BIO BLAST PHARMA LTD.
Form 20-F
March 31, 2015

United States

Securities and Exchange Commission

Washington, D.C. 20549

FORM 20-F

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES

EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2014

Commission file number: 001-36578

Bio Blast Pharma Ltd.

(Exact name of Registrant as specified in its charter)

State of Israel

(Jurisdiction of incorporation or organization)

37 Dereh Menachem Begin St.,
15th Floor
Tel Aviv 6522042 Israel
(Address of principal executive offices)

Mr. Colin Foster

Chief Executive Officer and President

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(Name, Telephone 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 of NIS 0.01	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.

14,230,480 Ordinary Shares, par value NIS 0.01 per share

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

¨ Yes x 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 x 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.

x Yes ¨ No

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

x Yes ¨ No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer (as defined in Rule 12b-2 of the Act).

¨ Large Accelerated Filer ¨ Accelerated Filer x Non-Accelerated Filer

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

U.S. GAAP x

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 x No

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INTRODUCTION

We are a development-stage biopharmaceutical company focused on the identification, licensing, acquisition, development and commercialization of drugs for rare and ultra-rare genetic and metabolic diseases. We seek to identify therapeutic platforms that offer solutions for several diseases that share a common pathophysiological mechanism, which are the functional changes that accompany a particular syndrome or disease. We focus on diseases with severe and debilitating manifestations, where the unmet medical need is clear, the biological mechanism of action is understood and for which there is no satisfactory treatment.

Unless otherwise indicated, all references to the "Company," "we," "our" "us" and "BioBlast" refer to Bio Blast Pharma Ltd. a its subsidiary, Bio Blast Pharma, Inc., a Delaware corporation. References to "U.S. dollars" and "$" are to the currency of the United States of America, and references to "NIS" are to New Israeli Shekels. References to "Ordinary Shares" are to our Ordinary Shares, par value of NIS 0.01 per share.

We do not endorse or adopt any third-party research or forecast firms' statements or reports referred to in this annual report and assume no responsibility for the contents or opinions represented in such statements or reports, nor for the updating of any information contained therein.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This annual report contains express or implied "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 and other U.S. Federal securities laws. These forward-looking statements include, but are not limited to:

- our expectations regarding the timing of commencing clinical studies with respect to SBMA, BB-FA, BB-OTC, BBrm1 and other product candidates;
- our expectations regarding the progress of our clinical studies, including the duration, cost and whether such studies will be conducted at all;

- the number, scope, size and design of our planned development programs, including pre-clinical and clinical studies;
- our intention to apply for regulatory approval for our product candidates, and the costs and timing of such regulatory approvals;
- the likelihood of regulatory approvals for our product candidates;
- the timing, cost or other aspects of the commercial launch of our product candidates, including our intention to a build a commercial infrastructure to support commercialization of our product candidates;
- future sales of our product candidates or any other future products or product candidates;
- our ability to achieve favorable pricing for our product candidates;
- the potential for our product candidates to receive designation as an orphan drug and implications if it does not receive such designation;
- that our product candidates potentially offer effective solutions for various diseases;
- our expectations regarding the manufacturing and supply of our product candidate for use in our clinical trials, and the commercial supply of our product candidates;
- third-party payor reimbursement for our product candidates;

- our estimates regarding anticipated expenses, capital requirements and our needs for substantial additional financing;
- the ultra-rare diseases patient market size and market adoption of our product candidates by physicians and patients;
- completion and receiving favorable results of clinical trials for our product candidates;
- protection of our intellectual property, including issuance of patents to us by the U.S. Patent and Trademark Office, or USPTO, and other governmental patent agencies;
- the development and approval of the use of our product candidates for additional indications other than ultra-rare diseases; and
- our expectations regarding licensing, acquisitions and strategic operations.

In some cases, forward-looking statements are identified by terminology such as “may,” “will,” “could,” “should,” “expects,” “plans,” “anticipates,” “believes,” “intends,” “estimates,” “predicts,” “potential,” or “continue” or the negative of these terms o comparable terminology. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results or performance to differ materially from those projected. These statements are only current predictions and are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry’s actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements. In addition, historic results of scientific research and clinical and preclinical trials do not guarantee that the conclusions of future research or trials would not suggest different conclusions or that historic results referred to in this annual report would not be interpreted differently in light of additional research and clinical and preclinical trials results. The forward-looking statements contained in this annual report are subject to risks and uncertainties, including those discussed under Item 3.D. – “Risk Factors” and in our other filings with the Securities and Exchange Commission, or the SEC. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance, or achievements. Except as required by law, we are under no duty to (and expressly disclaim any such obligation to) update or revise any of the forward-looking statements, whether as a result of new information, future events or otherwise, after the date of this annual report.

PART ONE

Item 1. Identity of directors, senior management and advisErs

Not applicable.

Item 2. Offer statistics and expected timetable

Not applicable.

Item 3. Key information

3.A. Selected financial data

Our historical financial statements are prepared in accordance with generally accepted accounting principles in the United States and are presented in U.S. dollars. The selected historical financial information as of December 31, 2013 and 2014 and for the years ended December 31, 2012, 2013 and 2014 have been derived from, and should be read in conjunction with, the financial statements of BioBlast Pharma Ltd. and notes thereto appearing elsewhere in this annual report. The selected financial data as of December 31, 2012 have been derived from the audited financial statements of BioBlast Pharma Ltd. not included in this annual report.

The information presented below is qualified by the more detailed historical financial statements set forth in this annual report, and should be read in conjunction with those financial statements, the notes thereto and the discussion under Item 5 – “Operating and Financial Review and Prospects.”

As an "emerging growth company," and pursuant to the Jump Start our Business Startups Act of 2012, or the JOBS Act, we are not required to include selected financial data for periods before the earliest audited period presented in our initial public offering registration statement. Accordingly, we are not yet required to present five years of historical financial data.

Statement of Operations Data – Year Ended December 31

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

	2014	2013	2012
Research and Development	$4,441	$732	$140
General and Administrative	2,639	416	86
Operating loss	7,080	1,148	226
Financial expenses (Income), net	(58)	(3)	3
Loss	7,022	1,145	229
Deemed dividend	-	26	-
Net loss attributable to holders of Ordinary Shares	$7,022	$1,171	$229
Net basic and diluted loss per Ordinary Share	0.57	0.14	0.03
Weighted average number of Ordinary Shares used in computing basic and diluted net loss per share	12,259,600	8,423,018	7,551,427

Balance Sheet Data – Year Ended December 31

(in thousands of U.S. dollars, except for share data)

	2014	2013	2012
Working capital	$30,605	$168	$75
Total assets	32,954	306	156
Shareholders' equity	$30,674	$175	$75
Number of Ordinary Shares outstanding	14,230,480	9,182,867	7,551,427

3.B. Capitalization and indebtedness

Not applicable.

3.C. Reasons for the offer and use of proceeds

Not applicable.

3.D. Risk factors

You should carefully consider the risks described below, together with all of the other information in this annual report. The risks described below are not the only risks facing us. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial may also materially and adversely affect our business operations. If any of these risks actually occurs, our business and financial condition could suffer and the price of our shares could decline.

Risks Related to Our Financial Condition and Capital Requirements

We are a development-stage company and have a limited operating history on which to assess our business, we have incurred significant losses since our inception, and anticipate that we will continue to incur significant losses for the foreseeable future.

We are a development-stage biopharmaceutical company with a limited operating history. We have incurred net losses since our inception in January 2012, including a net loss of $7.0 million for the year ended December 31, 2014. As of December 31, 2014, we had an accumulated deficit of $8.4 million.

We have devoted substantially all of our financial resources to identify, acquire, license, and develop our product candidates, including conducting preclinical and clinical studies and providing general and administrative support for these operations. To date, we have financed our operations primarily through the sale of equity securities. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations, or grants. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. With respect to most of our product candidates, we are in the early stages of clinical development. We have commenced a Phase 2/3 clinical trial for two of our product candidates, and it may be several years, if ever, before we have any product candidates approved for commercialization. Even if we obtain regulatory approval to market a product candidate, our future revenue will depend upon the size of any markets in which our product candidates may receive approval, and our ability to achieve sufficient market acceptance, pricing, reimbursement from third-party payors, and adequate market share for our product candidates in those markets.

We have incurred continuing losses. We depend on outside financing resources to continue our activities. On August 5, 2014, we completed a successful initial public offering that raised net proceeds of approximately $31.4 million. In the opinion of our management and based on our current business plans, our balances of cash and cash equivalents including short-term bank deposits will enable us to fund our activities until the end of 2016 or early 2017. However, the actual amount of cash we will need to fund our operations is subject to many factors, including, but not limited to, the timing, design and execution of the clinical trials of our existing drug candidates, any future projects which may be in-licensed or any other business development activities. For example, changing circumstances and/or acquisition of new technologies may cause us to consume capital significantly faster than management currently anticipates and we may need to spend more money than currently expected because of, among others, circumstances beyond our control.

Additionally, we expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our research and preclinical and clinical development of our product candidates;
- expand the scope of our current clinical studies for our product candidates;
- advance our programs into more expensive clinical studies;
- initiate additional preclinical, clinical, or other studies for our product candidates;
- change or add additional manufacturers or suppliers;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies;
- establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- seek to identify, assess, acquire, license, and/or develop other product candidates;
- make milestone or other payments under any license agreements;
- seek to maintain, protect, and expand our intellectual property portfolio;
- seek to attract and retain skilled personnel;
- create additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts; and
- experience any delays or encounter issues with any of the above, including but not limited to failed studies, complex results, safety issues, or other regulatory challenges that require longer follow-up of existing studies, additional major studies, or additional supportive studies in order to pursue marketing approval.

Further, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We have never generated any revenue from product sales and may never be profitable.

We have no products approved for commercialization and have never generated any revenue. Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize one or more of our product candidates. We do not anticipate generating revenue from product sales for the foreseeable future. Our ability to generate future revenue from product sales depends heavily on our success in many areas, including but not limited to:

- completing research and preclinical and clinical development of our product candidates;
- obtaining regulatory and marketing approvals for product candidates for which we complete clinical studies;
- developing a sustainable and scalable manufacturing process for any approved product candidates and establishing and maintaining supply and manufacturing relationships with third parties that can conduct the process and provide adequate (in amount and quality) products to support clinical development and the market demand for our product candidates, if approved;
- launching and commercializing product candidates for which we obtain regulatory and marketing approval, either directly or with a collaborator or distributor;

- obtaining market acceptance of our product candidates as viable treatment options;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or the EMA, or other regulatory agencies, domestic or foreign, to change our manufacturing processes or assays, or to perform clinical, nonclinical, or other types of studies in addition to those that we currently anticipate. In cases where we are successful in obtaining regulatory approvals to market one or more of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. If the number of our addressable rare disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably expected population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. Additionally, if we are not able to generate revenue from the sale of any approved products, we may never become profitable.

We expect that we will need to raise substantial additional funding before we can expect to become profitable from sales of our products. This additional financing may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit, or terminate our product development efforts or other operations.

We are currently advancing our Cabaletta platform product candidates through clinical development and advancing our other product candidates, BB-FA, BB-OTC, and BBrm1, as well as our other early stage research projects, through preclinical development. Developing our product candidates is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidates through clinical studies.

As of December 31, 2014, our cash and cash equivalents including short-term bank deposits were $32.6 million. We expect that our existing cash, cash equivalents and short-term bank deposits will be sufficient to fund our current operations for at least the next 12 months; however, we expect that we will require substantial additional capital to obtain regulatory approval for, and to commercialize, our product candidates. In addition, our operating plans may change as a result of many factors that may currently be unknown to us, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including but not limited to:

- the scope, rate of progress, results and cost of our clinical studies, preclinical testing, and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates and any products that we may develop;
- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing sales, marketing, and distribution capabilities; and

- the terms and timing of any collaborative, licensing, and other arrangements that we may establish, including any required milestone and royalty payments thereunder.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our shareholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our Ordinary Shares to decline. The incurrence of indebtedness could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell, or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results, and prospects. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay, or discontinue one or more of our research or development programs or the commercialization of any product candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, and results of operations.

Raising additional capital would cause dilution to our existing shareholders, and may restrict our operations or require us to relinquish rights.

We may seek additional capital through a combination of private and public equity offerings, debt financings and collaborations and strategic and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a shareholder. Debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions such as incurring debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration, strategic alliance and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates, or grant licenses on terms that are not favorable to us.

Risks Related to the Discovery and Development of Our Product Candidates

We are heavily dependent on the success of our product candidates, which are in the early stages of preclinical or clinical development. We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized.

To date, we have invested substantially all of our efforts and financial resources to identify, acquire, license, and develop our product candidates, including conducting preclinical and clinical studies and providing general and administrative support for these operations. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize one or more product candidates. We currently generate no revenue from sales of any drugs, and we may never be able to develop or commercialize a marketable drug.

Each of our product candidates is in the early stages of development and will require additional clinical development (and in some cases additional preclinical development), management of nonclinical, clinical, and manufacturing activities, regulatory approval, obtaining adequate manufacturing supply, building of a commercial organization, and significant marketing efforts before we generate any revenue from product sales. We currently have one product candidate in Phase 2 clinical studies and another one of our product candidates has advanced into a Phase 2/3 trial which, if the results are positive, we believe could be a pivotal trial. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates.

We as a company have never submitted marketing applications to the FDA or comparable foreign regulatory authorities. We cannot be certain that any of our product candidates will be successful in clinical studies or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical studies. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

We generally plan to seek regulatory approval to commercialize our product candidates in the United States, the European Union, and in additional foreign countries where we have commercial rights. To obtain regulatory approval in other countries, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing and controls, clinical studies, commercial sales, pricing, and distribution of our product candidates. Even if we are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue and results of operations could be negatively affected.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, typically takes many years following the commencement of clinical studies, and depends upon numerous factors. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. We have not obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical studies;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's safety-benefit ratio for its proposed indication is acceptable;
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the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;

- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical studies;

- the data collected from clinical studies of our product candidates may not be sufficient to support the submission of a new drug application, or NDA, or biologics license application, or BLA, or other submission or to obtain regulatory approval in the United States or elsewhere;

- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical studies, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies may not be predictive of future study results.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical study process. The results of preclinical studies and early clinical studies of our product candidates may not be predictive of the results of later-stage clinical studies. Product candidates that have shown promising results in early-stage clinical studies may still suffer significant setbacks in subsequent registration clinical studies. For example, the safety or efficacy results generated to date in preclinical and clinical studies for Cabaletta, BBrm1, BB-FA and BB-OTC do not ensure that later clinical studies will demonstrate similar results. There is a high failure rate for drugs and biologics proceeding through clinical studies, and product candidates in later stages of clinical studies may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical studies. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical studies due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses. We do not know whether any Phase 2, Phase 3, or other clinical studies we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain regulatory approval to market our drug candidates.

We may find it difficult to enroll patients in our clinical studies given the limited number of patients who have the diseases for which our product candidates are being studied. Difficulty in enrolling patients could delay or prevent clinical studies of our product candidates.

Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of our clinical studies depends in part on the speed at which we can recruit patients to participate in testing our product candidates, and, although we have not yet experienced difficulty enrolling patients in clinical studies in the past, we may experience delays in our clinical studies if we encounter difficulties in enrollment in the future.

Each of the conditions for which we plan to evaluate our current product candidates is a rare genetic disease. Accordingly, there are limited patient pools from which to draw for clinical studies. For our current product candidates:

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we estimate that several thousand patients in the United States suffer from OPMD for which Cabaletta is being studied;

- we estimate that a few thousand patients in the United States suffer from SCA3 for which Cabaletta is being studied;
- we estimate a few thousand patients in the United States suffer from SBMA for which Cabaletta is being studied;
- we estimate that several thousand patients in the United States suffer from Friedreich's Ataxia for which BB-FA is being studied;
- we estimate that a few thousand patients in the United States suffer from OTC deficiency for which BB-OTC is being studied;
- we estimate that several thousand patients in the United States suffer from SMA deficiency for which BBrm1 is being studied; and
- we estimate that the worldwide prevalence of the foregoing diseases is similar and sometimes higher than the total number of patients in the United States.

