work, but no later than one year from the contract completion date, or within 120 days after settlement of the final indirect cost rates covering the year in which the contract is physically complete (whichever date is later). The Contractor shall submit the completion invoice when all costs have been assigned to the contract and it completes all performance provisions.
(c) **Final Invoice:** A final invoice may be required after the amounts owed have been settled between the Government and the Contractor (e.g., resolution of all suspensions and audit exceptions).
Preparation and Itemization of the Invoice/Financing Request: The Contractor shall furnish the information set forth in the instructions below. The instructions are keyed to the entries on the Sample Invoice/Financing Request.
(a) **Designated Billing Office Name and Address:** Enter the designated billing office name and address, as identified in the Invoice Submission Instructions in SECTION G of the Contract Schedule.
(b) **Contractor's Name, Address, Point of Contact, VIN, and DUNS or DUNS+4 Number:** Show the Contractor's name and address exactly as they appear in the contract, along with the name, title, phone number, and e-mail address of the person to notify in the event of an improper invoice or, in the case of payment by method other than Electronic Funds Transfer, to whom payment is to be sent. Provide the Contractor's Vendor Identification Number (VIN), and Data Universal Numbering System (DUNS) number or DUNS+4. The DUNS number must identify the Contractor's name and address exactly as stated on the face page of the contract. When an approved assignment has been made by the Contractor, or a different payee has been designated, provide the same information for the payee as is required for the Contractor (i.e., name, address, point of contact, VIN, and DUNS).
(c) **Invoice/Financing Request Number:** Insert the appropriate serial number of the payment request. Include numbering in format of year_month #.
(d) **Date Invoice/Financing Request Prepared:** Insert the date the payment request is prepared.
(e) **Contract Number and Order Number (if applicable):** Insert the contract number and order number (if applicable).
(f) **Effective Date:** Insert the effective date of the contract or if billing under an order, the effective date of the order.
(g) **Total Estimated Cost of Contract/Order:** Insert the total estimated cost of the contract, exclusive of fixed-fee. If billing under an order, insert the total estimated cost of the order, exclusive of fixed-fee. For incrementally funded contracts/orders, enter the amount currently obligated and available for payment.
(h) **Total Fixed-Fee:** Insert the total fixed-fee (where applicable) or the portion of the fixed-fee applicable to a particular invoice as defined in the contract.
(i) **Two-Way/Three-Way Match:** Identify whether payment is to be made using a two-way or three-way match. To determine required payment method, refer to the Invoice Submission Instructions in SECTION G of the Contract Schedule.
(j) **Office of Acquisitions:** Insert the name of the Office of Acquisitions, as identified in the Invoice Submission Instructions in SECTION G of the Contract Schedule.
(k) **Central Point of Distribution:** Insert the Central Point of Distribution, as identified in the Invoice Submission Instructions in SECTION G of the Contract Schedule.
(l) **Billing Period:** Insert the beginning and ending dates (month, day, and year) of the period in which costs were incurred and for which reimbursement is claimed.

(m) **Amount Billed - Current Period:** Insert the amount claimed for the current billing period by major cost element, including any adjustments and fixed-fee. If the Contract Schedule contains separately priced line items, identify the contract line item(s) on the payment request and include a separate breakdown (by major cost element) for each line item.

(n) **Amount Billed - Cumulative:** Insert the cumulative amounts claimed by major cost element, including any adjustments and fixed-fee. If the Contract Schedule contains separately priced line items, identify the contract line item(s) on the payment request and include a separate breakdown (by major cost element) for each line item.

(o) **Direct Costs:** Insert the major cost elements. For each element, consider the application of the paragraph entitled "Costs Requiring Prior Approval" on page 1 of these instructions.

(1) **Direct Labor:** Include salaries and wages paid (or accrued) for direct performance of the contract. List individuals by name, title/position, hourly/annual rate, level of effort (actual hours or % of effort), breakdown by task performed by personnel, and amount claimed.

(2) **Fringe Benefits:** List any fringe benefits applicable to direct labor and billed as a direct cost. Do not include in this category fringe benefits that are included in indirect costs.

(3) **Accountable Personal Property:** Include any property having a unit acquisition cost of $5,000 or more, with a life expectancy of more than two years, and sensitive property regardless of cost see the HHS *Contractor's Guide for Control of Government Property (*http://www.google.com/url?sa=t&rct=j&q=&esrc=s&frm=1&source=web&cd=1&cad=rja&uact=8&ved=0CB4QFjAA&url=http%3A%2F%2Fncioa.cancer.gov%2Foa-internet%2Freference%2FAppendix_Q_HHS_Contracting_Guide-508.pdf&ei=NRraVO6WGsqAygTz7oL4Cw&usg=AFQjCNG-0KqILRbM1IgEntH08pUZhXTV4A&sig2=XUvZkNK95EJ7uvFs0A83ig)(e.g. personal computers). Note this is not permitted for reimbursement without pre-authorization from the CO.

On a separate sheet of paper attached to the payment request, list each item for which reimbursement is requested. Include reference to the following (as applicable):

- Item number for the specific piece of equipment listed in the Property Schedule, and
- COA number, if the equipment is not covered by the Property Schedule.

The Contracting Officer may require the Contractor to provide further itemization of property having specific limitations set forth in the contract.

(4) **Materials and Supplies:** Include all consumable material and supplies regardless of amount. Detailed line-item breakdown (e.g. receipts, quotes, etc.) is required.

(5) **Premium Pay:** List remuneration in excess of the basic hourly rate.

(6) **Consultant Fee:** List fees paid to consultants. Identify consultant by name or category as set forth in the contract or COA, as well as the effort (i.e., number of hours, days, etc.) and rate billed.

(7) **Travel:** Include domestic and foreign travel. Foreign travel is travel outside of Canada, the United States and its territories and possessions. However, for an organization located outside Canada, the United States and its territories and possessions, foreign travel means travel outside that country. Foreign travel must be billed separately from domestic travel.

(8) **Subcontract Costs:** List subcontractor(s) by name and amount billed. Provide subcontract invoices/receipts as backup documentation. If subcontract is of the cost-reimbursement variety, detailed breakdown will be required. Regardless, include backup documentation (e.g. subcontractor invoices, quotes, etc.).

(9) **Other:** Include all other direct costs not fitting into an aforementioned category. If over $1,000, list cost elements and dollar amounts separately. If the contract contains restrictions on any cost element, that cost element must be listed separately.

(p) **Cost of Money (COM):** Cite the COM factor and base in effect during the time the cost was incurred and for which reimbursement is claimed, if applicable.

(q) **Indirect Costs:** Identify the indirect cost base (IDC), indirect cost rate, and amount billed for each indirect cost category.

(r) **Fixed-Fee:** Cite the formula or method of computation for fixed-fee, if applicable. The fixed-fee must be claimed as provided for by the contract.

(s) **Total Amounts Claimed:** Insert the total amounts claimed for the current and cumulative periods.