In addition to the rarity of these diseases, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. Additionally, the process of finding and diagnosing patients may prove costly. We also may not be able to identify, recruit, and enroll a sufficient number of patients to complete our clinical studies because of the perceived risks and benefits of the product candidate under study, the availability and efficacy of competing therapies and clinical studies, the proximity and availability of clinical study sites for prospective patients, and the patient referral practices of physicians. If patients are unwilling to participate in our studies for any reason, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of potential products may be delayed.

If we experience delays in the completion of, or termination of, any clinical study of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenue from any of these product candidates could be delayed or prevented. In addition, any delays in completing our clinical studies will increase our costs, slow down our product candidate development and approval process, and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition, and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may also ultimately lead to the denial of regulatory approval of our product candidates.

We may encounter substantial delays in our clinical studies, or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, time consuming, and uncertain as to outcome. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical studies can occur at any stage of testing, and our future clinical studies may not be successful. Events that may prevent successful or timely completion of clinical development include but are not limited to:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation of human clinical studies;
- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical study sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical study sites;

- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical study site;
- imposition of a clinical hold by regulatory agencies, after review of an investigational new drug, or IND, application, or equivalent application, or an inspection of our clinical study operations or study sites;
- delays in recruiting suitable patients to participate in our clinical studies;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties, or us to adhere to clinical study requirements;
- failure to perform in accordance with the FDA's good clinical practices requirements, or applicable regulatory guidelines in other countries;
- delays in having patients complete participation in a study or return for post-treatment follow-up;
- patients dropping out of a study;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- the cost of clinical studies of our drug candidates being greater than we anticipate;

- clinical studies of our drug candidates producing negative or inconclusive results, which may result in us deciding, or regulators requiring us, to conduct additional clinical studies or abandon drug development programs; and

- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical studies or the inability to do any of the foregoing.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue. In addition, we may need to conduct additional studies to bridge our repurposed product candidates to generic products in the market. We may also be required to conduct additional safety, efficacy and comparability studies before we will be allowed to start clinical studies with our repurposed drugs. Clinical study delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to obtain orphan exclusivity and to successfully commercialize our product candidates and may harm our business and results of operations.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical studies and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Patients enrolled in our studies of Cabaletta for OPMD, known as our HOPEMD study, and for Spinocerebellar Ataxia, known as our SCA3 study, may suffer side effects associated with the use of Cabaletta. Other enzyme replacement therapies have been associated with infusion-associated reactions due to a developing allergy to the product, which can cause rashes, pain, significant clinical disease, or even death. Our BB-FA and BB-OTC product candidates may also cause these or similar side effects. Results of our studies could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our studies could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny or withdraw approval of our product candidates for any or all targeted indications.

The drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the study, or result in potential product liability claims. We do not currently hold product liability insurance and do not anticipate obtaining product liability insurance until such time as we have received FDA or other comparable foreign authority approval for a product and there is a product that is being provided to third parties outside of clinical trials.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, or if a patient suffers a serious complication, including death, with respect to one of our products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such product;

- regulatory authorities may require additional warnings on the label;

- we may be required to create a Risk Evaluation and Mitigation Strategy, or REMS, plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and/or other elements to assure safe use;

- we could be sued and held liable for harm caused to patients; and

- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations, and prospects.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.

If our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States. In addition, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practices, or cGMP, regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA or BLA. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or 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. We will also be required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have FDA approval. The holder of an approved NDA or BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical studies to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval were obtained via the accelerated approval pathway, we could be required to conduct a successful post-marketing clinical study to confirm clinical benefit for our products. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval. Furthermore, any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. Foreign regulatory authorities impose similar requirements.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning letters;
- impose civil or criminal penalties;

- suspend or withdraw regulatory approval;
- suspend any of our ongoing clinical studies;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- seize or detain products, or require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

Risks Related to our Reliance on Third Parties

We rely on third parties to conduct our preclinical and clinical studies and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third-party CROs to monitor and manage data for our ongoing preclinical and clinical programs. We rely on these parties for execution of our preclinical and clinical studies, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with cGMP, current good clinical practices, or cGCP, and Good Laboratory Practices, or GLP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites, and other contractors. If we or any of our CROs or vendors fail to comply with applicable regulations, the clinical data generated in our clinical studies may be deemed unreliable and the FDA, EMA, or comparable foreign regulatory authorities may require us to perform additional clinical studies before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical studies comply with cGCP regulations. In addition, our clinical studies must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical studies, which would delay the regulatory approval process.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our on-going clinical, nonclinical, and preclinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements, or for other reasons, our clinical studies may be extended, delayed, or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. CROs may also generate higher costs than anticipated. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that

these delays or challenges will not have a material adverse impact on our business, financial condition, and prospects.

We rely completely on third parties to manufacture our preclinical and clinical drug supplies. Our business could be harmed if those third parties fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality levels or prices.

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture our preclinical and clinical drug supplies for use in the conduct of our clinical studies, and we lack the resources and the capability to manufacture any of our product candidates on a clinical or commercial scale. We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical studies. There are a limited number of suppliers for raw materials that are used to manufacture our drugs, and there may be a need to identify alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our product candidates for our clinical studies, and, if approved, ultimately for commercial sale. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Although we generally do not begin a clinical study unless we believe we have a sufficient supply of a product candidate to complete such study, any significant delay or discontinuity in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical study due to the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing, and potential regulatory approval of our product candidates, which could harm our business and results of operations.

We are subject to a multitude of manufacturing risks, any of which could substantially increase our costs and limit supply of our product candidates.

The process of manufacturing our product candidates is complex, highly regulated, and subject to several risks, including but not limited to:

- the process of manufacturing biologics, such as BB-FA and BB-OTC, is extremely susceptible to 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 for any of our product candidates could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination; and

- the manufacturing facilities in which our product candidates are made could be adversely affected by equipment failures, labor shortages, natural disasters, power failures, and numerous other factors.

Any adverse developments affecting manufacturing operations for our product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls, or other interruptions in the supply of our product candidates. We may also have to take inventory write-offs and incur other charges and expenses for product candidates that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives.

The drug substance and drug product for our product candidates are currently acquired from single suppliers. The loss of these suppliers, or their failure to supply us with the drug substance or drug product, could materially and adversely affect our business.

In specific instances we may rely on a single provider or manufacturer for our product candidates. For example, the raw materials used to manufacture our Cabaletta product candidate are acquired from a single third party drug products supplier. Additionally, Cabaletta is manufactured by a single third party manufacturer. It is possible that we will be required to switch providers in the future. In such case, the process of switching suppliers and/or manufacturers may be costly and/or time consuming for us, and that may include the temporary or permanent suspension of a clinical study or commercial sales of our candidate products.

We do not currently have any other suppliers for the drug substance or drug product of our product candidates and, although we believe that there are alternate sources of supply that could satisfy our clinical and commercial

requirements, we cannot assure you that identifying alternate sources and establishing relationships with such sources would not result in significant delay in the development of our product candidates. Additionally, we may not be able to enter into supply arrangements with alternative suppliers on commercially reasonable terms, or at all. A delay in the development of our product candidates or having to enter into a new agreement with a different third party on less favorable terms than we have with our current suppliers could have a material adverse impact upon on our business.

We and our collaborators and contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and have limited capacity.

All entities involved in the preparation of therapeutics for clinical studies or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We, our collaborators, or our contract manufacturers must supply all necessary documentation in support of an NDA, BLA, or Marketing Authorization Application, or MAA, on a timely basis and must adhere to GLP and cGMP regulations enforced by the FDA and other regulatory agencies through their facilities inspection program. Some of our contract manufacturers have never produced a commercially approved pharmaceutical product and therefore have not obtained the requisite regulatory authority approvals to do so. The facilities and quality systems of some or all of our collaborators and third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the products may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever.

The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our collaborators and third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we, our collaborators, or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or other applicable regulatory authority can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, withdrawal of an approval, or suspension of production. As a result, our business, financial condition, and results of operations may be materially harmed.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through an NDA or BLA supplement or MAA amendment, or equivalent foreign regulatory filing, which

could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause us to incur higher costs and could cause the delay or termination of clinical studies, regulatory submissions, required approvals, or commercialization of our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenue.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to develop and manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements, or other similar agreements with our collaborators, advisors, employees, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor’s discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

Risks Related to Commercialization of Our Product Candidates

If the market opportunities for our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Because the target patient populations of our product candidates are small, we must be able to successfully identify patients and achieve a significant market share to maintain profitability and growth.

We focus our research and product development on treatments for rare and ultra-rare genetic diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare and ultra-rare genetic diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business.

We intend to rely on third-party manufacturers to produce our product candidates, but we have not entered into binding agreements with any such manufacturers to support commercialization. Additionally, these manufacturers do not have experience producing our product candidates at commercial levels and may not achieve the necessary regulatory approvals or produce our product candidates at the quality, quantities, locations, and timing needed to support commercialization.

We have not yet secured manufacturing capabilities for commercial quantities of our product candidates. Although we intend to rely on third-party manufacturers for commercialization, we have only entered into agreements with such manufacturers to support our clinical studies. We may be unable to negotiate binding agreements with the manufacturers to support our commercialization activities at commercially reasonable terms.

Manufacturers may not have the experience or ability to produce our product candidates at commercial levels. We may run into technical or scientific issues related to manufacturing or development that we may be unable to resolve in a timely manner or with available funds. We also have not completed all of the characterization and validation activities necessary for commercialization and regulatory approvals. If our manufacturing partners do not conduct all such necessary activities, our commercialization efforts will be harmed.

Even if we timely develop a manufacturing process and successfully transfer it to the third-party product manufacturers, if such third-party manufacturers are unable to produce the necessary quantities of our product candidates, or in compliance with cGMP or other pertinent regulatory requirements, and within our planned timeframe and cost parameters, the development and sales of our products, if approved, may be materially harmed.

We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are similar, more advanced, or more effective than ours, which may adversely affect our financial condition and our ability to successfully commercialize our product candidates.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We are currently aware of various existing therapies in the market and in development that may in the future compete with our product candidates.

Gene therapy, cell therapy, bone marrow transplantation and other approaches may also emerge for the treatment of any of the disease areas in which we focus.

We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies. Some of the pharmaceutical and biotechnology companies we expect to compete with include Shire, Sanofi, BioMarin, Alexion, Ultragenyx and Roche, other smaller companies or biotechnology startups, as well as other large multinational pharmaceutical companies. Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products as well. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring, or licensing on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization, and market penetration than we do. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

We currently have no marketing and sales organization. If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenue.

Although our employees may have sold other similar products in the past while employed at other companies, we as a company have no experience selling and marketing our product candidates and we currently have no marketing or sales organization. To successfully commercialize any products that may result from our development programs, we will need to develop these capabilities, either on our own or with others. If our product candidates receive regulatory approval, we intend to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize our product candidates in major markets, which will be expensive, difficult,

and time consuming. Any failure or delay in the development of our internal sales, marketing, and distribution capabilities would adversely impact the commercialization of our products.

Further, given our lack of prior experience in marketing and selling biopharmaceutical products, our initial estimate of the size of the required sales force may be materially more or less than the size of the sales force actually required to effectively commercialize our product candidates. As such, we may be required to hire substantially more sales representatives to adequately support the commercialization of our product candidates or we may incur excess costs as a result of hiring more sales representatives than necessary. With respect to certain geographical markets, we may enter into collaborations with other entities to utilize their local marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We may be competing with companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

The commercial success of any current or future product candidate will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community.

Even with the requisite approvals from the FDA and comparable foreign regulatory authorities, the commercial success of our product candidates will depend in part on the medical community, patients, and third-party payors accepting our product candidates as medically useful, cost-effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, third-party payors, and others in the medical community. The degree of market acceptance of any of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy of the product as demonstrated in clinical studies and potential advantages over competing treatments;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;
- the clinical indications for which approval is granted;
- relative convenience and ease of administration;
- the cost of treatment, particularly in relation to competing treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party insurance coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical and clinical studies, market acceptance of the product will not be fully known until after it is launched. Our efforts to educate the medical community and third-party payors on the benefits of the product candidates may require significant resources and may never be successful. If our product candidates are approved but fail to achieve an adequate level of acceptance by physicians, patients, third-party payors, and others in the medical community, we will not be able to generate sufficient revenue to become or remain profitable.

While orphan drug products are typically sold at a high price relative to other medications, the market may not be receptive to high pricing of our products.

We develop our product candidates to treat rare and ultra-rare diseases, a space where medications are usually sold at high prices compared with other medications. However, several of our product candidates are repurposed drugs, which means, among other things, that they are available in pharmacies for the purpose of treating indications that are different from the indications for which we plan to use. Accordingly, even if regulatory authorities approve our product candidates, the market may not be receptive to, and it may be difficult for us to achieve, a per-patient per-year price high enough to allow us to realize a return on our investment.

The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

Our target patient populations are small, and accordingly the pricing, coverage, and reimbursement of our product candidates, if approved, must be adequate to support our commercial infrastructure. Our per-patient prices must be sufficient to recover our development and manufacturing costs and potentially achieve profitability. Accordingly, the availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to be able to afford expensive treatments such as ours, assuming approval. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other third-party payors. If coverage and reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about coverage and reimbursement for new drugs are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for products such as ours.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicinal products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Health Care Reform Law, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Health Care Reform Law, among other things, subjects biologic products to potential competition by lower-cost biosimilars, addresses 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, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and promotes a new Medicare Part D coverage gap discount

program.

In addition, other legislative changes have been proposed and adopted in the United States since the Health Care Reform Law was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by the U.S. Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. On March 1, 2013, the President signed an executive order implementing sequestration, and on April 1, 2013, the 2% Medicare payment reductions went into effect. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain effective patent rights for our product candidates or any future product candidates, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to our technologies and product candidates. Our success depends in large part on our and our licensors' ability to obtain and maintain patent and other intellectual property protection in the United States and in other countries with respect to our proprietary technology and products.

We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unsolved. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue, and even if such patents cover our product candidates, third parties may challenge their validity, enforceability, or scope, which may result in such patents being narrowed, found unenforceable or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates, or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

We, independently or together with our licensors, have filed several patent applications covering various aspects of our product candidates. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

We have a number of patent applications directed to methods of use and certain compositions of matter. For example, we have a pending patent application covering the use of intravenously administered trehalose in several orphan diseases associated with trinucleotide repeat expansion (PolyA/PolyQ) diseases. With regards to our mitochondrial protein replacement therapy we do not have patent protection for the concept of attaching TAT to a protein generally but do have patent protection for attaching TAT to our mitochondrial protein targets, such as for example, frataxin. With our read-through technology, we do not have composition of matter protection. Instead, we have filed a use patent application of a generic family of molecules in a non-systemic route of administration for genetic neuro degenerative and neuro developmental diseases and new route of administration through direct injection to the central nervous system. In addition, our patent applications have not resulted in issued patents.

If we cannot obtain and maintain effective patent rights for our product candidates, we may not be able to compete effectively and our business and results of operations would be harmed.

We may not have sufficient patent terms to effectively protect our products and business.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications.

While patent term extensions under the Hatch-Waxman Act in the United States and under supplementary protection certificates in Europe may be available to extend the patent exclusivity term for Cabaletta, BB-FA and BB-OTC as well as the BBrm family of molecules we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long. In addition, upon issuance in the United States any patent term can be adjusted based on certain delays caused by the applicant(s) or the USPTO. For example, a patent term can be reduced based on certain delays caused by the patent applicant during patent prosecution. If we do not have sufficient patent terms or regulatory exclusivity to protect our products, our business and results of operations will be adversely affected.