(t) **Adjustments:** Include amounts conceded by the Contractor, outstanding suspensions, and/or disapprovals subject to appeal.

(u) **Grand Totals**

(v) **Certification of Salary Rate Limitation:** If required by the contract (see Invoice Submission Instructions in the Contract Schedule), the Contractor shall include the following certification at the bottom of the payment request:

"I hereby certify that the salaries billed in this payment request are in compliance with the HHS Salary Rate Limitation Provisions in Section H of the contract."

**Note the Contracting Officer may require the Contractor to submit detailed support for costs claimed on payment requests. Every cost must be determined to be allocable, reasonable, and allowable per FAR Part 31.

Attachment 3-SAMPLE INVOICE/PAYMENT REQUEST AND CONTRACT FINANCIAL REPORT

(a) Designated Billing Office Name and Address: DHHS/OS/ASPR/AMCG Attn: Contracting Officer US DEPT OF HEALTH & HUMAN SERVICES ASST SEC OF PREPAREDNESS & RESPONSE ACQ MGMT, CONTRACTS, & GRANTS O'NEILL HOUSE OFFICE BUILDING Washington DC 20515 (b) Contractor's Name, Address, Point of Contact, VIN, and DUNS or DUNS+4 Number: ABC CORPORATION 100 Main Street Anywhere, USA Zip Code Name, Title, Phone Number, and E-mail Address of person to notify in the event of an improper invoice or, in the case of payment by method other than Electronic Funds Transfer, to whom payment is to be sent. **VIN:** **DUNS or DUNS+4:**	(c) Invoice/Financing Request No.: (d) Date Invoice Prepared: (e) Contract No. and Order No. (if applicable): _____ (f) Effective Date: (g) Total Estimated Cost of Contract/Order: (h) Total Fixed-Fee (if applicable): (i) ☐Two-Way Match: ☐Three-Way Match: (j) Office of Acquisitions: (k) Central Point of Distribution:

(l) This invoice/financing request represents reimbursable costs for the period from _____ to

Expenditure Category* A	Cumulative Percentage of Effort/Hrs.		Amount Billed		Cost at Completion F	Contract Amount G	Variance H
	Negotiated B	Actual C	(m) Current D	(n) Cumulative E			
(o) Direct Costs:							
(1) Direct Labor							
(2) Fringe Benefits							
(3) Accountable Property							
(4) Materials & Supplies							
(5) Premium Pay							
(6) Consultant Fees							
(7) Travel							
(8) Subcontracts							
(9) Other							
Total Direct Costs							
(p) Cost of Money							
(q) Indirect Costs							
(r) Fixed Fee							
(s) Total Amount Claimed							
(t) Adjustments							
(u) Grand Totals							

I certify that all payments are for appropriate purposes and in accordance with the contract.

_____ _____

(Name of Official) (Title)

* Attach details as specified in the contract

Attachment 4

FINANCIAL REPORT OF INDIVIDUAL PROJECT/CONTRACT Note: Complete this Form in Accordance with Accompanying Instructions.	**Project Task:**	**Contract No.:**	**Date of Report:**	**0990-0134** **0990-0131**
	Reporting Period:	**Contractor Name and Address:**		

Expenditure Category	**Percentage of Effort/Hours**		**Cumulative Incurred Cost at End of Prior Period**	**Incurred Cost-- Current Period**	**Cumulative Cost to Date (D + E)**	**Estimated Cost to Complete**	**Estimated Cost at Completion (F + G)**	**Negotiated Contract Amount**	**Variance (Over or Under) (I - H)**
	Negotiated	**Actual**							
A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**

Attachment 5
INSTRUCTIONS FOR COMPLETING
"FINANCIAL REPORT OF INDIVIDUAL PROJECT/CONTRACT"

GENERAL INFORMATION
Purpose. This Quarterly Financial Report is designed to: (1) provide a management tool for use by the Government in monitoring the application of financial and personnel resources to the BARDA funded contracts; (2) provide contractors with financial and personnel management data which is usable in their management processes; (3) promptly indicate potential areas of contract underruns or overruns by making possible comparisons of actual performance and projections with prior estimates on individual elements of cost and personnel; and (4) obtain contractor's analyses of cause and effect of significant variations between actual and prior estimates of financial and personnel performance.

REPORTING REQUIREMENTS

Scope. The specific cost and personnel elements to be reported shall be established by mutual agreement prior to award. The Government may require the contractor to provide detailed documentation to support any element(s) on one or more financial reports.

Number of Copies and Mailing Address. An original and two (2) copies of the report(s) shall be sent to the contracting officer at the address shown on the face page of the contract, no later than 30 working days after the end of the period reported. However, the contract may provide for one of the copies to be sent directly to the Contracting Officer's Representative.

REPORTING STATISTICS

A modification which extends the period of performance of an existing contract will not require reporting on a separate quarterly report, except where it is determined by the contracting officer that separate reporting is necessary. Furthermore, when incrementally funded contracts are involved, each separate allotment is not considered a separate contract entity (only a funding action). Therefore, the statistics under incrementally funded contracts should be reported cumulatively from the inception of the contract through completion.

Definitions and Instructions for Completing the Quarterly Report. For the purpose of establishing expenditure categories in Column A, the following definitions and instructions will be utilized. Each contract will specify the categories to be reported.

(1) **Key Personnel.** Include key personnel regardless of annual salary rates. All such individuals should be listed by names and job titles on a separate line including those whose salary is not directly charged to the contract but whose effort is directly associated with the contract. The listing must be kept up to date.

(2) **Personnel--Other.** List as one amount unless otherwise required by the contract.

(3) **Fringe Benefits.** Include allowances and services provided by the contractor to employees as compensation in addition to regular salaries and wages. If a fringe benefit rate(s) has been established, identify the base, rate, and amount billed for each category. If a rate has not been established, the various fringe benefit costs may be required to be shown separately. Fringe benefits which are included in the indirect cost rate should not be shown here.

(4) **Accountable Personal Property.** Include nonexpendable personal property with an acquisition cost of $1,000 or more and with an expected useful life of two or more years, and sensitive items regardless of cost. Form HHS 565, "Report of Accountable Property," must accompany the contractor's public voucher (SF 1034/SF 1035) or this report if not previously submitted. See "Contractor's Guide for Control of Government Property."

(5) **Supplies.** Include the cost of supplies and material and equipment charged directly to the contract, but excludes the cost of nonexpendable equipment as defined in (4) above.

(6) **Inpatient Care.** Include costs associated with a subject while occupying a bed in a patient care setting. It normally includes both routine and ancillary costs.

(7) **Outpatient Care.** Include costs associated with a subject while not occupying a bed. It normally includes ancillary costs only.

(8) **Travel.** Include all direct costs of travel, including transportation, subsistence and miscellaneous expenses. Travel for staff and consultants shall be shown separately. Identify foreign and domestic travel separately. If required by the contract, the following information shall be submitted: (i) Name of traveler and purpose of trip; (ii) Place of departure, destination and return, including time and dates; and (iii) Total cost of trip.