Patent policy and rule changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. We therefore cannot be certain that we or our licensors were the first to make the invention claimed in our owned and licensed patents or pending applications, or that we or our licensor were the first to file for patent protection of such inventions. Assuming the other requirements for patentability are met, in the United States prior to March 15, 2013, the first to make the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. After March 15, 2013, under the Leahy-Smith America Invents Act, or the Leahy-Smith Act, enacted on September 16, 2011, the United States has moved to a first to file system. The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and may also affect patent litigation. The effects of these changes are currently unclear as USPTO, must still implement various regulations, the courts have yet to address any of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. In general, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

If we are unable to maintain effective proprietary rights for our product candidates or any future product candidates, we may not be able to compete effectively in our markets.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors, and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, and reexamination proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture, or methods for treatment related to the use or manufacture of our product candidates. We have conducted freedom to operate analyses with respect to only certain of our product candidates, and therefore we do not know whether there are any third-party patents that would impair our ability to commercialize these product candidates. We also cannot guarantee that any of our analyses are complete and thorough, nor can we be sure that we have identified each and every patent and pending application in the United States and abroad that is relevant or necessary to the commercialization of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable.

Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture, or methods of use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such

patent expires or is finally determined to be invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license, or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities.

For example, we sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, we may have to abandon development of that program and our business and financial condition could suffer.

We may face competition from biosimilars, which may have a material adverse impact on the future commercial prospects of our mitochondrial protein replacement platform.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars with respect to BB-FA and BB-OTC and future product candidates based on our protein replacement platform. In the United States, the Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biological products that are demonstrated to be "highly similar," or biosimilar, to or "interchangeable" with an FDA-approved biological product. This new pathway could allow competitors to reference data from innovative biological products 12 years after the time of approval of the innovative biological product. This data exclusivity does not prevent another company from developing a product that is highly similar to the innovative product, generating its own data, and seeking approval. Data exclusivity only assures that another company cannot rely upon the data within the innovator's application to support the biosimilar product's approval. In his proposed budget for fiscal year 2014, President Obama proposed to cut this 12-year period of exclusivity down to seven years. He also proposed to prohibit additional periods of exclusivity due to minor changes in product formulations, a practice often referred to as "evergreening." It is possible that the U.S. Congress may take these or other measures to reduce or eliminate periods of exclusivity. The Biologics Price Competition and Innovation Act of 2009 is complex and only beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when any such processes may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for BB-FA and BB-OTC.

In Europe, the European Commission has granted marketing authorizations for several biosimilars pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to get on the market until 10 years after the time of approval of the innovative product. This 10-year marketing exclusivity period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with

existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with our products.

If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

The patent protection and patent prosecution for some of our product candidates is dependent on third parties.

While we normally seek and gain the right to fully prosecute the patents relating to our product candidates, there may be times when patents relating to our product candidates are controlled by our licensors.

In addition, even where we now have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to us assuming control over patent prosecution.

If we fail to comply with our obligations in the agreements under which we license intellectual property and other rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalties, and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, we may be required to make certain payments to the licensor, we may lose the exclusivity of our license, or the licensor may have the right to terminate the license, in which event we would not be able to develop or market products covered by the license. Additionally, the milestone and other payments associated with these licenses will make it less profitable for us to develop our drug candidates. See Item 4.B. – "Business Overview – License Agreements" for a description of our license agreements with the Hebrew University in Jerusalem and the Tel-Aviv University.

In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding intellectual property subject to a licensing agreement, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;

- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our collaborators; and
- the priority of invention of patented technology.

If disputes over intellectual property and other rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We may not be able to identify infringements of our patents and accordingly the enforcement of our intellectual property rights may be difficult.

The drug substance in some of our product candidates is a repurposed drug. It is possible that if we receive FDA approval of such drug candidates patients that we target with this drug would receive prescriptions for the same substance but not by using our product. It would be difficult, if not impossible for us to identify such instances that may constitute an infringement of our patents. In addition, because the drug substance of some of our product candidates is a repurposed drug, such substance may not be eligible for protection by composition of matter patents. Patent protection for these product candidates is limited to method of use formulation and other types of patents.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. If we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable.

Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our Ordinary Shares.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary

information, of any of our employee's former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Therefore, we may receive less revenue from future products if such claims are successful which in turn could impact our future profitability.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity. Therefore, obtaining and enforcing biotechnology patents is costly, time consuming, and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Employees may be entitled to seek compensation for their inventions irrespective of their agreements with us.

In 2012, the Israeli Supreme Court ruled that an employee who receives a patent or contributes to an invention during his or her employment may be allowed to seek compensation for it from his or her employer, even if the employee's contract of employment specifically states otherwise and the employee has transferred all intellectual property rights to the employer. The Supreme Court ruled that the fact that a contract revokes the employee's right for royalties and compensation, does not rule out the right of the employee to claim his or her right for royalties. However, in a more recent ruling, issued in May 2014, the government-appointed Compensation and Royalties Committee, established under the Israeli Patents Law, 5727-1967, determined that an employee's remuneration rights for service inventions may be waived by an explicit contractual waiver. It is our understanding that a petition has been filed with the Israeli Supreme Court. In light of the petition and the inconsistency in rulings it is still unclear if, and to what extent, our employees may be able to claim compensation with respect to our future revenue. Therefore, although we enter into agreements with our employees pursuant to which they waive their right to special remuneration for inventions created in the scope of their employment or engagement and agree that any such inventions are owned exclusively by us, we may face claims by employees demanding remuneration beyond their regular salary and benefits, and we may receive less revenue from future products if such claims are successful, which in turn could impact our future profitability.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual

property rights to the same extent as federal and state laws in the United States. Among these countries is China where we intend to protect our intellectual property rights to the extent possible.

Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks Related to Our Business Operations

Our future success depends in part on our ability to retain our executive officers and management level employees and to attract, retain, and motivate other qualified personnel.

We are highly dependent on Colin Foster, our Chief Executive Officer, and Dalia Megiddo, M.D., our Founder and Chief Development Officer. The loss of their services without a proper replacement may adversely impact the achievement of our objectives. Mr. Foster and Dr. Megiddo may leave our employment at any time (subject to contractual notice periods, as applicable), as each one is an “at will” independent contractor. Recruiting and retaining other qualified employees, consultants, and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled personnel in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical studies may make it more challenging to recruit and retain qualified personnel. The inability to recruit and retain qualified personnel, or the loss of the services of Mr. Foster or Dr. Megiddo without proper replacement, may impede the progress of our research, development, and commercialization objectives.

If we fail to obtain or maintain orphan drug exclusivity for our products, our competitors may sell products to treat the same conditions and our revenue will be reduced.

Our business strategy focuses on the development of drugs that are eligible for FDA and European Union orphan drug designation. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the EMA’s Committee

for Orphan Medicinal Products, or COMP, 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 Community. 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 necessary investment in developing the drug or biological product.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. 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 is granted 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.

Because the extent and scope of patent protection for our products may in some cases be limited, orphan drug designation is especially important for our products for which orphan drug designation may be available. For eligible drugs, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products and biologic products that do not have broad patent protection, our competitors may then sell the same drug to treat the same condition sooner than if we had obtained orphan drug exclusivity and our revenue will be reduced.

Even though we have obtained orphan drug designation for OPMD in the United States, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even with orphan drug exclusivity, if a third party were to prepare or market a trehalose IV preparation which infringes upon our intellectual property, we may need to initiate litigation, which may be costly, to enforce our rights against such party. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.

As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, sales, marketing, financial, legal, and other resources. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We may not be successful in our efforts to identify, license, or discover additional product candidates.

Although a substantial amount of our effort will focus on the continued clinical testing, potential approval, and commercialization of our existing product candidates, the success of our business also depends upon our ability to

identify, license, or discover additional product candidates. Our research programs or licensing efforts may fail to yield additional product candidates for clinical development for a number of reasons, including but not limited to the following:

- our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates;
- we may not be able or willing to assemble sufficient resources to acquire or discover additional product candidates;
- our product candidates may not succeed in preclinical or clinical testing;
- our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and

- a product candidate may not be accepted as safe and effective by patients, the medical community, or third-party payors.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, or we may not be able to identify, license, or discover additional product candidates, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives.

As a public company, we incur significant legal, accounting, and other expenses. In addition, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, as well as rules subsequently implemented by the SEC and the NASDAQ Stock Market, or NASDAQ, have imposed various requirements on public companies. Emerging growth companies may implement some of these requirements over a longer period and up to five years from the date of their initial public offering. We intend to take advantage of this legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment, and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and will make some activities more time consuming and costly. For example, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal control over financial reporting and disclosure controls and procedures. In particular, we will be required to perform system and process evaluation and testing of our internal control over financial reporting to allow management to report, commencing in our annual report on Form 20-F for the year ending December 31, 2015, on the effectiveness of our internal control over financial reporting, if then required by the SEC's rules pursuant to Section 404 of the Sarbanes-Oxley Act. Our testing may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses. Our compliance with the SEC's rules pursuant to Section 404 will require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. Moreover, if we are not able to comply with the SEC's requirements in a timely manner or if we identify or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by NASDAQ, the SEC, or other regulatory authorities, which would require additional financial and management resources.

New laws and regulations as well as changes to existing laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act and rules adopted by the SEC and by NASDAQ, would likely result in increased costs to us as we respond to their requirements.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly or indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations. These laws may impact, among other things, our proposed sales, marketing, and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information;

- the federal physician sunshine requirements under the Health Care Reform Laws requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers, state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state 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 laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the Health Care Reform Law, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the Health Care Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

International expansion of our business exposes us to business, regulatory, political, operational, financial, and economic risks associated with doing business outside of the United States or Israel.

Other than our headquarters and other operations which are located in Israel, we currently have limited international operations, but our business strategy incorporates potentially significant international expansion, particularly in anticipation of approval of our product candidates. We plan to maintain sales representatives and conduct physician and patient association outreach activities, as well as clinical trials, outside of the United States and Israel. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting, and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- failure by us to obtain regulatory approvals for the use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection and enforcing our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism, and political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions;
- certain expenses including, among others, expenses for travel, translation, and insurance; and

- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, or FCPA, its books and records provisions, or its anti-bribery provisions.

Any of these factors could significantly harm our future international expansion and operations and, consequently, our results of operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use, and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently, and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. We do not currently carry biological or hazardous waste insurance coverage.

Risks Related to Our Ordinary Shares

We may be a "passive foreign investment company", or PFIC, for U.S. federal income tax purposes in the current taxable year or may become one in any subsequent taxable year. There generally would be negative tax consequences for U.S. taxpayers that are holders of our Ordinary Shares if we are or were to become a PFIC.

We would be treated as a PFIC for U.S. federal income tax purposes in any taxable year in which either (1) at least 75% of our gross income is "passive income" or (2) on average at least 50% of our assets by value produce passive income or are held for the production of passive income. Passive income for this purpose generally includes, among other things, certain dividends, interest, royalties, rents and gains from commodities and securities transactions and from the sale or exchange of property that gives rise to passive income. Passive income also includes amounts derived by reason of the temporary investment of funds, including those raised in a public offering. In determining whether a non-U.S. corporation is a PFIC, a proportionate share of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account. Based on the nature of our business, the projected composition of our income and the projected composition and estimated fair market values of our assets, we cannot rule out that we will not be a PFIC for our current taxable year or in the future. The tests for determining PFIC status are applied annually, and it is difficult to make accurate projections of future income and assets which are relevant to this determination. In addition, our PFIC status may depend in part on the market value of our Ordinary Shares. Accordingly, there can be no assurance that we currently are not or will not become a PFIC in the future. If we are a PFIC in any taxable year during which a U.S. taxpayer holds our Ordinary Shares, such U.S. taxpayer would be subject to certain adverse U.S. federal income tax rules. In particular, if the U.S. taxpayer did not make an election to treat us as a "qualified electing fund," or QEF, or make a "mark-to-market" election, then "excess distributions" to the U.S. taxpayer, and any gain realized on the sale or other disposition of our Ordinary Shares by the U.S. taxpayer: (1) would be allocated ratably over the U.S. taxpayer's holding period for the Ordinary Shares; (2) the amount allocated to the current taxable year and any period prior to the first day of the first taxable year in which we were a PFIC would be taxed as ordinary income; and (3) the amount allocated to each of the other taxable years would be subject to tax at the highest rate of tax in effect for the applicable class of taxpayer for that year, and an interest charge for the deemed deferral benefit would be imposed with respect to the resulting tax attributable to each such other taxable year. In addition, if the Internal Revenue Service, or IRS, determines that we are a PFIC for a year with respect to which we have determined that we were not a PFIC, it may be too late for a U.S. taxpayer to make a timely QEF or mark-to-market election. U.S. taxpayers that have held our Ordinary Shares during a period when we were a PFIC will be subject to the foregoing rules, even if we cease to be a PFIC in subsequent years, subject to exceptions for U.S. taxpayer who made a timely QEF or mark-to-market election. A U.S. taxpayer can make a QEF election by completing the relevant portions of and filing IRS Form 8621 in accordance with the instructions thereto. We do not intend to notify U.S. taxpayers that hold our Ordinary Shares if we believe we will be treated as a PFIC for any taxable year in order to enable U.S. taxpayers to consider whether to make a QEF election. In addition, we do not intend to furnish such U.S. taxpayers annually with information needed in order to complete IRS Form 8621 and to make and maintain a valid QEF election for any year in which we or any of our subsidiaries are a PFIC. U.S. taxpayers that hold our Ordinary Shares are strongly urged to consult their tax advisors about the PFIC rules, including tax return filing requirements and the eligibility, manner, and consequences to them of making a QEF or mark-to-market election with respect to our Ordinary Shares in the event that we are a PFIC. See Item 10.E. – "Taxation – United States Federal Income Tax Consequences — Passive Foreign Investment Companies" for additional information.

We do not know whether a market for our Ordinary Shares will be sustained or what the market price of our ordinary shares will be and as a result it may be difficult for you to sell your shares.

Although our Ordinary Shares are quoted on the NASDAQ Global Market, an active trading market for our Ordinary Shares may not be sustained. It may be difficult for you to sell your Ordinary Shares at all or without depressing the market price for the Ordinary Shares. As a result of these and other factors, you may not be able to sell your Ordinary Shares at or above the price you paid for such shares or at all. In addition, the trading price of our Ordinary Shares is likely to be volatile. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our Ordinary Shares:

- inability to obtain the approvals necessary to commence further clinical trials;
- unsatisfactory results of clinical trials;
- announcements of regulatory approval or the failure to obtain it, or specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to any candidate product of our in each of our platforms;
- any adverse changes to our relationship with manufacturers or suppliers;
- any intellectual property infringement actions in which we may become involved;
- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability or our failure to meet expectations;
- our commencement of, or involvement in, litigation;
- low daily trading volume of our shares;
- any major changes in our Board of Directors or management; and
- legislation in the United States relating to the sale or pricing of pharmaceuticals.

In addition, the stock market in general, and NASDAQ in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of small companies. Broad market and industry factors may negatively affect the market price of our Ordinary Shares, regardless of our actual operating performance. Further, a systemic decline in the financial markets and related factors beyond our control may cause our share price to decline rapidly and unexpectedly. If our share price falls below the listing

standards of NASDAQ, our Ordinary Shares may be delisted from trading.

We may be subject to securities litigation, which is expensive and could divert management attention.

In the past companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Litigation of this type could result in substantial costs and diversion of management's attention and resources, which could seriously hurt our business. Any adverse determination in litigation could also subject us to significant liabilities.

As of March 20, 2015, our officers and directors beneficially own approximately 71% of our Ordinary Shares. They will therefore be able to exert significant control over matters submitted to our shareholders for approval.

As of March 20, 2015, our officers and directors, in the aggregate, beneficially own approximately 71% of our Ordinary Shares. This significant concentration of share ownership may adversely affect the trading price for our Ordinary Shares because investors often perceive disadvantages in owning stock in companies with controlling shareholders. As a result, these shareholders, if they acted together, could significantly influence or even unilaterally approve matters requiring approval by our shareholders, including the election of directors and the approval of mergers or other business combination transactions. The interests of these shareholders may not always coincide with our interests or the interests of other shareholders.

Sales of a substantial number of our Ordinary Shares in the public market by our existing shareholders could cause our share price to fall.

Sales of a substantial number of our Ordinary Shares in the public market or the perception that these sales might occur, could depress the market price of our Ordinary Shares and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our Ordinary Shares.

If securities or industry analysts do not publish or cease publishing research or reports about us, our business or our market, or if they adversely change their recommendations or publish negative reports regarding our business or our Ordinary Shares, our share price and trading volume could decline.