(9) **Consultant Fee.** Include fees paid to consultant(s). Identify each consultant with effort expended, billing rate, and amount billed.

(10) **Premium Pay.** Include the amount of salaries and wages over and above the basic rate of pay.

(11) **Subcontracts.** List each subcontract by name and amount billed.

(12) **Other Costs.** Include any expenditure categories for which the Government does not require individual line item reporting. It may include some of the above categories.

(13) **Overhead/Indirect Costs.** Identify the cost base, indirect cost rate, and amount billed for each indirect cost category.

(14) **General and Administrative Expense.** Cite the rate and the base. In the case of nonprofit organizations, this item will usually be included in the indirect cost.

(15) **Fee.** Cite the fee earned, if any.

(16) **Total Costs to the Government.**

PREPARATION INSTRUCTIONS

These instructions are keyed to the Columns on the Quarterly Report.

Column A--Expenditure Category. Enter the expenditure categories required by the contract.

Column B--Percentage of Effort/Hours Negotiated. Enter the percentage of effort or number of hours agreed to during contract negotiations for each labor category listed in Column A.

Column C--Percentage of Effort/Hours-Actual. Enter the cumulative percentage of effort or number of hours worked by each employee or group of employees listed in Column A.

Column D--Cumulative Incurred Cost at End of Prior Period. Enter the cumulative incurred costs up to the end of the prior reporting period. This column will be blank at the time of the submission of the initial report.

Column E--Incurred Cost-Current Period. Enter the costs which were incurred during the current period.

Column F--Cumulative Incurred Cost to Date. Enter the combined total of Columns D and E.

Column G--Estimated Cost to Complete. Make entries only when the contractor estimates that a particular expenditure category will vary from the amount negotiated. Realistic estimates are essential.

Column H--Estimated Costs at Completion. Complete only if an entry is made in Column G.

Column I--Negotiated Contract Amount. Enter in this column the costs agreed to during contract negotiations for all expenditure categories listed in Column A.

Column J--Variance (Over or Under). Complete only if an entry is made in Column H. When entries have been made in Column H, this column should show the difference between the estimated costs at completion (Column H) and negotiated costs (Column I). When a line item varies by plus or minus 10 percent, i.e., the percentage arrived at by dividing Column J by Column I, an explanation of the variance should be submitted. In the case of an overrun (net negative variance), this submission shall not be deemed as notice under the Limitation of Cost (Funds) Clause of the contract.

Modifications. List any modification in the amount negotiated for an item since the preceding report in the appropriate cost category.
Expenditures Not Negotiated. List any expenditure for an item for which no amount was negotiated (e.g., at the discretion of the contractor in performance of its contract) in the appropriate cost category and complete all columns except for I. Column J will of course show a 100 percent variance and will be explained along with those identified under J above.

Attachment 6
INCLUSION ENROLLMENT REPORT

This report format should NOT be used for data collection from study participants

Study Title:				
Total Enrollment:		**Protocol Number:**		
Contract Number:				
PART A. TOTAL ENROLLMENT REPORT: Number of Subjects Enrolled to Date (Cumulative) by Ethnicity and Race				
Ethnic Category	Sex/Gender			
	Females	**Males**	**Unknown or Not Reported**	**Total**
Hispanic or Latino				
Not Hispanic or Latino				
Unknown (Individuals not reporting ethnicity)				
Ethnic Category: Total of All Subjects*				
Racial Categories				
American Indian/Alaska Native				
Asian				
Native Hawaiian or Other Pacific Islander				
Black or African American				
White				
More than one race				
Unknown or not reported				
Racial Categories: Total of All Subjects*				
PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)				
Racial Categories	**Females**	**Males**	**Unknown or Not Reported**	**Total**
American Indian or Alaska Native				
Asian				
Native Hawaiian or Other Pacific Islander				
Black or African American				
White				
More Than One Race				
Unknown or not reported				
Racial Categories: Total of Hispanics or Latinos**				
*These totals must agree **These totals must agree				

Attachment 7 - Research Patient Care Costs

Research Patient Care Costs

(a) Research patient care costs are the costs of routine and ancillary services provided to patients participating in research programs described in this contract.
(b) Research patient care costs shall be computed in a manner consistent with the principles and procedures used by the Medicare Program for determining the part of Medicare reimbursement based on reasonable costs. The Diagnostic Related Group (DRG) prospective reimbursement method used to determine the remaining portion of Medicare reimbursement shall not be used to determine research patient care costs. Research patient care rates or amounts shall be established by the Secretary of HHS or his/her duly authorized representative.
(c) Prior to submitting an invoice for research patient care costs under this contract, the contractor must make every reasonable effort to obtain third party payment, where third party payors (including Government agencies) are authorized or are under a legal obligation to pay all or a portion of the charges incurred under this contract for research patient care.
(d) The contractor must maintain adequate procedures to identify those research patients participating in this contract who are eligible for third party reimbursement.
(e) Only those charges not recoverable from third party payors or patients and which are consistent with the terms and conditions of the contract are chargeable to this contract.

Attachment 8 - Report of Government Owned, Contractor Held Property

REPORT OF GOVERNMENT OWNED, CONTRACTOR HELD PROPERTY

CONTRACTOR:	**CONTRACT NUMBER:**
ADDRESS:	**REPORT DATE:**
ADDRESS1:	
ADDRESS2:	**FISCAL YEAR:**
CITY:	
STATE:	
ZIP:	

CLASSIFICATION	**BEGINNING OF PERIOD**		**ADJUSTMENTS**			**END OF PERIOD**	
	#ITEMS	VALUE	GFP ADDED	CAP ADDED	DELETIONS	#ITEMS	VALUE
LAND >=$25K							
LAND <$25K							
OTHER REAL >=$25K							
OTHER REAL <$25K							
PROPERTY UNDER CONST >=$25K							
PROPERTY UNDER CONST <$25K							
PLANT EQUIP >=$25K							
PLANT EQUIP <$25K							
SPECIAL TOOLING >=$25K							
SPECIAL TOOLING <$25K							
SPECIAL TEST EQUIP >=$25K							
SPECIAL TEST EQUIP <$25K							
AGENCY PECULIAR >=$25K							
AGENCY PECULIAR <$25K							
MATERIAL >=$25K (CUMULATIVE)							
PROPERTY UNDER MFR >=$25K							
PROPERTY UNDER MFR <$25K							

SIGNED BY:			
SIGNATURE		DATE SIGNED:	
NAME PRINTED		Email	
TITLE		TELEPHONE	

Report of Government Owned, Contractor Held Property (Rev 10/2014)

End of Contract No. HHSO100201800023C

Confidential Portions of this Exhibit marked as [***] have been omitted pursuant to a request for confidential treatment and have been filed separately with the Securities and Exchange Commission.