The trading market for our Ordinary Shares will be influenced by the research and reports that industry or securities analysts may publish about us, our business, our market or our competitors. We do not have any control over these analysts and we cannot provide any assurance that analysts will cover us or provide favorable coverage. If any of the analysts who may cover us adversely change their recommendation regarding our Ordinary Shares, or provide more favorable relative recommendations about our competitors, our share price would likely decline. If any analyst who may cover us were to cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our share price or trading volume to decline.

Because we do not intend to declare cash dividends on our Ordinary Shares in the foreseeable future, shareholders must rely on appreciation of the value of our Ordinary Shares for any return on their investment.

We have never declared or paid cash dividends on our Ordinary Shares. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future.

The requirements associated with being a public company require significant company resources and management attention.

We are subject to the reporting requirements of the Exchange Act of 1934, as amended, or the Exchange Act, the Sarbanes-Oxley Act, the Listing Rules of NASDAQ, and other applicable securities rules and regulations. The Exchange Act requires that we file periodic reports with respect to our business and financial condition and maintain effective disclosure controls and procedures and internal control over financial reporting. In addition, subsequent rules

implemented by the SEC and NASDAQ may also impose various additional requirements on public companies. As a result, we will incur additional legal, accounting and other expenses that we did not incur as a nonpublic company, particularly after we are no longer an “emerging growth company” as defined in the JOBS Act. Further, the need to establish the corporate infrastructure demanded of a public company may divert management’s attention from implementing our development plans. We made changes to our corporate governance standards, disclosure controls and financial reporting and accounting systems to meet our reporting obligations. The measures we take, however, may not be sufficient to satisfy our obligations as a public company, which could subject us to delisting of our Ordinary Shares, fines, sanctions and other regulatory action and potentially civil litigation.

The JOBS Act and our status as a foreign private issuer will allow us to postpone the date by which we must comply with some of the laws and regulations intended to protect investors and to reduce the amount of information we provide in our reports filed with the SEC, which could undermine investor confidence in our company and adversely affect the market price of our Ordinary Shares.

For so long as we remain an "emerging growth company" as defined in the JOBS Act, we intend to take advantage of certain exemptions from various requirements that are applicable to public companies that are not emerging growth companies including:

- the provisions of the Sarbanes-Oxley Act requiring that our independent registered public accounting firm provide an attestation report on the effectiveness of our internal control over financial reporting;

- Section 107 of the JOBS Act, which provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. This means that an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We are electing to delay such adoption of new or revised accounting standards. As a result, our financial statements may not be comparable to companies that comply with the public company effective date;

- any rules that may be adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotation or a supplement to the auditor's report on the financial statements; and

- our ability to furnish two rather than three years of income statements and statements of cash flows in various required filings.

We intend to take advantage of these exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of our initial public offering which occurred in 2014, (b) in which we have total annual gross revenue of at least $1.0 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our Ordinary Shares that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Our status as a foreign private issuer also exempts us from compliance with certain SEC laws and regulations and certain regulations of NASDAQ, including the proxy rules, the short-swing profits recapture rules, and certain governance requirements such as independent director oversight of the nomination of directors and executive compensation.

We cannot predict if investors will find our Ordinary Shares less attractive because we may rely on these exemptions. 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 and may decline.

Risks Related to Israeli Law and Our Operations in Israel

Our headquarters and other significant operations are located in Israel and, therefore, our results may be adversely affected by political, economic and military instability in Israel.

Our executive offices are located in Tel Aviv, Israel. In addition, the majority of our officers and directors are residents of Israel. Accordingly, political, economic and military conditions in Israel may directly affect our business. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its neighboring countries. Any hostilities involving Israel or the interruption or curtailment of trade between Israel and its trading partners could adversely affect our operations and results of operations. During the summer of 2006, Israel was engaged in an armed conflict with Hezbollah, a Lebanese Islamist Shiite militia group and political party and since March 2011, there has been a civil war in Syria, Israel's neighboring country to the north. Occasionally, violence from Syria has spilled over into Israel, and Israel has responded militarily several times since the onset of the civil war. During November 2012 and July 2014, Israel was engaged in an armed conflict with a militia group and political party which controls the Gaza Strip. These conflicts involved missile strikes against civilian targets in various parts of Israel, including areas in which our employees and some of our consultants are located, and negatively affected business conditions in Israel. Any potential future conflict could also include such missile strikes against other parts of Israel, including our offices and laboratories. Any armed conflicts, terrorist activities or political instability in the region could adversely affect business conditions, could harm our results of operations and could make it more difficult for us to raise capital. Parties with whom we do business may sometimes decline to travel to Israel during periods of heightened unrest or tension, forcing us to make alternative arrangements when necessary in order to meet our business partners face to face. In addition, the political and security situation in Israel may result in parties with whom we have agreements involving performance in Israel claiming that they are not obligated to perform their commitments under those agreements pursuant to force majeure provisions in such agreements.

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. Although the Israeli government has in the past covered the reinstatement value of certain damages that were 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. Any armed conflicts or political instability in the region would likely negatively affect business conditions generally and could harm our results of operations.

Further, in the past, the State of Israel and Israeli companies have been subjected to economic boycotts. Several countries still restrict business with the State of Israel and with Israeli companies. These restrictive laws and policies may have an adverse impact on our operating results, financial conditions or the expansion of our business.

Our operations may be disrupted as a result of the obligation of management or key personnel to perform military service.

Our employees and consultants in Israel, including members of our senior management, may be obligated to perform one month, and in some cases longer periods, of annual military reserve duty until they reach the age of 40 (or older, for citizens who hold certain positions in the Israeli armed forces reserves), and, in the event of a military conflict, may be called to active duty. In response to increases in terrorist activity, there have been periods of significant call-ups of military reservists. It is possible that there will be similar large-scale military reserve duty call-ups in the future. Our operations could be disrupted by the absence of a significant number of our officers, directors, employees and consultants. Such disruption could materially adversely affect our business and operations.

Exchange rate fluctuations between the U.S. dollar and the New Israeli Shekel may negatively affect our earnings.

We incur expenses both in U.S. dollars and NIS, but our financial statements are denominated in U.S. dollars. As a result, we are exposed to the risks that the NIS may appreciate relative to the U.S. dollar, or, if the NIS instead devalues relative to the U.S. dollar, that the inflation rate in Israel may exceed such rate of devaluation of the NIS, or that the timing of such devaluation may lag behind inflation in Israel. In any such event, the U.S. dollar cost of our operations in Israel would increase and our U.S. dollar-denominated results of operations would be adversely affected. In 2014, approximately 23% of our expenses were denominated in NIS. Changes of 5% and 10% in the U.S. Dollar/NIS exchange rate would increase/decrease our operating expenses by 1.7% and 3.5%, respectively. These historical figures may not be indicative of future exposure, and we cannot predict any future trends in the rate of inflation in Israel or the rate of devaluation (if any) of the NIS against the U.S. dollar.

Furthermore, currently we do not hedge our foreign currency exchange risk. Even if we attempt to decrease the risk of financial exposure from fluctuations in the exchange rates of our principal operating currencies, these measures, may

not adequately protect us from the material adverse effects of such fluctuations.

Provisions of Israeli law and our articles of association may delay, prevent or otherwise impede a merger with, or an acquisition of, our company, which could prevent a change of control, 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 merger may not be consummated unless at least 50 days have passed from the date on which a merger proposal is filed by each merging company with the Israel Registrar of Companies and at least 30 days have passed from the date on which the shareholders of both merging companies have approved the merger. In addition, a majority of each class of securities of the target company must approve a merger. Moreover, 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, claim that the consideration for the acquisition of the shares does not reflect fair market value, and 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.

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. See Item 10.E. – "Taxation – Israeli Tax Considerations" for additional information.

Our articles of association also contain provisions that could delay or prevent changes in control or changes in our management without the consent of our Board of Directors. These provisions include the following:

- no cumulative voting in the election of directors, which limits the ability of minority shareholders to elect director candidates; and

- the right of our Board of Directors to elect a director to fill a vacancy created by the expansion of the Board of Directors or the resignation, death or removal of a director, which may prevent shareholders from being able to fill vacancies on our Board of Directors.

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

We were incorporated in Israel. Substantially all of our executive officers and directors reside outside of the United States, and all 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 necessarily be enforced by an Israeli court. It also may be difficult for you to affect service of process on these persons in the United States or to assert U.S. securities law claims in original actions instituted in Israel. Additionally, it may be difficult for an investor, or any other person or entity, to initiate an action with respect to United States securities laws in Israel. Israeli courts may refuse to hear a claim based on an alleged violation of United States 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 United States law is applicable to the claim. If United States law is found to be applicable, the content of applicable United States 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 United States 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.

The rights and responsibilities of the holders of our Ordinary Shares are governed by our articles of association and by Israeli law. These rights and responsibilities differ in some material respects from the rights and responsibilities of shareholders in typical U.S.-based corporations. In particular, a shareholder of an Israeli company has certain duties to act in good faith and fairness towards us and other shareholders, and to refrain from abusing its power in us. See Item 16G. – "Approval of Related Party Transactions under Israeli Law" for additional information. There is limited case law available to assist us in understanding the nature of this duty or the implications of these provisions. These provisions may be interpreted to impose additional obligations and liabilities on holders of our Ordinary Shares that are not typically imposed on shareholders of U.S. corporations.

Item 4. Information on the company

4.A. History and development

We are an Israeli corporation based in Tel Aviv and were incorporated on January 22, 2012. Our principal executive offices are located at 37 Dereh Menachem Begin St., Tel Aviv 6522042, Israel, and our telephone number is: +972 722409060. Our wholly owned U.S. subsidiary, BioBlast Pharma, Inc., incorporated in Delaware, has been appointed our agent in the United States and its registered address is 1811 Silverside Road, Wilmington, Delaware 19810. Our website address is http://bioblast-pharma.com. The information contained on, or that can be accessed through, our website is not part of this annual report. We have included our website address herein solely as an inactive textual reference.

We are an emerging growth company, as defined in Section 2(a) of the Securities Act, as implemented under the JOBS Act. As such, we are eligible to, and intend to, take advantage of certain exemptions from various reporting requirements applicable to other public companies that are not emerging growth companies including but not limited to not being required to comply with the auditor attestation requirements of the SEC rules under Section 404 of the Sarbanes-Oxley Act. We could remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of our initial public offering, which occurred in 2014, (b) in which we have total annual gross revenue of at least $1.0 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our Ordinary Shares that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Our capital expenditures for 2014, 2013, and 2012 amounted to $63,000, $2,000, and $0, respectively. These expenditures were primarily for computers, other electrical equipment and office furniture. Our current capital expenditures are primarily for leasehold improvements, computers and other electronic equipment, and we expect to finance these expenditures primarily from cash on hand.

4.B. Business overview

Who We Are

We are a development-stage biopharmaceutical company focused on the identification, licensing, acquisition, development and commercialization of drugs for rare and ultra-rare genetic and metabolic diseases. We seek to identify therapeutic platforms that offer solutions for several diseases that share a common pathophysiological mechanism, which are the functional changes that accompany a particular syndrome or disease. We focus on diseases

with severe and debilitating manifestations, where the unmet medical need is clear, the biological mechanism of action is understood and for which there is no satisfactory treatment. Since our inception in 2012, we have developed and in-licensed potential treatments for six diseases. Our three principal product candidate platforms are as follows:

Our current pipeline is based on three platforms:

Protein Stabilizing Platform: Cabaletta is a mutant protein stabilizing and autophagy enhancer based on a small repurposed molecule, namely, trehalose. Trehalose is currently used as an excipient, or non-active ingredient, for protein-based drugs that are administered intravenously, such as Avastin® or Herceptin®. Mutant unstable cellular proteins are the cause of several genetic diseases known as PolyA/PolyQ, including oculopharyngeal muscular dystropy, or OPMD, spinocerebellar ataxia type 3, or Machado Joseph disease, or SCA3 and spino bulbar muscular atrophy, or SBMA. These pathological proteins aggregate within cells, eventually leading to cell death. Our data to date from preclinical studies from both cells and animal models, indicates that our Cabaletta platform has the potential to prevent mutant protein aggregation and enhanced autophagy in humans.

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We are currently conducting a Phase 2/3 clinical trial for Cabaletta in treating OPMD. In March 2015, the FDA granted us clearance to proceed with an IND with respect to the Phase 2/3 clinical trial for OPMD with Cabaletta. Concurrently, we are conducting a Phase 2 clinical trial to assess Cabaletta's efficacy and safety in treating SCA3. Subject to planned discussions with the FDA regarding trial design, we intend to pursue a multicenter clinical study in 2015 for SCA3. With respect to OPMD and SCA3, we plan to continue to pursue pre-commercial activities in 2015.

Additionally, Cabaletta is in preclinical development for SMBA. In 2015, we plan to continue to pursue preclinical studies as well as clinical planning for SMBA. Based on the biology of trehalose and our intellectual property, we believe that this drug platform has the potential to treat several diseases.

- ***Read-through Platform***: BBrm is our lead product candidate in our read-through platform and is a proprietary formulation of a small repurposed molecule, azithromycin for intrathecal delivery. The platform enables the read-through (or bypassing) of genetic defects called nonsense mutations or stop codons that interfere with normal protein formation and cause disease. Based on our preclinical data, we believe that this drug platform has the potential to treat several diseases caused by nonsense mutation. Subject to regulatory approval, we plan to conduct Phase 2 clinical studies in 2015 for our lead indication in spinal muscular atrophy, or SMA.

- ***Mitochondrial Protein Replacement Platform***: mPRT is a mitochondrial protein replacement platform that is based on biological components that we synthesize in bacteria. Mitochondria are cell components that supply chemical energy for normal cell functioning. This platform is currently in preclinical development for two diseases: Friedreich's Ataxia and ornithine transcarbamylase deficiency. These diseases are among hundreds of genetic diseases that are caused by a missing or mutant protein that has a critical role in the normal mitochondrial function. While lysosomal protein replacement platforms have been successful in replacing a missing protein in lysosomes, we believe that our mPRT platform is the first one to potentially be successful in replacing mitochondrial proteins. Our product candidates are new "fusion proteins" that are a combination of the replaced protein fused with two additional sequences that facilitate its transport through biological membranes. Based on the biology of this platform and our intellectual property, we believe that this drug platform has the potential to treat a significant number of diseases.

Two of the drugs in our current drug candidate pipeline has been in-licensed from academic institutions and one was developed internally. Our strategy is based on risk diversification through multiple therapeutic platforms, diversified clinical and pre-clinical stages of our programs, and diversified diseases addressed. We use strict selection criteria for our pipeline platforms and focus on drugs that we believe will be cost-efficient to develop.

We believe that our strategy and special business operation model is especially suitable for commercializing effective and safe products in a timely and cost efficient manner.

Strict selection criteria of our platforms and clinical program.

We target rare and ultra-rare diseases that:

- cause severely shortened life expectancy or severe debilitation;

- do not have an approved or effective therapy currently available;

- have a drug candidate that we believe will either be lifesaving or significantly ameliorate the disease course;
- have tangible and validated tests where initial efficacy can be demonstrated in a reasonable time frame; and
- preferably have validated biomarkers and where natural history study is available.

As part of this selection process, we:

- estimate the scope and availability of research tools for the preclinical studies required;

- limit the diseases selected to those in which the full pre-clinical tool kit is available or can be obtained through collaboration with patient organizations;

- estimate the size and structure of the clinical studies that will be required and confine our selections to fit what we believe will be a cost effective program that will not require unreasonable financial resources;

- select diseases in which the regulatory path to approval is clear and well defined;

- strictly evaluate the strength of the intellectual property that we license for further development;

- estimate the required chemistry, manufacturing and control development program;

- exclude drug candidates that are known to have any safety issues and prefer, when possible and feasible, repurposed drugs; and

- part of our screening and selection criteria involves accessing key opinion leaders and aligning ourselves with the patient advocacy group for the specific disease we are considering our decision to move forward is often taken in consensus with them.

Because these diseases are rare or ultra-rare, no prenatal diagnosis is widely offered that might reduce the incidence of the diseases. Optimally, our target diseases have geographic clusters around a small number of clinics with a sufficient number of patients to avoid large multi-center studies. Due to our location in Israel, we prefer to focus on diseases for which we can find a disease cluster in Israel where we can start a proof of concept study promptly.

Risk diversification through multiple platforms, clinical programs and stages of development.

Drug development is a complex and unpredictable process with multiple risks. We believe that a biopharmaceutical company such as ours should diversify the inherent risk associated with drug development. Drug development occurs in both the preclinical and clinical stages, each of which must satisfy separate criteria with different risks, including safety and efficacy.

We have begun to diversify risk by initially focusing on three therapeutic platforms that each can be applied to several diseases. In each case, we have identified a lead program, but we believe we have the opportunity to benefit from the shorter and less expansive route to additional indications based on the same platform. In addition there are different risks associated with the development of a small molecule drug, a biological drug, or a repurposed drug. Our portfolio is comprised of all three, thereby balancing the systemic risk associated with it.

Variable lean cost structure.

We believe in keeping a small, select and highly professional core team while relying on experienced service providers and CROs for an efficient and time – saving development process. We carefully screen our service providers and CROs for their expertise in the specific project required and work with them closely to complete the task assigned to them efficiently and professionally. This business operation model enables us to develop multiple programs while avoiding the exorbitant costs associated with learning curves, setup times, and high fixed costs associated with in-house development.

Our Current Product Pipeline

The following table summarizes our product candidate pipeline:

Product Candidates — Overview

Our current product candidate pipeline has been either in-licensed from academic institutions or developed internally. Where possible, our strategy is to acquire and retain global commercialization rights to our products to maximize long-term value. Over time, we intend to build our own commercial organization, which we believe will be of modest size due to the relatively small number of specialists who treat patients with rare and ultra-rare diseases.

The diseases which we are addressing have devastating consequences on the patient's health, quality of life and life expectancy. In addition these diseases create significant burdens on the patient's family and care takers as well as on the public health resources. In all the diseases we are addressing, patients cannot be offered an alternative therapy or the current solutions are inadequate in their abilities to change the course of the disease. We believe that prompt and efficient drug development can be of substantial benefit to the patients who are suffering from these incurable diseases.

We have assembled an experienced team of employees, consultants, service providers and Board of Directors with extensive drug development and commercialization capabilities, particularly in the orphan drug area.

Cabaletta for the treatment of OPMD

Cabaletta is our proprietary intravenous (IV) solution of trehalose for the treatment of OPMD. OPMD is an inherited myopathy. It is a muscle disease caused by a primary defect in muscle cells caused by aggregation of a protein called PABPN1, and is characterized by dysphagia (difficulty in swallowing), the loss of muscular strength and weakness in multiple parts of the body. As the dysphagia becomes more severe, patients become malnourished, lose significant weight, become dehydrated and suffer from repeated incidents of aspiration pneumonia. These last two are often the cause of death.

Trehalose is naturally occurring and is well known for its protein-stabilizing and autophagy enhancing properties. It is used in several biological systems, such as freeze drying of red blood cells and the preservation of organs for donation and as a protein stabilizer in IV pharmaceutical products. Trehalose is approved by the FDA as a GRAS (Generally Recognized as Safe) food ingredient and is listed in the U.S. National Formulary, which is a compendium of public pharmacopeial standards, which are guidelines for the identification of compound medicines, as well as in Europe and Japan. It is a disaccharide chemical chaperone, which is a chemical molecule comprised of two sugar components that stabilize the folding of proteins and that buffer abnormal protein aggregation, thus protecting against pathological processes in cells. It has been shown to prevent pathological aggregation of proteins within cells in several diseases associated with abnormal cellular-protein aggregation as well as acting as an autophagy enhancer. Autophagy is the basic catabolic mechanism that involves cell degradation of unnecessary or dysfunctional cellular components. Autophagy in healthy adults, or if regulated in those with abnormalities, ensures the synthesis, degradation and recycling of cellular components. Trehalose has been documented as demonstrating significant efficacy in preclinical animal models of OPMD and other PolyA/PolyQ diseases.

Trehalose is not effective when given orally since it is almost completely metabolized in the small intestine into glucose and often causes diarrhea and flatulence after ingestion of more than 50g. Cabaletta is our proprietary IV solution of trehalose that has been designed to circumvent the breakdown of trehalose in the gastrointestinal tract, and to enable therapeutic doses of trehalose to reach muscles and nerve cells.

We are currently conducting a Phase 2/3 trial of Cabaletta to treat OPMD; if the results are positive, we believe this could be a pivotal trial. We believe, based on discussions with the FDA, that if the Phase 2/3 trial shows positive results, the data could be considered pivotal data, considering, among other things, the applicable FDA guidance for the industry called “Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products.”

The study is planned to include 70 patients in three centers in Israel, Canada and the United States. All patients will be treated with 30g trehalose IV weekly for the first 6 months. After 6 months, patients will be randomized into a treatment arm that will continue with the weekly IV 30g regimen and a non-treatment control group that will be followed up under the same protocol for an additional 12 months. As of the date hereof, all 14 patients in Israel have been treated. 13 of them have completed the first six months of the study and are randomized into a treatment and non-treatment control group. In Canada, we are targeting to treat 40 patients. Treatment started in January 2015, and eight patients have already been dosed. In March 2015, the FDA granted us clearance to proceed with an IND with respect to the Phase 2/3 clinical trial for OPMD with Cabaletta. If the trial is successful, we are planning to submit an NDA to the FDA.

Cabaletta for the treatment of SCA3

SCA3, also known as Machado Joseph disease, is the most common of the cerebellar ataxias, and is one of a group of genetic diseases that are characterized by memory deficits, spasticity, difficulty with speech and swallowing,

weakness in arms and other muscular disorders. Symptoms can begin in early adolescence and get worse over time. Eventually SCA3 leads to paralysis, and severe cases can lead to an early death in the fourth decade of life. SCA3 is incurable, and there is currently no approved treatment for the disease.

SCA3 is caused by a mutation in the DNA that leads to the creation of a pathological protein — Ataxin 3. Ataxin 3 is unstable, and aggregates within the cells, and eventually leads to cell death.

Multiple reported studies in cell models have shown that trehalose, both as an anti-mutant protein aggregation agent and as an autophagy enhancer, is able to reduce protein aggregates and improve cell survival in several spinocerebellar ataxias including SCA3 cells. Additional animal studies show that activation of autophagy may be beneficial in alleviating disease symptoms. We recently started our Phase 2 clinical trial of Cabaletta to treat SCA3 in Israel.

Cabaletta for the treatment of SBMA

SBMA, also known as Kennedy's disease, is characterized by the degeneration and loss of lower motor neurons in the brainstem and spinal cord. Patients with SBMA often have weakness in muscle function, severe difficulty in swallowing, repeated aspiration pneumonia, and other symptoms. SBMA is caused by an abnormal androgen receptor (AR) protein. Patients suffering from SBMA suffer from progressive neuromuscular deterioration that can end up in extreme disability and repeated aspiration pneumonia. There is currently no approved therapy for SBMA.

Studies in cell models have shown that trehalose is both an anti-mutant protein aggregation and an autophagy enhancer is able to reduce protein aggregates and improve cell survival in SBMA cells. Additional studies in animal models show that activation of autophagy may be beneficial in alleviating disease symptoms.

We have entered into an agreement with NINDS (a group within the U.S. National Institutes of Health, or NIH) pursuant to which NINDS will conduct animal studies on SBMA mouse models to validate the potential efficacy of Cabaletta. NINDS will conduct the study using its own resources, and we will supply the research material. If the animal studies are successful, and subject to regulatory allowance, we may commence a Phase 2/3 clinical trial for this application.

BBrm — our read-through platform

BBrm is our family of small molecule non-glycosides repurposed drugs for the treatment of patients with genetic disorders that arise from a type of genetic mutation known as a nonsense mutation (stop codon). The platform enables the read-through (deactivation) of the genetic defects that stop synthesis of normal full length proteins. Deactivation of disease-causing nonsense mutation can alleviate the symptoms of genetic diseases caused by these mutations. Our BBrm family of repurposed drugs is able to induce translational read-through, restoring full-length functional proteins in diseases where the nonsense mutation results in truncated ineffective proteins. We licensed the exclusive worldwide commercial rights for our BBrm technology for stop codon inhibition of orphan diseases from the Tel Aviv University in January 2014.

BBrm1 for the treatment of SMA

Using our BBrm platform, we developed a unique therapeutic candidate for SMA, a proprietary intrathecal formulation of azythromycin. SMA is the leading genetic cause of infantile death and is caused by the loss of a functional Survival Motor Neuron 1 (SMN1). The disease is manifested by loss of muscle mass and mobility as well as severe compromise of vital functions such as respiration. Another protein called SMN2 is a nearly identical copy of SMN1, differentiated only by a silent, single-nucleotide mutation within the DNA. SMN2 partially compensates for the dysfunction of SMN1; however, the small amount of the functional protein that is produced from the SMN2 gene is not able to fully compensate for the loss of SMN1. Prior independent studies proposed that read-through agents, such as aminoglycosides, can induce the read-through of the stop codon located in the SMN2-protein, thus elongating the SMN2 and creating a full length functional protein that can compensate for the non-functioning SMN1 and alleviate the disease. This approach was also successfully tested in SMA animal models. Nonetheless, chronic administration of aminoglycosides was found to be associated with prohibitive toxicity.

Nevertheless, we believe that drug-induced read-through of premature stop codons remains a promising approach to elevate active protein expression from the SMN2 gene which is an ideal therapeutic target as it is found in all SMA patients. Our family of repurposed FDA-approved non-glycosides molecules (BBrm) induced significantly higher levels of full length functional SMN2 protein in several *in vitro* and *in vivo* studies. These molecules are ineffective if administered orally or intravenously since they do not penetrate into the brain to create high enough therapeutic levels within nerve cells. Our BBrm1 product can be injected directly into the central nervous system (CNS), creating adequate drug concentration. This method of administration has the added benefit of further protection against off label use. We plan to continue our preclinical development of BBrm1 for SMA through 2015, and, if successful and subject to regulatory approval, expect to start a Phase 2 study in 2015.

Mitochondrial protein replacement platform (mPRT)

Mitochondrial disorders are diseases, for which no cure has been found that are caused by a missing or mutated critical enzyme or protein in the cell organelle called mitochondria. Our fusion proteins, comprised of two delivery moieties, transactivator of transcription, or TAT, and mitochondrial targeting sequence, or MTS, and the replacement proteins, help move proteins across biological membranes to facilitate the creation of mature proteins inside the mitochondria. Our replacement proteins are able to enter human cells and mitochondria and replace the damaged or missing proteins in the mitocmtshondria. Our breakthrough platform technology demonstrated efficacy in several mitochondrial protein deficiencies in cells and animal models. Currently, Frataxin for Friedreich’s Ataxia (BB-FA) is our most advanced mPRT preclinical program, followed by Ornithine Transcarbamylase (BB-OTC) for Ornithine Transcarbamylase Deficiency (OTCD).

Our studies demonstrated the superiority of our proprietary approach of using a heterologous (non-native) MTS as part of our fusion proteins in four different aspects: expression by bacteria, cell penetration, mitochondrial processing and anchorage of target proteins, and rescue of cells in oxidative stress.

We have an exclusive worldwide royalty-bearing license to commercialize, develop and use the technology, including certain patent applications, from the Hebrew University in Jerusalem. These patent applications, as well as our internally developed intellectual property assets, cover our unique approach of using homologous and heterologous MTS in the fusion proteins.

BB-FA for the treatment of Friedreich's Ataxia (FA)

Friedreich's Ataxia is an inherited disease characterized by progressive deterioration of muscles and nerves, resulting in gait disturbance (ataxia), cognitive impairment, progressive heart disease and diabetes. Patients are usually diagnosed in the first or second decade of life, and are typically wheelchair-bound within 15 years of diagnosis. Most do not survive beyond the fourth decade of life. In many cases the cause of death is myopathic heart disease. The underlying cause of Friedreich's Ataxia is reduced levels of Frataxin — a protein responsible for iron sulfur clusters in the mitochondria that are critical for mitochondria activity. Our preclinical data demonstrated successful placement of Frataxin into the mitochondria and in the treatment of oxidative stress in Friedreich's Ataxia patients' cells. In addition, our studies in FA mice models demonstrate improvement in the biochemical as well as the clinical characteristics of the disease following treatment with BB-FA. We are advancing the Friedreich's Ataxia program through its preclinical development throughout 2015.

BB-OTC for the treatment of ornithine transcarbamylase deficiency (OTCD)

OTCD is the most common disorder among urea cycle disorders — a group of rare genetic diseases characterized by the body's inability to detoxify ammonia. Ammonia is a toxic breakdown product of proteins. OTCD is caused by a mutated and ineffective form of the enzyme, ornithine transcarbamylase, that is part of the urea cycle complex in the mitochondria. As a result, the normal breakdown of ammonia is disrupted and toxic ammonia accumulates in the blood causing severe damage to the brain and other vital organs. Newborn males affected with OTCD may suffer devastating hepatic coma in the first few days after birth, and survivors typically suffer from severe cognitive, mental and metabolic disorders and growth retardation. Many do not survive the first decade of life. We are using our mitochondrial protein replacement platform to replace this enzyme in the mitochondria. Our preclinical data indicates that our OTC fusion protein is well able to be transferred into the mitochondria and be processed in it, resulting in improved mitochondrial metabolism. We are advancing the BB-OTC program through its preclinical development during 2015.

Our Approach

Our approach is to identify, acquire, license, develop, and commercialize novel products for the treatment of rare and ultra-rare diseases in the United States, the European Union, and select international markets, with the goal of becoming a leading rare disease biotechnology company.

The patients we seek to treat have diseases with limited or no treatment options, and their lives and well-being are highly dependent upon our efforts to develop new therapies. We strive to build a company that is faster, better and smarter about advancing multiple product candidates through approval.

The critical components of our business strategy include the following:

- *Focus on rare and ultra-rare diseases with significant unmet medical need.* There are numerous rare and ultra-rare metabolic genetic diseases that currently have no approved drug therapy and for which no therapies, to our knowledge, are currently in development. Patients suffering from these diseases often have a high unmet medical need with significant morbidity and/or mortality. We are focused on developing and commercializing therapies for multiple such indications.

- *Focus on diseases and therapies with clear mechanisms of action*. We also focus on diseases that have biology and root causes that are well understood. For example, several of our product candidates are replacement therapies for a single deficient enzyme or substrate in the body. We believe that developing drugs that directly impact known disease pathways will increase the probability of success of our development programs.

- *Leverage our experience and relationships to in-license promising product candidates*. Our management and Board of Directors has strong relationships with key opinion leaders in the metabolic genetic field, as well as a history of success in the development and commercialization of therapies for rare and ultra-rare genetic diseases. Accordingly, we enjoy access to many in-licensing opportunities. Most of our current product candidates are in-licensed from academic institutions. We believe these parties have agreed to license product candidates to us because they are confident in our drug development capabilities and experience in bringing rare disease therapies to market.

- *Develop and commercialize multiple product candidates in parallel*. Clinical studies for rare and ultra-rare diseases can often be smaller, fewer in number, and less expensive than those for larger market indications. Development of multiple programs in the metabolic genetics field also generates organizational efficiencies and economies of scale. As a result of these efficiencies, we can feasibly develop multiple clinical-stage product candidates in parallel, resulting in a more diversified portfolio that provides multiple opportunities to create value.

- *Focus on excellent and rapid clinical and regulatory execution*. We believe that building a successful and sustainable rare disease-focused company requires very specific expertise in the areas of patient identification, clinical study design and conduct, and regulatory strategy. We have assembled a team with a successful track record in managing global clinical development activities in an efficient manner, and with multinational experience in obtaining regulatory approvals for rare disease products.

- *Seek to retain global commercialization rights to product candidates*. We intend to seek and retain global commercialization rights to our product candidates whenever possible to maximize the potential value of our product portfolio. Our plan is to establish our own commercial organization in major pharmaceutical markets and develop a network of third-party distributors in smaller markets. We believe this commercial organization can be modest and targeted due to the relatively small number of specialists who typically treat patients with the diseases to be addressed by our product candidates. As a result, we do not expect that we will require pharmaceutical partners for commercialization of our product candidates, although we may consider partnering for certain territories or indications or for other strategic purposes.