Exhibit 4.20

Addendum to Unprotected Sublease Contract dated March 18th, 2018

made and signed in Tel Aviv on February 3rd, 2019

Between: **CLAL LIFE SCIENCES Limited Partnership (registered partnership 55-020837-5**)
At 132 Derech Menachem Begin street, Azrieli Center, Triangular Tower, Tel Aviv
(hereinafter – the "**Lessor**")

on the one hand

And: **MEDIWOUND LTD (public company 512894940)**
At 42 Hayarkon street Yavne
(hereinafter – the "**Lessee**")

on the other hand

Whereas on 18.03.2018, an unprotected sublease contract was signed between the Lessor and the Lessee (the "**Lease Agreement**") in relation to the leasehold as defined in the Lease Agreement, which is located at parcel 3 on block 4939 in Yavne Industrial Zone including the structure built on it (the "**Original Leasehold**");

Whereas The Original Leasehold included the entire property (as defined in the Lease Agreement), except for the premises which were leased to CURETECH LTD. ("**Curetech**") at the same time, which are marked on the sketch hereby attached to this addendum as **Appendix A**, as well as 10 parking spaces which were leased to Curetech at the same time (the premises which were leased to Curetech Ltd. as specified in Appendix A and the said parking spaces will be hereinafter jointly called – the **"Rest of The Property** ");

And Whereas the lease of Curetech ended on 31.12.2018 and the Lessee turned to the Lessor requesting to hire the Rest of The Property as well, commencing on 1.1.2019, in its condition as-is, so that the Lessee will hire the property as a whole, without exception, and the Lessor granted the request of the Lessee, all in accordance with and subject to the terms of this addendum as specified below;

Now, therefore, it is declared, stipulated and agreed between the parties as follows:

1. **General**

1.1. The introduction to this addendum becomes an integral part hereof.

1.2. The captions of the addendum articles are for orientation and convenience purposes only, they are not part of the addendum and they will not be used for its interpretation.

1.3. This addendum becomes an integral part of the Lease Agreement and unless provided otherwise, all of its terms will be construed as defined in the Lease Agreement.

1.4. This addendum will come into force only after the parties sign it.

1.5. All provisions of the Lease Agreement which were not explicitly changed in accordance with the contents of this addendum, will continue binding the parties, mutatis mutandis.

2. **The transaction**

2.1 Commencing on January 1st, 2019 (the "**Effective Date**"), the Lessee hires from the Lessor, and the Lessor rents to the Lessee, within an unprotected sublease, the Rest of The Property as well, in accordance with the provisions of this addendum.

2.2 The Rest of The Property was delivered to the Lessee on the Effective Date in its condition as-is, and the Lessee confirms that it has been given the option to see and to examine the Rest of The Property within a reasonable lessee's examination, as well as any detail which can influence its decision to hire the Rest of The Property, and that it found the Rest of The Property suitable for its goal and needs, and that it waives any claim regarding a discrepancy and/or a fault in the Rest of The Property, except for a discrepancy or hidden defects which were known to the Lessor prior to the signing of this Agreement and which were not disclosed by it.

2.3 The lease period in respect of the Rest of The Property will begin on the Effective Date and it will end at the completion of the Lease period or the option period (as far as it is fulfilled), as these periods are defined in the Lease Agreement.

The original leasehold jointly with the Rest of The Property will be referred to hereinafter as the "**Updated Leasehold**".

2.4 Without derogating from the generality of the above stated, and for the avoidance of doubt, it is clarified that commencing on the Effective Date, the Lessee shall be the exclusive lessee and possessor of the Updated Leasehold, i.e., of the property as a whole, without exception, and the provisions of the Lease Agreement relating to the Leasehold, will relate to it commencing on the Effective Date for the Updated Leasehold, mutatis mutandis and as one piece.

3. **The rent**

Despite anything stated in the Lease Agreement:

3.1 The rent for the Updated Leasehold in respect of the period lasting from 1.1.2019 until 30.10.2019, will be in the amount of NIS 116,000 in respect of each month of lease.

3.2 The rent for the Updated Leasehold in respect of the period lasting from 1.11.2019 until 30.10.2022, will be in the amount of NIS 119,000 in respect of each month of lease.

3.3 The rent for the Updated Leasehold in respect of the option period (as much as it is extended) (i.e. in respect of the period lasting from 1.11.2022 until 30.10.2025), will be in the amount of NIS 125,500 in respect of each month of lease.

3.4 For the avoidance of doubt, the rent as stated above will be paid in addition to VAT by its lawful rate, as well as linkage differentials in accordance with the provisions of the Lease Agreement.

4. The rest of the provisions of the Lease agreement which were not explicitly changed in this addendum, will continue to apply mutatis mutandis only, and with respect to the Updated Leasehold, i.e., the property as a whole, without exception.

In WITNESS WHEREOF the parties have signed
at the place and on the date mentioned at the top of this contract:

/s/ Ofer Gonen /s/ Assaf Segal
Clal Life Sciences Limited Partnership

/s/ Gal Cohen /s/ Sharon Malka
Mediwound Ltd.

I hereby certify that the above signatures are the signatures of the Messrs.: Ofer Gonen and Assaf Segal and that these signatures legally bind the Lessor

/s/ Shiran Manor
Shiran Manor, Adv.

I hereby certify that the above signatures are the signatures of the Messrs.: Gal Cohen and Sharon Malka and that these signatures legally bind the Lessee

/s/ Yaron Meyer
Yaron Meyer, Adv.

Exhibit 4.21

SETTLEMENT AGREEMENT AND MUTUAL GENERAL RELEASE

THIS SETTLEMENT AGREEMENT AND MUTUAL GENERAL RELEASE (the "Settlement Agreement") is made and entered into this 24th day of March, 2019 (the "Effective Date"), by and between Teva Pharmaceutical Industries Ltd. ("Teva"), on the one hand, and MediWound Ltd. ("MediWound"), on the other hand. Teva and MediWound are together referred to as the "Parties" and individually referred to as a "Party".

WITNESSETH:

WHEREAS, the Parties have previously collaborated and in conjunction therewith were parties (whether alone or in concert with others) to certain transactions and agreements entered into during the years 2007 through 2013 (collectively, the "Collaboration Agreements"), which have terminated effective as of December 31, 2012 and September 2, 2013, as applicable; and

WHEREAS, following such termination of the Collaboration Agreements, each Party raised, and asserted that it further has, certain claims and demands against the other Party in connection with rights and obligations arising from and/or related to the Collaboration Agreements, including claims and demands by MediWound regarding, inter alia, damages related to production, development, loss of potential profits, commercialization costs of the products underlying said collaboration, and unpaid reimbursement obligations, amounting to an aggregate of NIS ~110,000,000, which were allegedly suffered by MediWound as a result of such collaboration and the termination thereof, and including claims and demands by Teva regrading, inter alia, certain unpaid amounts (collectively, the "Asserted Claims"); and

WHEREAS, the Parties have been actively discussing their claims and demands since the year 2013 and, in light of the costs and delays associated with litigating the disputes between the Parties, the Parties desire to fully and finally settle all matters arising from and/or related to the their business relationship and the termination of such relationship, including without limitation the Asserted Claims, as more fully set forth herein;

NOW, THEREFORE, in consideration of the mutual promises herein contained, it is agreed as follows:

1. Non-Admission of Liability.

This Settlement Agreement shall not in any way be construed as an admission by either Party that it has acted wrongfully with respect to the other Party or any other person, and each Party specifically disclaims any liability to or wrongful acts against the other Party or any other person, on the part of itself, its employees, its agents or its other Releasors (as defined in Section 5.1 below). The Parties specifically acknowledge and agree that this Agreement is made to compromise and settle the Asserted Claims and the Parties' respective rights and defenses in connection therewith, and that neither this Agreement nor any action taken pursuant to this Agreement shall be offered or received in evidence in any action or proceeding by one Party against the other Party.