Product Candidates — Disease background, rationale for treatment, development plan and market potential

Oculopharyngeal Muscular Dystropy (OPMD)

Disease background:

OPMD is a rare inherited myopathy characterized by dysphagia (difficulty in swallowing), the loss of muscular strength and weakness in multiple parts of the body. Patients typically suffer from severe dysphagia, ptosis (eye lid drooping), tongue atrophy, lower limb proximal weakness, dysphonia (altered and weak voice), limitation in looking upward, facial muscle weakness and upper limb proximal weakness. The disease is most often diagnosed in the fifth or sixth decade of life and progresses throughout the patient's life. As the dysphagia becomes more severe, patients become malnourished, lose significant weight, become dehydrated and suffer from repeated incidents of aspiration pneumonia. These last two are often the cause of death.

OPMD is one of a larger group of diseases called tri-nucleotide repeat diseases that are associated with the presence of an abnormal cellular protein, that aggregates in the cells eventually causing cell death. In OPMD the mutant protein PABPN1 was found to be correlated with disease severity in animal models and was identified within the typical cellular protein aggregates-the intranuclear inclusion body (INI) that are the diagnostic hallmark of the disease.

There is no medical treatment or, to our knowledge, potential cure for OPMD. Current therapeutic strategies are confined to surgical interventions that have limited efficacy and need to repeated often while the progressive loss of muscle's contractility continue relentlessly.

Rationale for treatment:

The naturally occurring disaccharide trehalose is well known for its protein-stabilizing properties. It is used extensively in many applications as a stabilizer of frozen food, in freeze drying of biological systems and cells, as a stabilizer of therapeutic parenteral proteins and as an excipient in tablets and IV solutions. Trehalose has been shown to prevent pathological aggregation of proteins within cells in several diseases associated with mutant cellular-protein aggregation such as PolyA/PolyQ and taupathy diseases (for example OPMD, Huntington's disease, Spinocerebellar ataxia, Parkinson and Alzheimer disease and more). Recent studies demonstrated that trehalose enhances autophagy — a natural mechanism of debris-clearance within cells.

Trehalose was found to be effective in cell studies and in a mouse model of OPMD. In this disease there are characteristic intracellular aggregations of the abnormal protein PABPN1 (INI). Animal studies showed a direct correlation between reduction of mutant PABPN1 aggregates (INI) in cells and reduced cell death. Trehalose effectively reduced the aggregation and toxicity of mutant PABPN1 proteins in OPMD cell models. Furthermore, treatment of an OPMD mouse model with trehalose resulted in the attenuation of muscle weakness, decreased aggregate formation and a reduced number of TUNEL-positive nuclei in skeletal muscle fibers.

Like all disaccharides, trehalose is metabolized at the epithelial brush border of the intestine into two D-glucose molecules. Less than 0.5% of ingested trehalose is absorbed into the blood stream where it is further metabolized by the liver and kidney. Oral trehalose in amounts exceeding 40 – 50 g per day causes diarrhea, bloating and abdominal pain. To achieve therapeutic amounts of trehalose in the muscle cells, it is necessary to circumvent the massive metabolism in the gastrointestinal tract. Cabaletta is our proprietary IV formulation of trehalose developed for the treatment of diseases characterized by unstable mutant protein aggregates causing cellular damage and eventually cell death.

During 2014, we showed both in preclinical and human pharmacokinetic studies that Cabaletta is able to reach muscle cells and remain within the cells for considerable periods of time consistent with our dosing regimen.

Trehalose was approved by the FDA, EMEA and several other authorities as a GRAS food ingredient and is also registered on the U.S. National Formulary, as well as in Europe and Japan. Its safety in preclinical studies was extensively researched and validated. In addition, we have conducted a 3 month safety study in two animal species of Cabaletta with amounts that far exceed the intended dose we will be using in clinical trials. These studies showed that Cabaletta is safe and well tolerated.

Clinical development plan:

Our clinical plan will include eventually three centers that will look at the safety and efficacy of trehalose in OPMD patients across centers in Israel and North America.

The study is planned to include 70 patients in 3 centers, in Israel, Canada and the United States. All patients will be treated with 30g trehalose IV weekly for the first 6 months. After 6 months, patients will be randomized into a treatment arm that will continue with the weekly IV 30g regimen and a non-treatment control group that will be followed up under the same protocol for an additional 12 months. As of January 2015, all fourteen patients in Israel have been treated. Nine of them have already completed the full six months treatment and are randomized into the second phase of the study. In Canada, we are targeting to treat 40 patients. Treatment started in January 2015, and eight patients have already been dosed. Subject to regulatory approval the U.S. center is planned to start recruiting patients in 2015. During 2014, we released the interim results from the Israeli center showing that Cabaletta is safe and well tolerated by patients. There were no drug related serious adverse events. During the trial we had two non-drug related adverse events. One of our patients suffered aspiration pneumonia as a complication of her disease and later on passed away. Another patient was hospitalized for urinary tract infection probably as a complication of prior renal surgery. This patient fully recovered and returned to the study. If the trial is successful, we are planning to submit an NDA to the FDA. Endpoints in the trial include (i) penetration aspiration scale based on video fluoroscopy, (ii) muscle strength, and (iii) quality of life.

The market potential for OPMD:

The prevalence of OPMD is estimated at 1:100,000. The disease is more prevalent among people of French Canadian origin residing in Canada and in the United States, and among Hispanics in New Mexico, Arizona and the other U.S. Southwestern states and in Israel. The prevalence of OPMD among French Canadians in the Montreal, Canada area is 1:1,000. There are estimated 4,000 – 5,000 patients in Canada. In Israel, the prevalence of OPMD among Bukharian Jews is 1:600. There are an estimated 1,200 – 1,500 patients in Israel. It has been reported to occur in 33 countries in

the world. In the United States, the estimated number of patients is approximately 6,000, and accordingly, the North American opportunity for OPMD represents approximately 10,000 patients.

Spinocerebellar Ataxia type 3 (SCA3 or Machado Joseph disease)

Disease background:

Spinocerebellar ataxia Type 3, also known as SCA3 or Machado-Joseph disease, is a dominantly inherited ataxia, and is the most common disease among the cerebellar ataxias. SCA3 is characterized by memory deficits, clumsiness in movements in the arms and legs, unstable gait, difficulty with speech and swallowing, impaired eye movements that may be accompanied by double vision or bulging eyes, and lower limb spasticity. In most individuals with SCA3, symptoms typically begin in the third to fifth decade of life but can start as early as young childhood or as late as 70 years of age. The cause of death is often aspiration pneumonia.

SCA3 is a caused by a repeat expansion in the DNA code causing the creation of an abnormal and unstable cellular protein Ataxin 3. Typically the longer the expansion, the more severe the disease which may manifest earlier in life and exert a broader range of neurological symptoms. Cellular aggregations of Ataxin 3 inclusion bodies are found in SCA3 patients' brain and nerve cells.

There is no medical treatment for SCA3 and current approaches are focused on alleviating disease symptoms and supportive care.

Rationale for treatment and development plan:

It has been established that enhancement of autophagy in SCA3 is an effective approach that reduces intracellular aggregates and increase cell survivals. Trehalose was found to be effective in SCA3 cells as a stabilizer of the mutant Ataxin 3 and as an enhancer of autophagy. We have conducted animal studies in several disease models. We have found that treatment with trehalose reduced the level of the pathological protein in nerve cells and reduced the disease symptoms in the model animals. We recently started our Phase 2 clinical trial of Cabaletta to treat SCA3 in Israel. This randomized trial will treat patients for six months. We intend to enroll twelve to twenty patients. Subject to regulatory approvals we intend to conduct a multicenter pivotal study in the United States and Europe. Most recently, we announced positive *in vivo* proof of concept results for Cabaletta for SCA3 in two different mouse models of the disease.

Market potential:

The prevalence of SCA3 is estimated as 1 to 2 cases per 100,000 people. The prevalence of the disease is highest among people of Portuguese/Azorean descent. For example, among immigrants of Portuguese ancestry in New England, the prevalence is around one in 4,000, and the highest prevalence in the world, about one in 140, occurs on the small Azorean island of Flores. There are an estimated 4,000 to 6,000 patients in the United States, and an estimated 2,000 patients in each of Portugal and Brazil. SCA3 has been reported in over a dozen European countries with a few effected families mentioned in each of the reported case studies.

Spino Bulbar muscular atrophy (SBMA)

Disease background:

SBMA, also known as Kennedy’s disease, is a rare inherited X linked disease, characterized by the degeneration and loss of lower motor neurons in the brainstem and spinal cord resulting in progressive muscle weakness, atrophy, and fasciculation. The disease is typically manifested in the fourth or fifth decade of life. As the disease progresses, disability is increased until the patient is wheelchair bound.

Rationale for treatment and development plan:

SBMA is caused by an expansion of the CAG trinucleotide repeat in exon 1 of the human androgen receptor (*AR*) gene. A disease causing protein — a mutant AR - has been identified in a patient's cells, where it aggregates both in the cytoplasm and in the nucleus. Several studies demonstrated the ability of trehalose as a protein stabilizer and an autophagy enhancer to protect SBMA cells from the toxic effects of the mutant AR protein. We are now conducting a study in animal models.

Market potential:

The estimated incidence of SBMA in the United States is approximately 1 case in 40,000 men, or approximately 3,775 patients. There is a general impression that SBMA may be under-diagnosed, owing in part to misdiagnosis and to the mild symptoms exhibited by some patients. The estimated prevalence in the rest of the world (Europe, Japan and Australia) is similar. Some regions, such as western Finland and Japan, may have a higher prevalence. There are an estimated 10,000 patients in Europe, 1,500 patients in Japan and 300 patients in Australia.

Friedreich's Ataxia (FA)

Disease background:

Friedreich's Ataxia is a rare inherited disease that causes muscle and nerve damage. It usually begins in childhood and is caused by progressive degeneration of the spinal cord and peripheral nerves. The cerebellum — the part of the brain that coordinates balance and movement, also degenerates. This damage results in clumsy, unsteady movements and gait and impaired sensory functions. The disease also causes severe heart disease, spinal deformity and diabetes. Typically patients are diagnosed within the first two decades of life and may become wheelchair bound within 15 years of diagnosis. Life expectancy is severely shortened and most patients do not live beyond the fourth decade of life.

Friedreich's Ataxia is caused by a defect (mutation) in a gene labeled *FXN*. As a result, the corresponding protein called Frataxin is mutated and dysfunctional. Fratxin plays a pivotal role in the normal mitochondrial metabolism: Without a normal level of Frataxin, certain cells in the body (especially peripheral nerve, spinal cord, brain and heart muscle cells) cannot effectively produce energy, and buildup toxic byproducts leading to what is called "oxidative stress." Frataxin deficiency may also lead to increased levels of iron in the mitochondria. When the excess iron reacts with oxygen, free radicals can be produced. Although free radicals are essential molecules in the body's metabolism, they can also destroy cells and harm the body.

Rationale for treatment and development plan:

Unlike successful lysosomal Enzyme-Protein Replacement Therapy (ERT)- mitochondrial ERT has yet to be established. We have developed a novel mPRT platform based on a recombinant protein containing targeting signals (TAT-MTS-protein). Based on our approach, PRT therapy has been studied in a FA mouse model with some success, using the native MTS of Frataxin (MTSfa). We have made a scientific leap by replacing the native MTS with a heterologous MTS (one that is native to another protein). Our approach was tested in preclinical studies and was found to be highly superior in four major parameters: The expression of the fusion protein by bacterial cells, the penetration of the protein into FA patient's cells, the breakout of the fusion protein into its components leaving the Frataxin protein in the mitochondria, and finally, the correction of the pathological "oxidative stress" of the cells. Most recently, we announced positive *in vitro* and *in vivo* proof of concept results for BB-FA in several patient cell lines and in two different and well established animal models of Friedreich's Ataxia.

We continue our preclinical development of our BB-FA candidate and will advance into a full preclinical regulatory route and manufacturing scale-up in 2015 and 2016. Upon completion, we plan to initiate clinical studies in the United States and Europe.

Market potential for BB-FA:

Although rare, Friedreich's Ataxia is the most common form of hereditary ataxia, affecting about 1 in every 50,000 people in the United States. It is estimated that the number of Friedreich's Ataxia patients in the United States is about 6,000, with approximately 15,000 patients worldwide.

Ornithine transcarbamylase deficiency

Disease background:

Ornithine transcarbamylase deficiency (OTCD) is the most common urea cycle disorder, a group of rare genetic metabolic disorders characterized by the body's inability to detoxify ammonia. OTCD is caused by a mutated and ineffective form of the enzyme ornithine transcarbamylase (OTC).

OTC is one of the critical enzymes that participate in the "Urea cycle" — a metabolic process that helps the body get rid of ammonia, the toxic breakdown product of proteins. As a result, the normal breakdown of ammonia is disrupted and toxic ammonia accumulates in the blood causing severe damage to the brain and other vital organs, especially in the highly vulnerable nervous system.

Ornithine transcarbamylase deficiency often becomes evident in the first few days of life; however, it can present at middle age. The typical initial symptoms of a child with hyperammonemia are failure to feed, loss of thermoregulation with a low core temperature, and somnolence. Symptoms progress from somnolence to lethargy and coma. Abnormal posturing and encephalopathy are often related to the degree of central nervous system swelling and pressure upon the brain stem. In cases where OTC enzyme production is low or non-existent, death can occur within the first days of life. Complications from ornithine transcarbamylase deficiency may include developmental delay and mental retardation. Progressive liver damage, skin lesions, and brittle hair may also be seen. Other symptoms include irrational behavior (caused by encephalitis), mood swings, and poor performance in school. In milder (or partial) urea cycle enzyme deficiencies, ammonia accumulation may be triggered by illness or stress at almost any time of life, resulting in multiple mild elevations of plasma ammonia concentration.

Rationale for treatment and development plan:

Loss of OTC blocks the normal metabolism of ammonia into the less toxic urea that can be cleared from the blood by the kidneys. Replacement of the missing or mutated protein can restore the normal function of the urea cycle and prevent the toxic accumulation of ammonia. Based on our PRT platform, we have developed a fusion protein that is comprised of TAT-MTS OTC. We are developing it towards proof of concept in human cells and in animal models. We continue our preclinical development and expect to start a full preclinical regulatory phase in mid-2015. We expect to start a Phase 1 study late in 2016 in the United States and Europe.

Market potential for BB-OTC:

The incidence of OTCD is 1 in 70,000, with approximately 4,000 patients in the United States, of which 2,000 males suffer from the severe lethal form. This incidence may be an underestimation due to under diagnosis. In some affected individuals, signs and symptoms of ornithine transcarbamylase may be less severe, and may not appear until later in life. Some female carriers become symptomatic later in life in times of metabolic stress. Despite milder presentations in adulthood, hyperammonemia, encephalopathy, cerebral edema, and death can occur. On February 1, 2013, the FDA approved RAVICTI® (glycerol phenylbutyrate) Oral Liquid for use as a nitrogen-binding agent for chronic management of adult and pediatric patients 2 years of age or older with urea cycle disorders (UCDs) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone. In clinical studies, RAVICTI was shown to be noninferior to sodium phenylbutyrate, and kept ammonia at safe levels throughout the day and night and over the long-term (1 year). Despite RAVCITI’s effectiveness in lowering blood ammonia levels it has some significant limitations in that it is not approved for patients suffering from liver or kidney disease and many OTCD patients have some disturbance in liver or kidney functions. In addition, over 10% of RAVCITI users suffer from diarrhea, bloating, and abdominal pain. We believe there exists a place for a therapy that will prevent the accumulation of ammonia in the first place.

Spinal Muscular atrophy

Disease background:

SMA is a neuromuscular disorder for which there is no available therapy. SMA is the number one autosomal recessive cause of infantile death. SMA is caused by loss or mutation of the survival motor neuron 1 gene, SMN1, while the nearly identical copy gene, SMN2 is retained. In contrast to SMN1, most SMN2 DNA lack a segment called exon 7. The alternative, Δ7-SMN, translates into a prematurely terminated protein that is rapidly degraded. It has been established that read-through of the stop codon in exon 8 of the Δ7 -SMN2 protein increases the amount of full-length SMN2 — a protein that can significantly attenuate disease severity in SMA patients.