2. No Other Claims.

Each Party represents and warrants to the other Party that it has not filed any complaints, charges or lawsuits against the other Party with any governmental agency, court, or administrative entity.

3. Settlement Payment; Payment Undertaking.

Following MediWound's Asserted Claims, but without admitting of any of the Asserted Claims:

3.1. On or before April 2, 2019, Teva will pay MediWound an amount in cash equal to US$4,000,000 (" Settlement Payment"), as full and final settlement, termination and satisfaction of all Claims (as defined in Section 5.1 below) released by MediWound below. Such Settlement Payment shall be made in accordance with wiring instructions to be provided by MediWound.

3.2. MediWound hereby undertakes to pay Teva an amount equal to 15% of any recognized revenues of MediWound (according to MediWound's financial statements, which will be prepared in accordance with International Financial Reporting Standards (IFRS) generally accepted accounting principles) (the "Recognized Revenues") generated, from time to time after January 1, 2019, from the sale or the license by MediWound or its Affiliates of the Licensed Products (including, for the avoidance of doubt, any Recognized Revenues generated from time to time after January 1, 2019 from any agreement between MediWound and Biomedical Advanced Research and Development Authority dated September 29, 2015 (the "BARDA Agreement" - MediWound confirms that it had not received any Recolonized Revenues from the BARDA Agreement prior to January 1, 2019)(the " Revenues-Based Payments"); all, up to an aggregate amount equal to US$ 10,200,000 *(the term "Licensed Product" shall have the meaning ascribed thereto in that certain License and Collaboration Agreement dated August 21, 2007, as amended, by and between MediWound and Teva, which definition is hereby incorporated by reference into this Agreement to constitute an integral part hereof)*; each such payment shall be made by MediWound to Teva from time to time within 45 days following the later of actual receipt by MediWound of the applicable Recognized Revenues and the recognition of such Recognized Revenues by MediWound in its annual financial statements under applicable financial principals; provided however that, on the date on which MediWound is to pay Teva the Revenue-Based Payment (if any) in respect of the 12-month period ending December 31, 2028 (and regardless of whether or not any such Revenue-Based Payment is at all due in respect of such period at that time), MediWound shall pay Teva an amount equal to the lesser of:

(i) the sum (if positive) of (A) US$ 10,200,000 *minus* (B) the aggregate amount of all Revenues-Based Payments that have been paid by MediWound to Teva until such time pursuant to this Section 3.2 (such sum being inclusive of the amount of the Revenue-Based Payment that may be due by MediWound to Teva at that time in respect of the 12-month period ending December 31, 2028; i.e. no double payment); in which case, MediWound's obligations under this Section 3.2 shall terminate and be of no further force and effect;

or

(ii) US$ 1,700,000, which amount shall be credited against and be deducted from any future payments that may become due by MediWound to Teva under this Section 3.2 at any time thereafter (in which case, Mediwound's obligations under this Section 3.2 shall continue until such time as the aggregate amount of all payments that have been paid by Mediwound to Teva until such time pursuant to this Section 3.2, inclusive of the amount paid under this clause 3.2(ii), equal an aggregate of US$10,200,000).

3.3. Anything to the contrary notwithstanding:

(i) in no event shall the aggregate of all payments by MediWound to Teva pursuant to this Agreement, exceed the amount of US$10,200,000, and once such aggregate has been paid in full a aforesaid, all payment obligations of MediWound under this Agreement shall terminate and be of no further force and effect;

(ii) on or prior to the sixtieth (60^{th}) calendar day following the last day of each calendar year during the period commencing on the Effective Date and expiring upon the time by which the Company shall have completed the payment to Teva of an aggregate amount equal to US$10,200,000, the Company shall deliver to Teva a certificate, executed by an officer of the Company and certified by an outside accountant to the Company (being a firm of Independent Certified Public Accountants who are members of the Israeli Institute of Certified Public Accountants and are associated with one of the "big four" independent public accountants of internationally recognized standing), setting forth the Company's determination of the amount of Recognized Revenues, which were generated from the sale or license of the Licensed Products for such preceding calendar year;

(iii) No Assurances. Teva hereby acknowledges that the commercialization of any of the Licensed Products as well as the amount of Recognized Revenues, if any, that may be generated at any time hereafter, are uncertain, and that (A) MediWound or its Affiliates may not (i) commercialize any of the Licensed Products, and/or (ii) generate any revenues from the Licensed Products, and (B) it is therefore not assured that the Company will be required to pay the consideration set forth in Section 3.2(i);

(iv) Without limiting the other provisions of Section 3.3, MediWound shall have sole discretion over all matters relating to the Licensed Products or other technology, including, but not limited to, any development, testing, manufacturing, regulatory, marketing and sales decisions relating to any Licensed Product, and MediWound and its Affiliates shall have no obligations to Teva with respect to such decisions or the development, sales and marketing of the Licensed Products other than with respect to the applicable payments under Section 3.2 above, if any, that may become due and payable pursuant to Section 3.2;

(v) MediWound shall be entitled to assign its rights and obligations pursuant to Sections 3.2 and 3.3 - (A) to any third party who (a) is a recipient of all or substantially all of the assets of MediWound or (b) who (x) is a recipient of all or substantially all marketing and/or commercialization rights of the Licensed Products, in either the United States or Europe, and (y) has either a market capitalization in excess of $3 billion or annual revenues for the most recent fiscal year (calculated in accordance with GAAP) in excess of $200 million, or (B) to any trustee or escrow agent for the benefit of MediWound or its shareholders.

4. Waiver and Termination.

4.1. Teva on behalf of itself and on behalf of its Releasors (as defined in Section 5 below) hereby irrevocably terminates, waives and forever discharges MediWound and its respective Releasees (as defined in Section 5 below) from any and all Claims, debts, obligations or liabilities that MediWound or any of its Releasees had or has to Teva or any of its Releasors under, in connection with or arising out of the Collaboration Agreements (or any of them) or the termination thereof, or the subsequent repurchase by MediWound of Teva's shares in MediWound, or any subject matter of the Teva 2013 Waiver and Termination (as defined in Section 10 below); without, however, annulling or otherwise abrogating the binding effect of the Teva 2013 Waiver and Termination or of any other release, waiver, termination, share purchase, share transfer deed, payment or other action or transaction that has been given, made or taken prior to the Effective Date.

4.2. MediWound on behalf of itself and on behalf of its Releasors hereby irrevocably terminates, waives and forever discharges Teva and its respective Releasees from any and all debts, obligations or liabilities that Teva or any of its Releasees had or has to MediWound or any of its Releasors under, in connection with or arising out of the Collaboration Agreements (or any of them) or the termination thereof, or the subsequent repurchase by MediWound of Teva's shares in MediWound, or any subject matter of the Teva 2013 Waiver and Termination; without, however, annulling or otherwise abrogating the binding effect of any other release, waiver, termination, share purchase, share transfer deed, payment or other action or transaction that has been given, made or taken prior to the Effective Date.

4.3. Each Party, on behalf of itself and on behalf of its Releasors, hereby irrevocably and unconditionally (subject in the case of MediWound, to Section 3.1 above) waives and forever discharges the other Party and its respective Releasees - in consideration for the waivers and releases (and, in the case of MediWound, also in consideration for the Settlement Payment, and in the case of Teva, also in consideration for the payment undertaking in Section 3.2) by the other Party and its Releasors contained in this Settlement Agreement - from any and all claims and demands arising out of any act or omission by such other Party occurring prior and up to the Effective Date relating to, in connection with or arising out of the Collaboration Agreements (or any of them) or the termination thereof, or the subsequent repurchase by MediWound of Teva's shares in MediWound, or any subject matter of the Teva 2013 Waiver and Termination, or any other agreement, understanding, covenant or promise, whether written or oral, entered into, prior to the Effective Date, between the Parties or their respective Releasors (whether alone or in concert with others), including without limitation MediWound's demand that Teva pay to MediWound certain consideration, costs, loss of profits, damages and expenses underlying the Asserted Claims; without, however, annulling or otherwise abrogating the binding effect of the Teva 2013 Waiver and Termination or any other release, waiver, termination, share purchase, share purchase, payment or other action or transaction that has been given, made or taken prior to the Effective Date.

5. Release.

In addition to the provisions of Section 4 above, each Party, on behalf of itself, its past, present and future Affiliates, and its and their respective past, present and future subsidiaries, agents, directors, officers, employees, representatives, attorneys, heirs, administrators, executors, successors and assigns, and all persons acting by, through, under or in concert with any of them (collectively, such Party's " Releasors"), hereby irrevocably and unconditionally releases, acquits and forever discharges the other Party, each of its past, present and future Affiliates, and its and their respective past, present and future subsidiaries, agents, directors, officers, employees, representatives, attorneys, heirs, administrators, executors, successors and assigns, and all persons acting by, through, under or in concert with any of them (collectively, such Party's " Releasees"), from any and all charges, complaints, claims, liabilities, obligations, promises, agreements, damages, actions, causes of action, suits, rights, demands, costs, losses, debts and expenses (including attorneys' fees and costs actually incurred) of any nature whatsoever, known or unknown, suspected or unsuspected, whether in law or equity, including, but not limited to, rights arising out of alleged violations of any contracts, express or implied, any covenant of good faith and fair dealing, express or implied, or any tort, or any governmental statute, regulation, or ordinance (any of the foregoing a "Claim," and collectively, the "Claims") which each Party at any time had, has or may have, against the other Party or any of the Releasees by reason of any act or omission concerning any matter, cause or thing prior and up to the Effective Date.

"Affiliate" shall mean, with respect to any Party hereto, any person, organization or entity directly or indirectly controlled by such Party. For purposes of this definition only, "control" of another person, organization or entity shall mean the ability, directly or indirectly, to direct the activities of the relevant entity, and shall include, without limitation (i) ownership or direct control of fifty percent (50%) or more of the outstanding voting stock or other ownership interest of the other organization or entity, or (ii) possession of, or the power to elect or appoint fifty percent (50%) or more of the members of the governing body of the organization or other entity.

6. Certain Exceptions.

Anything to the contrary notwithstanding, it is hereby agreed between the Parties that the waivers and releases set forth in this Settlement Agreement do not include and do not intend to include (i) a waiver or release of Claims resulting from a Party's breach of the terms, conditions and covenants of this Settlement Agreement or of the Teva 2013 Waiver and Termination, nor of any claim relating to a breach of one Party's confidentiality obligations to the other Party, other than any breach of confidentiality obligations which was already known to a party hereto on or prior to the Effective Date; or (ii) an annulment or other abrogation of the binding effect of the of the Teva 2013 Waiver and Termination or of any other release, waiver, termination, share purchase, share transfer deed, payment or other action or transaction that has been given, made or taken prior to the Effective Date.

7. Knowing and Voluntary Waiver by the Parties.

For the purpose of implementing a full and complete release, each Party expressly acknowledges that this Settlement Agreement is intended to include in its effect, without limitation, all Claims which a Party does not know or suspect to exist at the time of execution hereof, and that this Settlement Agreement contemplates the extinguishment of any such Claims.

8. Confidentiality; Publicity.

8.1. The Parties represent and agree that they will keep the terms and conditions of this Settlement Agreement completely confidential, other than as specifically set forth hereunder. Neither Party shall disclose any information concerning this Settlement Agreement except (i) in response to an order of a court of competent jurisdiction, a subpoena issued by a government agency, or as required by applicable law or regulations including applicable securities laws and stock exchange regulations, (ii) to any other party to the Collaboration Agreements (or any of them), (iii) as required by any due diligence or inquiry in connection with any current or future contemplated investment, license, acquisition or other transaction (subject, however, to a nondisclosure agreement), and (iv) to such Party's auditors or legal or tax advisors, or as necessary to enforce the terms of this Agreement. Except in the cases listed above in this Section 8.1, each Party, if being asked, will only be entitled to respond that the matter has been resolved.

8.2. Neither MediWound, Teva or any person acting on their behalf, nor any of their respective Affiliates or any person acting on their behalf, shall issue, without the consent of the MediWound and Teva, any public statement or press release or make any other disclosure concerning the terms and content of this Settlement Agreement, except for such public statement or press release or other disclosure which is required to be made pursuant to any applicable law or stock exchange regulations in which event the party required to make such disclosure shall, to the extent permissible and reasonably feasible, provide both MediWound and Teva with a copy of such public statement or press release or other disclosure reasonably in advance, to enable such MediWound and Teva to comment on such press release or public statement or other disclosure, and shall take into consideration any such comments, provided that the final determination shall be at the sole discretion of the party required to make such disclosure. The press release, regarding the execution of this Settlement Agreement is attached hereto as Schedule A.