Rationale for therapy and development plan:

Drug-induced read-through of the premature termination codon enables full-length translation of SMN, thus serving as an ideal therapeutic target as it is found in all SMA patients. This approach was successfully tested in SMA cells and animal models using a known family of antibiotics called aminoglycosides. Unfortunately, chronic administration of aminoglycosides is impossible due to their well-known prohibitive toxicity.

Our family of FDA-approved molecules (BBrm) are non-glycosides that were found to be significantly superior to aminoglycosides (Gentamycin) in enabling read-through and enabling the expression of full length functional SMN2 and rescue of cells.

We continue our preclinical development of our BBrm program and expect to start Phase 2 clinical study by 2015 in Israel to be expanded to the United States and Europe in 2016.

Market potential for SMA:

SMA has a carrier frequency of one in every 35 to 40 people, affecting every one in 6,000 live births. It is estimated that some 30,000 children suffer from SMA in the United States and in similar numbers in Europe.

There are several drugs in development for SMA; however, there is no approved therapy for this disease.

Competition

The commercialization of new drugs is competitive, and we may face worldwide competition from individual investigators, major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, nutraceutical companies, and ultimately biosimilar and generic companies. Our competitors may develop or market therapies that are more effective, safer, or less costly than any that may be commercialized by us, or may obtain regulatory approval for their therapies more rapidly than we may obtain approval for ours. Many of our competitors have substantially greater financial, technical, and human resources than we have. Additional mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields. Our success will be based in part on our ability to build and actively manage a portfolio of drugs that addresses unmet medical needs and creates value in patient therapy.

The acquisition or licensing of pharmaceutical products is also very competitive, and a number of more established companies, which have acknowledged strategies to license or acquire products, may have competitive advantages as may other emerging companies taking similar or different approaches to product acquisitions. These established companies may have a competitive advantage over us due to their size, cash flows, and institutional experience.

With respect to our programs in Cabaletta for OPMD, although we are not aware of any other products currently in clinical development for the treatment of OPMD, it is possible that competitors may produce, develop, and commercialize therapeutics, or utilize other approaches, such as gene therapy, to treat OPMD. An academic based study testing the use of injected myoblasts has completed a Phase 2 study.

With respect to our programs in Cabaletta for SCA3, although we are not aware of any other products currently in clinical development for the treatment of SCA3, it is possible that competitors may produce, develop, and commercialize therapeutics, or utilize other approaches such as gene therapy, to treat SCA3. In the last few years several academic researches where conducted to explore the efficacy of approved drugs such as Lithium, Varenicline (Chantix), riluzol, and Dalfampridine.

We are not aware of any competitive products approved or in late-stage clinical development for the treatment of SBMA. However, it is possible that competitors may produce, develop, and commercialize therapeutics, or utilize other approaches such as gene therapy to treat SBMA.

Although we believe that Cabaletta should be considered a drug and that only insignificant amounts of trehalose can be absorbed through an oral administration — it is possible that other companies or individuals may attempt to use food grade trehalose as a substitute, and others may attempt to sell the product via a nutraceutical or food pathway. We believe that following the approval of our patent applications, if approved, we will be well protected in our intellectual property from the use of trehalose as an IV product.

With respect to our programs in protein replacement platform although we are not aware of any other similar products currently in clinical development for the treatment of Friedreich's Ataxia, there are a number of competitors trying to develop and commercialize therapeutics, or utilize other approaches such as mitochondria protecting agents, anti-oxidants, HDAC inhibitors, cell therapy or gene therapy, to treat Friedreich's Ataxia. The table below from www.curefa.org, describes, to our knowledge, the current therapeutic approaches for Friedreich's Ataxia in different stages of development. To our knowledge, none of these product candidates have received regulatory approval in the United States or Europe.

With respect to our programs in protein replacement platform, although we are not aware of any other similar products currently in clinical development for the treatment of Ornithine transcarbamylase deficiency, there are a number of clinical approaches currently used to treat OTCD patients in emergency situation: Intravenous administration of sodium benzoate, arginine, and sodium phenylacetate might be beneficial for patients in hepatic coma; however, they can only be administered in a large medical facility setting with close laboratory monitoring available. Intravenous sodium benzoate and phenylacetate (Ammonul) was approved in the United States in February 2005.

Glycerol phenylbutyrate (Ravicti) is a pre-prodrug that undergoes metabolism to form phenylacetate. Results of a Phase 3 study comparing ammonia control in adults showed glycerol phenylbutyrate was non-inferior to sodium phenylbutyrate. In a separate study involving young children ages 2 months through 5 years, glycerol phenylbutyrate resulted in a more evenly distributed urinary output of phenyl butyrate main metabolite (PAGN) over 24 hours and accounted for fewer symptoms from accumulation of phenylacetate. Ravicti was approved by the FDA early in 2013 (Hyperion).

With respect to our program in BBrm- read-through platform there are a number of competitors developing read-through molecules, both small molecules (PTC) and exon- skipping RNA based platform (ISIS, Prosensa, Sarepta). Although not all have focused so far on SMA, it is possible that they will develop in the future programs that will attempt to utilize their technology for SMA. In addition it is possible that competitors may produce, develop, and commercialize therapeutics, or utilize other approaches such as gene therapy, cell therapy or bone marrow transplantation, to treat SCA3. The table below, from www.curesma.org, outlines, to our knowledge, the different approaches for developing drugs for SMA.

We believe that our read-through platform could be synergistic to most technologies outlined above since most are focused on either generally enhancing the total production of SMN2 through exon skipping, or focused on the downstream effects of lack of SMN1.

License Agreements

We have entered into two license agreements with respect to two of our three platform technologies. On December 18, 2011, we entered into a Research and Exclusive License Agreement with Yissum Research Development Company of the Hebrew University in Jerusalem Ltd., whereby we licensed exclusively two patent applications covering our mitochondrial protein replacement platform. One patent application covers the use of TAT-MTS-Protein for protein replacement in mitochondrial diseases. The second patent application covers the use of heterologous MTS in a fusion protein for treatment of mitochondrial protein deficiency diseases. These patent applications, if issued, will expire in 2029 and 2033, respectively. In addition, on January 1, 2014 we entered into an Exclusive License Agreement with Ramot at Tel Aviv University Ltd. for the use, development and commercialization of our read-through platform.

Intellectual Property and Patents and Proprietary Rights

The proprietary nature of, and protection for, our product candidates, processes, and know-how are important to our business. Our success depends in part on our ability to protect the proprietary nature of our product candidates, technology, and know-how, to operate without infringing on the proprietary rights of others, and to prevent others from infringing our proprietary rights. We seek patent protection in the United States and internationally for our product candidates and other technology. Our policy is to patent or in-license the technology, inventions and improvements that we consider important to the development of our business. In addition to patent protection, we intend to use other means to protect our proprietary rights, including pursuing marketing or data exclusivity periods, orphan drug status, and similar rights that are available under regulatory provisions in certain countries, including the United States, Europe, Japan, and China. See "U.S. Government Regulation — Orphan Designation and Exclusivity," "U.S. Government Regulation — Pediatric Studies and Exclusivity," "U.S. Government Regulation — Patent Term Restoration," "U.S. Government Regulation — Biosimilars and Exclusivity," "U.S. Government Regulation — Abbreviated New Drug Applications for Generic Drugs," "U.S. Government Regulation — Hatch-Waxman Patent Certification and the 30-Month Stay," and "European Union/Rest of World Government Regulation — Orphan Designation and Exclusivity" below for additional information.

We also rely on trade secrets, know-how, and continuing innovation to develop and maintain our competitive position. We cannot be certain that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents granted to us in the future will be commercially useful in protecting our technology.

We seek regulatory approval for our products in disease areas with high unmet medical need, great market potential, and where we have a proprietary position through patents covering various aspects of our products, such as composition, dosage, formulation, use, and manufacturing process, among others. Our success depends on an intellectual property portfolio that supports our future revenue streams and erects barriers to our competitors. We are maintaining and building our patent portfolio through filing new patent applications, prosecuting existing applications, and licensing and acquiring new patents and patent applications.

Despite these measures, any of our intellectual property and proprietary rights could be challenged, invalidated, circumvented, infringed or misappropriated, or such intellectual property and proprietary rights may not be sufficient to permit us to take advantage of current market trends or otherwise to provide competitive advantages. For more information, please see Item 3.D. – "Risks Related to our Intellectual Property."

As of December 31, 2014, we own and/or are the exclusive licensee of five pending U.S. patent applications, one issued U.S. patent and corresponding patents and patent applications internationally. With respect to any patents that may issue in the United States and Europe, we may also be entitled to obtain a patent term extension to extend the patent expiration date. For example, in the United States, we can apply for a patent term extension of up to five years

for one of the patents covering a product once the product is approved by the FDA. The exact duration of the extension depends on the time we spend in clinical studies as well as getting a new drug application approval from the FDA. The patent portfolios for our three leading platform and product candidates as of December 31, 2014 are summarized below.

Cabaletta

We have filed two patent applications that relate to the use of trehalose for the treatment of PolyA/PolyQ diseases and Taupathies. The patent applications are directed to a novel therapeutic regime using parenteral administration of trehalose, thereby achieving higher bioavailability and therapeutic efficacy in the treatment of myopathic and neurodegenerative diseases associated with abnormal protein aggregation, specifically polyalanine or polyglutamine expansion protein and tauopathies disorders such as OPMD, SCA, SBMA, Huntington and more. We have received a notice of allowance from the USPTO relating to a patent for Cabaletta and OPMD.

The expiring patent terms for such pending patent applications in the United States would be 2034. We intend to pursue marketing and orphan drug exclusivity periods that are available to us under regulatory provisions in certain countries.

In addition we have received orphan drug designation for the use of trehalose in OPMD and SCA3 patients.

mPRT

We have filed two patent applications and have licensed exclusively two patent applications from the Hebrew University in Israel that relate to our mitochondrial protein replacement platform. These patent applications, as well as our internally developed intellectual property assets, cover our unique approach of using homologous and heterologous MTS. We have one granted patent covering TAT-citrate synthase MTS-fraxatin fusion proteins that expires in 2033.

Read-through

We are the exclusive licensee of one Patent Cooperation Treaty, or PCT, patent application and one U.S. patent application covering our read-through platform that we licensed from Tel Aviv University (See “License Agreements” above). We also filed one U.S. patent application that relates to our read-through platform. The licensed PCT patent application and the patent application that we filed are directed to a method of treatment for orphan genetic neurodegenerative and neurodevelopmental diseases through non-systemic administration and specific injectable formulations.

The expiration dates on these patents are 2027 and 2033, respectively.

Trademarks

We have filed with the USPTO an intent to use application for the trademark Cabaletta in International Class 5 for certain pharmaceutical preparations.

Other

We rely upon unpatented trade secrets, know-how, and continuing technological innovation to develop and maintain our competitive position. We seek to protect our ownership of know-how and trade secrets through an active program of legal mechanism including assignments, confidentiality agreements, material transfer agreements, research collaborations, and licenses.

Manufacturing

We currently contract with third parties for the manufacturing and testing of our product candidates for preclinical studies and clinical studies and intend to do so in the future. We do not own or operate manufacturing facilities for the production of clinical quantities of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. The use of contracted manufacturing and reliance on collaboration partners is relatively cost-efficient and has eliminated the need for our direct investment in manufacturing facilities and additional staff early in development. Although we rely on contract manufacturers, we have personnel with extensive manufacturing experience to oversee our contract manufacturers.

To date, our third-party manufacturers have met our manufacturing requirements. We expect third-party manufacturers to be capable of providing sufficient quantities of our product candidates to meet anticipated full scale commercial demands. To meet our projected needs for commercial manufacturing, third parties with whom we currently work might need to increase their scale of production or we will need to secure alternate suppliers. We believe that there are alternate sources of supply that can satisfy our clinical and commercial requirements, although we cannot be certain that identifying and establishing relationships with such sources, if necessary, would not result in significant delay or material additional costs.

The drug substance for Cabaletta is purchased from a third party supplier and drug product for Cabaletta is manufactured by a third party manufacturer. There are other suppliers for pharmaceutical grade trehalose in the market. We have not yet started the development of our clinical trial material for our pre-clinical programs in mPRT and read-through platforms.

Sales and Marketing

We intend to build the commercial infrastructure in the United States and Europe necessary to effectively support the commercialization of all of our product candidates, if and when we believe a regulatory approval of the first of such product candidates in a particular geographic market appears imminent. The commercial infrastructure for orphan products typically consists of a targeted, specialty sales force that calls on a limited and focused group of physicians supported by sales management, medical liaisons, internal sales support, an internal marketing group, and distribution support. One challenge unique to commercializing therapies for rare diseases is the difficulty in identifying eligible patients due to the very small and sometimes heterogeneous disease populations. Our management team is experienced in maximizing patient identification for both clinical development and commercialization purposes in rare diseases.

Additional capabilities important to the orphan marketplace include the management of key accounts such as managed care organizations, group-purchasing organizations, specialty pharmacies, and government accounts. To develop the appropriate commercial infrastructure, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that any of our product candidates will be approved.

Outside of the United States and Europe, where appropriate, we may elect in the future to utilize strategic partners, distributors, or contract sales forces to assist in the commercialization of our products. In certain instances we may consider building our own commercial infrastructure.

Government Regulation

Clinical trials, the drug approval process, and the marketing of drugs are intensively regulated in the United States and in all major foreign countries. Governmental authorities in the United States (including federal, state, and local authorities) and in other countries, extensively regulate, among other things, the manufacturing, research and clinical development, marketing, labeling and packaging, storage, distribution, post-approval monitoring and reporting, advertising and promotion, pricing, and export and import of pharmaceutical products, such as those we are developing. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and related regulations, and biologics under the FDCA and the Public Health Service Act, or PHSA, and its implementing regulations. FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. Drugs and biologics are also subject to other federal, state and local statutes and regulations. Failure to comply with the applicable United States regulatory requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include the imposition by the FDA or an IRB of a clinical hold on trials, the FDA's refusal to approve pending applications or supplements, license suspension or revocation, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, distribution, record keeping, approval, advertising and promotion of our products.

The FDA's policies may change and additional government regulations may be enacted that could prevent or delay regulatory approval of our platforms and candidate products or any future product candidates or approval of new disease indications or label changes. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the United States or abroad.

Marketing Approval

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests and preclinical animal studies, all performed in accordance with GLP regulations;
- submission to the FDA of an IND which must become effective before human clinical studies may begin and must be updated annually;
- approval by an IRB or ethics committee representing each clinical site before each clinical study may be initiated;
- performance of adequate and well-controlled human clinical studies to establish the safety and efficacy of the product candidate for each proposed indication;
- preparation of and submission to the FDA of an NDA or BLA after completion of all pivotal clinical studies;
- potential review of the product application by an FDA advisory committee, where appropriate and if applicable;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities where the proposed product drug substance is produced to assess compliance with cGMP; and
- FDA review and approval of an NDA or BLA prior to any commercial marketing or sale of the drug in the United States.

The testing and approval process requires substantial time and financial resources, and we cannot be certain that any approvals for our candidate products will be granted on a timely basis, if at all.

An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational new drug. An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical studies. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical studies can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical studies to commence.

We will need to successfully complete extensive additional clinical trials in order to be in a position to submit a new drug application to the FDA. Our planned future clinical trials for our candidate products may not begin or be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays in:

- obtaining regulatory approval to commence a study;
- reaching agreement with third-party clinical trial sites and their subsequent performance in conducting accurate and reliable studies on a timely basis;
- obtaining institutional review board approval to conduct a study at a prospective site;
- recruiting patients to participate in a study; and
- supply of the drug.

We must reach agreement with the FDA on the proposed protocols for our future clinical trials in the United States. A separate submission apart from any IND application we submit must be made for each successive clinical trial to be conducted during product development. Further, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that site. Informed consent must also be obtained from each study subject. Regulatory authorities, an IRB, a data safety monitoring board or the sponsor, may suspend or terminate a clinical trial at any time on various grounds, including a finding that the participants are being exposed to an unacceptable health risk.