9. Voluntary Act.

Each Party represents and acknowledges that it has carefully read and fully understands all of the provisions of this Settlement Agreement and that it is voluntarily entering into this Settlement Agreement wholly of its own free will and volition. Each Party further represents that it has been represented by counsel of its own choice in the negotiations leading to its execution of this Settlement Agreement and that it has received independent legal advice, or has had the opportunity to receive independent legal advice, from such Party's respective legal counsel with respect to the advisability of executing this Settlement Agreement.

10. Sole and Entire Agreement.

This Settlement Agreement constitutes the full and entire understanding and agreement between the Parties, and fully supersedes any and all prior agreements or understandings between the Parties hereto pertaining to the subject matter hereof and any other written or oral agreement existing between the Parties are expressly terminated, excluding that certain Irrevocable Waiver and Termination Agreement by Teva dated September 2, 2013, a copy of which is attached hereto as Schedule B (the "Teva 2013 Waiver and Termination") which shall remain in full force and effect notwithstanding the termination of the obligations of MediWound referred to therein.

11. Miscellaneous

11.1. For the purposes of this Settlement Agreement, neither Party shall be deemed the writer of this document. This Settlement agreement may not be amended, revised or modified in whole or in part, except pursuant to a separate written agreement signed by both Parties.

11.2. The terms and conditions of this Settlement Agreement shall inure to the benefit of and be binding upon the respective, Releasors, Releasees, successors and assigns of the Parties hereto. Nothing in this Settlement Agreement, express or implied, is intended to confer upon any party other than the Parties hereto, the Releasees or their respective successors and assigns any rights, remedies, obligations, or liabilities under or by reason of this Settlement Agreement, except as expressly provided in this Settlement Agreement.

11.3. This Settlement Agreement and any controversy arising out of or relating to this Settlement Agreement shall be governed by and construed in accordance with the internal laws of the State of Israel, without regard to conflict of law principles that would result in the application of any law other than the laws of the State of Israel. The parties hereto (a) hereby irrevocably and unconditionally submit to the jurisdiction of the competent courts of Tel Aviv-Jaffa, Israel for the purpose of any suit, action or other proceeding arising out of or based upon this Settlement Agreement, (b) agree not to commence any suit, action or other proceeding arising out of or based upon this Settlement Agreement except in the competent courts of Tel Aviv-Jaffa, Israel.

11.4. This Settlement Agreement may be executed and deliv-ered by facsimile or electronically-transmitted PDF signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

11.5. No delay or omission to exercise any right, power or remedy accruing to any Party under this Settlement Agreement, upon any breach or default of any other Party under this Settlement Agreement, shall impair any such right, power or remedy of such non-breaching or non-defaulting Party nor shall it be construed to be a waiver of any such breach or default, or an acquiescence therein, or of or in any similar breach or default thereafter occurring; nor shall any waiver of any single breach or default be deemed a waiver of any other breach or default previously or thereafter occurring. Any waiver, permit, consent or approval of any kind or character on the part of any Party of any breach or default under this Settlement Agreement, or any waiver on the part of any Party of any provisions or conditions of this Settlement Agreement, must be in writing and shall be effective only to the extent specifically set forth in such writing. All remedies, either under this Settlement Agreement or by law or otherwise afforded to any Party, shall be cumulative and not alternative.

11.6. The invalidity or unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision.

11.7. Each Party to this Settlement Agreement agrees to execute and to deliver such additional documents and instruments, and to perform such additional acts, as may be necessary to effectuate, consummate or perform any of the terms, provisions or conditions of this Settlement Agreement.

[Signature Block Follows]

IN WITNESS WHEREOF, this Settlement Agreement and Mutual General Release has been duly executed on the date herein above set forth:

MediWound Ltd.

By: /s/ Gal Cohen
Name: Gal Cohen
Title: Chief Executive Officer

By: /s/ Sharon Malka
Name: Sharon Malka
Title: Chief Financial Officer

Teva Pharmaceutical Industries Ltd.

By: /s/ Michael Mcclellan
Name: Michael Mcclellan
Title: EVP, Chief Financial Officer

By: /s/ Eli Shani
Name: Eli Shani
Title: SVP, Business Development

List of attachments:

- *Schedule A – Form of Press Release*
- *Schedule B - Irrevocable Waiver and Termination Agreement by Teva, dated September 2, 2013*

[Signature Page to
Settlement Agreement and Mutual General Release / 2019]

March 24, 2019

STRICTLY CONFIDENTIAL

Teva Pharmaceutical Industries Ltd.
5 Basel Street
Petach Tikva 4951033, Israel

Re.: Certain Indemnity in connection with Settlement Agreement

MediWound Ltd. ("MediWound") and Teva Pharmaceutical Industries Ltd. ("Teva") are parties to that certain Settlement Agreement and Mutual General Release dated as of the date hereof (the "Settlement Agreement"), relating to certain collaborations and transactions entered into during the years 2007 through 2013, which have terminated effective as of December 31, 2012 and September 2, 2013, as applicable, and to which MediWound was a party (whether together with Teva or alone in concert with others).

One of the aforesaid collaborations was associated with, inter alia, a Buyout Agreement dated December 22, 2010, by and among MediWound, PolyHeal Ltd. ("PolyHeal"), the Equity Holders (as defined therein) and the Shareholders Representative Committee referred to therein (the "Buyout Agreement").

Teva was not a party to such Buyout Agreement.

MediWound informed Teva that claims were made by certain Equity Holders against MediWound concerning the achievement of a PH2 Milestone under the Buyout Agreement and the non-payment by MediWound to the Equity Holders of an amount of US$ 6,750,000 ("PH2 Milestone Payment"), and, to its defense, MediWound relied, inter-alia, on the back-to-back structure of such transactions and suggested a direct rivalry under which the plaintiffs may file their claims directly against Teva.

As it is the Parties' intention to settle all Asserted Claims (as such term is defined in the Settlement Agreement), then, in order to induce Teva to enter into the Settlement Agreement:

1. MediWound hereby agrees, subject to the terms and conditions of this letter agreement, to indemnify, defend and hold harmless Teva and its directors, officers, agents, and employees (Teva and each such person being referred to as an "Indemnified Person"), from and against any amount actually paid by such Indemnified Party to any Equity Holder (as defined in the Buyout Agreement) that is not a Releasee of Teva (any such Equity Holder that is not a Releasee of Teva - a "Third Party") arising out of any and all suits, investigations, claims, or demands made by such Third Party and relating to the (i) achievement of the PH2 Milestone and (ii) the non-payment to such Third Party of all or any of its portion of the PH2 Milestone Payment under the Buyout Agreement (a "Collaboration Agreement Claim"); provided, however, that notwithstanding anything to the contrary: (a) any indemnity that may become payable by MediWound in accordance with this letter agreement shall be paid in cash, (b) subject only to Section 5(b) of this letter agreement, the maximum aggregate liability of MediWound under this letter shall not exceed an amount equal to $10,000,000 (the "Cap Amount"), (c) an Indemnified Person shall only be entitled to indemnification under this letter for a Third Party's Collaboration Agreement Claim with respect to which a notice has been received by MediWound prior to December 31, 2023 (in which case the indemnity hereunder shall survive with respect to such Third Party's Collaboration Agreement Claim until it has been finally resolved), and (d) notwithstanding anything to the contrary, the obligations of MediWound hereunder shall not apply to any special, indirect or consequential damages incurred by any Indemnified Persons themselves but will apply to any special indirect or consequential damages which may become payable by the Indemnified Persons to any Third Party in connection with any Collaboration Agreement Claim. The indemnity, defense and hold-harmless obligation set forth in this letter shall be the sole and exclusive remedy available to the Indemnified Persons with respect to or in connection with any Third Party's Collaboration Agreement Claim. In no event shall MediWound be required to indemnify, defend or hold harmless any Indemnified Person, from or against any claims, demands, losses, costs or expenses, other than as specifically set forth above.

2. Teva shall give MediWound prompt written notice within 10 days of becoming aware of any Third Party's Collaboration Agreement Claim asserted or threatened against an Indemnified Person that could give rise to a right of indemnification under this letter and; provided, however, that the failure to give such notification shall not affect the indemnification provided hereunder except to the extent that MediWound shall have been prejudiced as a result of such failure.

3. Upon receipt such notice MediWound will assume sole control and defense of such Third Party's Collaboration Agreement Claim, subject to the right of Teva, as set forth in Section 7 below, to waive its right to indemnity, defense and hold-harmless. Each Indemnified Person shall cooperate with MediWound's investigation and defense of such Third Party's Collaboration Agreement Claim, as may reasonably be requested by MediWound.

4. So long as the aggregate potential liability of MediWound under this letter has not exceeded the Cap Amount, MediWound shall assume the defense of any Third Party's Collaboration Agreement Claim by giving written notice to Teva and the Indemnified Person within 30 days after MediWound's receipt of Teva's notice thereof. Teva on behalf of the Indemnified Persons shall be entitled to participate in, but not control, the defense of the Third Party's claim or demand and to employ counsel of their choice for such purpose at the Indemnified Persons' sole cost and expense.

5. In the event MediWound has not assumed the defense of any Third Party's Collaboration Agreement Claim in accordance with the previous paragraph and it is determined by a final judgment of a competent court that MediWound has breached its obligations under this Settlement Agreement to assume the defense of such Third Party's Collaboration Agreement Claim, then (a) such breach shall not release MediWound from its indemnification obligation hereunder and, accordingly, in such event at the request of Teva, MediWound shall (subject to the Cap Amount and other limitations set forth above) (x) indemnify the Indemnified Persons for any amount actually paid by such Indemnified Persons to such Third Party arising out of such Third Party's Collaboration Agreement Claim, or (y) pay directly to such Third Party any reasonable settlement amount as requested by the Indemnified Person in settlement of the relevant Third Party's Collaboration Agreement Claim (provided such settlement (i) includes a release from all liabilities in respect of such claim and (ii) does not involve an obligation other than the payment of money, that would bind or impair MediWound), and (b) Teva shall be entitled to full reimbursement of its reasonable legal fees and expenses (notwithstanding the Cap Amount) in defending or settling such Third Party's Collaboration Agreement Claim, without derogating from any remedy which may be determined by the competent court with respect to MediWound's breach of its obligations hereunder.

6. MediWound shall have the sole right to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such third party claim, on such terms as MediWound, in its sole discretion, shall deem appropriate, provided that MediWound shall not settle any such claim without the prior written consent of Teva (which consent shall be binding upon all Indemnified Persons and shall not be unreasonably withheld or delayed) if such settlement (i) exceeds the Cap Amount less any amounts previously paid by Mediwound under this letter agreement, (ii) does not include a release by the applicable Third Party of the Indemnified Persons from all liabilities in respect of such claim or (iii) if such settlement would involve an obligation other than the payment of money, that would bind or impair any such Indemnified Person.

7. Notwithstanding the foregoing, if, in the reasonable judgment of Teva, such suit or claim involves an issue or matter which could have a material adverse effect on the business, operations or assets of any such Indemnified Person, then Teva may waive (which waiver shall apply to, and be binding upon Teva and all other Indemnified Persons) the rights to indemnity, defense and hold-harmless under this Agreement and shall have the rights to conduct the defense or settlement thereof on behalf of the Indemnified Persons (without derogating from MediWound's rights to the extent it is a party to any such proceeding), and in such a case MediWound shall have no obligations whatsoever under this letter agreement neither to Teva nor any other Indemnified Person.

The provisions of Sections 8 and 11 of the Settlement Agreement shall apply, *mutatis mutandis*, to this letter agreement.

This letter agreement shall be governed by and construed in accordance with the laws of the State of Israel, without reference to principles of conflicts of law that may result in the application of the law of any other jurisdiction. Any claim, controversy or dispute arising from this letter shall be referred to and resolved solely in the competent courts located in Tel-Aviv, Jaffa, Israel.

Breach of this letter agreement by Teva or Mediwound shall deemed a breach of the Settlement Agreement by such party.

[Signature Page Follows]

Very truly yours,

MediWound Ltd.

By: /s/ Gal Cohen
Name: Gal Cohen
Title: Chief Executive Officer

By: /s/ Sharon Malka
Name: Sharon Malka
Title: Chief Financial Officer

ACCEPTED AND AGREED:

Teva Pharmaceutical Industries Ltd.

By: /s/ Michael Mcclellan
Name: Michael Mcclellan
Title: EVP, Chief Financial Officer

By: /s/ Eli Shani
Name: Eli Shani
Title: SVP, Business Development

[Signature Page to
Letter re. Certain Indemnity in connection with Settlement Agreement/ 2019]

+רחוב הירקון 42 אזור תעשייה צפוני יבנה 8122745 טלפון: 972-77-9714100+ פקס: 972-77-9714111
42 Hayarkon St. Industrial Zone Yavne 8122745 Tel: +972-77-9714100 Fax: +972-77-9714111
E-mail: mediwound@mediwound.com website: www.mediwound.com

EXHIBIT 12.1

CERTIFICATIONS

I, Gal Cohen, 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/Gal Cohen
Gal Cohen
President and Chief Executive Officer
Date: March 25, 2019

EXHIBIT 12.2

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 Financial and Operations Officer
Date: March 25, 2019

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, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Gal Cohen, 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/Gal Cohen
Gal Cohen
President and Chief Executive Officer
Date: March 25, 2019

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, 2018 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 Financial and Operations Officer
Date: March 25, 2019

EXHIBIT 15.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in MediWound Ltd.'s Registration Statement on Form S-8 (No. 333-223767, 333-195517 and 333-210375) of our report dated March 25, 2019, with respect to the consolidated financial statements of MediWound Ltd. included in the Annual Report on Form 20-F of MediWound Ltd. for the year ended December 31, 2018.

/s/ KOST, FORER, GABBAY & KASIERER

Tel Aviv, Israel
March 25, 2019

KOST, FORER, GABBAY & KASIERER
A Member of Ernst & Young Global