Clinical Studies

Clinical studies involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with current cGCPs which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical studies are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Additionally, approval must also be obtained from each clinical study site’s IRB before the studies may be initiated, and the IRB must monitor the study until completed. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

Our objective is to conduct additional clinical trials for our candidate products and, if those trials are successful, seek marketing approval from the FDA and other worldwide regulatory bodies.

For purposes of NDA approval, human clinical trials are typically conducted in phases that may overlap.

- *Phase 1*. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- *Phase 2*. This phase involves trials in 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*. This phase involves trials undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population, often at geographically dispersed clinical trial sites. These trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

- *Phase 4*. In some cases, the FDA may condition approval of an NDA or BLA for a product candidate on the sponsor's agreement to conduct additional clinical studies after approval. In other cases, a sponsor may voluntarily conduct additional clinical studies after approval to gain more information about the drug. Such post-approval studies are typically referred to as Phase 4 clinical studies.

A pivotal study is a clinical study that adequately meets regulatory agency requirements for the evaluation of a drug candidate's efficacy and safety such that it can be used to justify the approval of the product. Generally, pivotal studies are Phase 3 studies, but the FDA may accept results from Phase 2 studies if the study design provides a well-controlled and reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need and the results are sufficiently robust.

The FDA, the IRB, or the clinical study sponsor may suspend or terminate a clinical study at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk.

Additionally, some clinical studies are overseen by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study. We may also suspend or terminate a clinical study based on evolving business objectives and/or competitive climate.

All of these trials must be conducted in accordance with good clinical practice requirements in order for the data to be considered reliable for regulatory purposes.

The clinical study process can take three to ten years or more to complete, and there can be no assurance that the data collected will support FDA approval or licensure of the product. Government regulation may delay or prevent marketing of product candidates or new drugs for a considerable period of time and impose costly procedures upon our activities. We cannot be certain that the FDA or any other regulatory agency will grant approvals for our candidate products or any future product candidates on a timely basis, if at all. Success in early stage clinical trials does not ensure success in later stage clinical trials. Data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval.

The NDA Approval Process

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational new drug product information is submitted to the FDA in the form of an NDA or BLA requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs and BLAs is subject to an application user fee. For fiscal year 2014, the application user fee exceeded $2.1 million, and the sponsor of an approved NDA or BLA is also subject to annual product and establishment user fees, set at $104,060 per product and $554,600 per establishment. These fees are typically increased annually. Applications for orphan drug products are exempted from the NDA and BLA user fees and may be exempted from product and establishment user fees, unless the application includes an indication for other than a rare disease or condition.

An NDA or BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product’s chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational new

drug product to the satisfaction of the FDA.

The FDA will initially review the NDA for completeness before it accepts it for filing. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that the application is sufficiently complete to permit substantive review. After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. The FDA may refer applications for novel drug products or drug products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and, if so, under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Based on pivotal Phase 3 trial results submitted in an NDA, upon the request of an applicant, the FDA may grant a priority review designation to a product, which sets the target date for FDA action on the application at six months, rather than the standard ten months. Priority review is given where preliminary estimates indicate that a product, if approved, has the potential to provide a significant improvement compared to marketed products or offers a therapy where no satisfactory alternative therapy exists. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

After the FDA completes its initial review of an NDA, it will communicate to the sponsor that the drug will either be approved, or it will issue a complete response letter to communicate that the NDA will not be approved in its current form and inform the sponsor of changes that must be made or additional clinical, nonclinical or manufacturing data that must be received before the application can be approved, with no implication regarding the ultimate approvability of the application.

Before approving an NDA or BLA, the FDA will typically inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications.

Additionally, before approving an NDA, the FDA may inspect one or more clinical sites to assure compliance with GCPs. If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it typically will outline the deficiencies and often will request additional testing or information. This may significantly delay further review of the application. If the FDA finds that a clinical site did not conduct the clinical trial in accordance with GCP, the FDA may determine the data generated by the clinical site should be excluded from the primary efficacy analyses provided in the NDA. Additionally, notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The testing and approval process for a drug requires substantial time, effort and financial resources, and this process may take several years to complete. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals, which could delay or preclude us from marketing our products.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 studies may be made a condition to be satisfied for continuing drug approval. The results of Phase 4 studies can confirm the effectiveness of a product candidate and can provide important safety information. In addition, the FDA now has express statutory authority to require sponsors to conduct post-market studies to specifically address safety issues identified by the agency.

Any approvals that we may ultimately receive could be withdrawn if required post-marketing trials or analyses do not meet the FDA requirements, which could materially harm the commercial prospects for our candidate products.

The FDA also has authority to require a REMS from manufacturers to ensure that the benefits of a drug or biological product outweigh its risks. A sponsor may also voluntarily propose a REMS as part of the NDA submission. The need for a REMS is determined as part of the review of the NDA. Based on statutory standards, elements of a REMS may include “dear doctor letters,” a medication guide, more elaborate targeted educational programs, and in some cases restrictions on distribution. These elements are negotiated as part of the NDA approval, and in some cases if consensus is not obtained until after the Prescription Drug User Fee Act review cycle, the approval date may be delayed. Once adopted, REMS are subject to periodic assessment and modification.

Even if a product candidate receives regulatory approval, the approval may be limited to specific disease states, patient populations and dosages, or might contain significant limitations on use in the form of warnings, precautions or contraindications, or in the form of onerous risk management plans, restrictions on distribution, or post-marketing study requirements. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Delay in obtaining, or failure to obtain, regulatory approval for our candidate products, or obtaining approval but for significantly limited use, would harm our business. In addition, we cannot predict what adverse governmental regulations may arise from future U.S. or foreign governmental action.

Expedited Review and Accelerated Approval Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate the FDA's review and approval of NDAs and BLAs. For example, Fast Track Designation may be granted to a drug intended for treatment of a serious or life-threatening disease or condition that has potential to address unmet medical needs for the disease or condition. The key benefits of fast track designation are the eligibility for priority review, rolling review (submission of portions of an application before the complete marketing application is submitted), and accelerated approval, if relevant criteria are met. Based on results of the Phase 3 clinical study(ies) submitted in an NDA or BLA, upon the request of an applicant, the FDA may grant the NDA or BLA a priority review designation, which sets the target date for FDA action on the application at six months after the FDA accepts the application for filing. Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the accelerated approval program, the FDA may approve an NDA or BLA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the drug's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In addition, the Food and Drug Administration Safety and Innovation Act which was enacted and signed into law in 2012, established the new Breakthrough Therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

FDA Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

Drug manufacturers are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

We rely, and expect to continue to rely, on third parties for the production of clinical quantities of our product candidates, and expect to rely in the future on third parties for the production of commercial quantities. Future FDA and state inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA or BLA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- injunctions or the imposition of civil or criminal penalties; or
- product seizure or detention, or refusal to permit the import or export of products.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Orphan Designation and Exclusivity

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making the drug for this type of disease or condition will be recovered from sales in the United States.

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and user-fee waivers. In addition, if a product receives FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity.

Pediatric Studies and Exclusivity

NDAs and BLAs must contain data (or a proposal for post-marketing activity) to assess the safety and effectiveness of an investigational new drug product for the claimed indications in all relevant pediatric populations in order to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. 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 if certain criteria are met. Discussions about pediatric development plans can be discussed with the FDA at any time, but usually occur any time between the end-of-Phase 2 meeting and submission of the NDA or BLA. The requirements for pediatric data do not apply to any drug for an indication for which orphan designation has been granted.

Pediatric exclusivity is another type of non-patent 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 five-year and three-year non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA or 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 the product to be effective in the pediatric population studied; rather, if the clinical study is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of FDA-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 relying on the NDA or BLA sponsor's data.

Patent Term Restoration

Depending upon the timing, duration, and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act.

The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA, plus the time between the submission date and the approval of that application. Only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical studies and other factors involved in the filing of the relevant NDA or BLA.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, or Affordable Care Act, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, which created an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product. This amendment to the PHSA attempts to minimize duplicative testing. 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 and, for

products administered multiple times, the biologic and the reference biologic may be 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, structure of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

A reference biologic is granted twelve years of exclusivity from the time of first licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitting under the abbreviated approval pathway for the lesser of (i) one year after the first commercial marketing,

(ii) eighteen months after approval if there is no legal challenge, (iii) eighteen months after the resolution in the applicant's favor of a lawsuit challenging the biologics' patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Act, the U.S. Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to an RLD if "the rate and extent of absorption of the generic drug do not show a significant difference from the rate and extent of absorption of the listed drug. . . ."

Upon approval of an ANDA, the FDA indicates that the generic product is "therapeutically equivalent" to the RLD and it assigns a therapeutic equivalence rating to the approved generic drug in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider an "AB" therapeutic equivalence rating to mean that a generic drug is fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of an "AB" rating often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. In cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant

is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

European Union/Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical studies and any commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies. In the European Union, for example, a clinical study application, or CTA, must be submitted for each clinical protocol to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is accepted in accordance with a country's requirements, the clinical study may proceed.

The requirements and process governing the conduct of clinical studies vary from country to country. In all cases, the clinical studies are conducted in accordance with cGCP, the applicable regulatory requirements, and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational medicinal product under European Union regulatory systems, we must submit a marketing authorization application. The content of the NDA or BLA filed in the United States is similar to that required in the European Union, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing product licensing, pricing, and reimbursement vary from country to country.

Countries that are part of the European Union, as well as countries outside of the European Union, have their own governing bodies, requirements, and processes with respect to the approval of pharmaceutical products. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Authorization Procedures in the European Union

Medicines can be authorized in the European Union by using either the centralized authorization procedure or national authorization procedures.

Centralized procedure. The EMA implemented the centralized procedure for the approval of human medicines to facilitate marketing authorizations that are valid throughout the EEA which is comprised of the 28 member states of the European Union plus Norway, Iceland, and Lichtenstein. This procedure results in a single marketing authorization issued by the EMA that is valid across the EEA. The centralized procedure is compulsory for human medicines that are: derived from biotechnology processes, such as genetic engineering, contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions, and officially designated orphan medicines.

- For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the European Commission following a favorable opinion by the EMA, as long as the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.

- *National authorization procedures*. There are also two other possible routes to authorize medicinal products in several European Union countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:

- *Decentralized procedure*. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one European Union country of medicinal products that have not yet been authorized in any European Union country and that do not fall within the mandatory scope of the centralized procedure.

- *Mutual recognition procedure.* In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

In some cases, a Pediatric Investigation Plan, or PIP, and/or a request for waiver or deferral, is required for submission prior to submitting a marketing authorization application. A PIP describes, among other things, proposed pediatric studies and their timing relative to clinical studies in adults.

New Chemical Entity Exclusivity

In the European Union, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Orphan Designation and Exclusivity

In the European Union, the EMA's COMP grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the European Union Community and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). 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 necessary investment in developing the medicinal product.

In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and 10 years of market exclusivity is granted following medicinal 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.

Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Exceptional Circumstances/Conditional Approval

Orphan drugs or drugs with unmet medical needs may be eligible for European Union approval under exceptional circumstances or with conditional approval. Approval under exceptional circumstances is applicable to orphan products and is used when an applicant is unable to provide comprehensive data on the efficacy and safety under normal conditions of use because the indication for which the product is intended is encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, when the present state of scientific knowledge does not allow comprehensive information to be provided, or when it is medically unethical to collect such information. Conditional marketing authorization is applicable to orphan medicinal products, medicinal products for seriously debilitating or life-threatening diseases, or medicinal products to be used in emergency situations in response to recognized public threats. Conditional marketing authorization can be granted on the basis of less complete data than is normally required in order to meet unmet medical needs and in the interest of public health, provided the risk-benefit balance is positive, it is likely that the applicant will be able to provide the comprehensive clinical data, and unmet medical needs will be fulfilled. Conditional marketing authorization is subject to certain specific obligations to be reviewed annually.

Accelerated Review

Under the Centralized Procedure in the European Union, the maximum timeframe 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 EMA's Committee for Medicinal Products for Human Use, or CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. In this circumstance, EMA ensures that the opinion of the CHMP is given within 150 days, excluding clock stops.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government 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 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 FDA-approved drugs for a particular indication. Moreover, a payor's decision to provide coverage for a drug product does not imply 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.

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. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Healthcare Reform Law, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very 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 a commercial pressure on pricing within a country.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on cost containment measures in the United States and other countries has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Other Healthcare Laws and Compliance Requirements

If we obtain regulatory approval for any of our product candidates, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent;

- HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

- the federal transparency laws, including the federal Physician Payment Sunshine Act, that requires drug manufacturers to disclose payments and other transfers of value provided to physicians and teaching hospitals;

- HIPAA, as amended by HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The Healthcare Reform Law broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. §1320a-7b, effective March 23, 2010. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Healthcare Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

We are also subject to the FCPA, which prohibits improper payments or offers of payments to foreign governments and their officials for the purpose of obtaining or retaining business.

Safeguards we implement to discourage improper payments or offers of payments by our employees, consultants, and others may be ineffective, and violations of the FCPA and similar laws may result in severe criminal or civil sanctions, or other liabilities or proceedings against us, any of which would likely harm our reputation, business, financial condition and result of operations.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, exclusion from participation in government healthcare programs, such as Medicare and Medicaid and imprisonment, damages, fines and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Labeling, Marketing and Promotion

The FDA closely regulates the labeling, marketing and promotion of drugs. While doctors are free to prescribe any drug approved by the FDA for any use, a company can only make claims relating to safety and efficacy of a drug that are consistent with FDA approval, and the company is allowed to actively market a drug only for the particular use and treatment approved by the FDA. In addition, any claims we make for our products in advertising or promotion must be appropriately balanced with important safety information and otherwise be adequately substantiated. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising, injunctions and potential civil and criminal penalties. Government regulators recently have increased their scrutiny of the promotion and marketing of drugs.

Pediatric Research Equity Act

The Pediatric Research Equity Act, or PREA, amended the FDCA to authorize the FDA to require certain research into drugs used in pediatric patients. The intent of PREA is to compel sponsors whose drugs have pediatric applicability to study those drugs in pediatric populations, rather than ignoring pediatric indications for adult indications that could be more economically desirable. The Secretary of Health and Human Services may defer or waive these requirements under specified circumstances.

Anti-Kickback and False Claims Laws

In the United States, the research, manufacturing, distribution, sale and promotion of drug products and medical devices are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice, state Attorneys General, and other state and local government agencies. For example, sales, marketing and scientific/educational grant programs must comply with the Anti-Kickback Statute, the False Claims Act, as amended, the privacy regulations promulgated under HIPAA and similar state laws. Pricing and rebate programs must comply with the Medicaid Drug Rebate Program requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Veterans Health Care Act of 1992, as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

In the United States, we are subject to complex laws and regulations pertaining to healthcare “fraud and abuse,” including, but not limited to, the Anti-Kickback Statute, the federal False Claims Act, and other state and federal laws and regulations. The Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid.

The federal False Claims Act prohibits anyone from knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services.

There are also an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the laws. In addition, a similar federal requirement will require manufacturers to track and report to the federal government certain payments made to physicians and teaching hospitals made in the previous calendar year. These laws may affect our sales, marketing, and other promotional activities by imposing administrative and compliance burdens on us. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state, and soon federal, authorities.

Patient Protection and Affordable Health Care Act

In March 2010, the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively PPACA, was enacted, which includes measures that have or will significantly change the way health care is financed by both governmental and private insurers. The fees, discounts and other provisions of this law are expected to have a significant negative effect on the profitability of pharmaceuticals.

Many of the details regarding the implementation of PPACA are yet to be determined, and at this time, it remains unclear the full effect that PPACA would have on our business.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

Israel

Clinical Testing in Israel

In order to conduct clinical testing on humans in the State of Israel, special authorization must first be obtained from the ethics committee and general manager of the institution in which the clinical studies are scheduled to be conducted, as required under the Guidelines for Clinical Trials in Human Subjects implemented pursuant to the Israeli Public Health Regulations (Clinical Trials in Human Subjects), as amended from time to time, and other applicable legislation. These regulations require authorization by the institutional ethics committee and general manager as well as from the Israeli Ministry of Health, except in certain circumstances, and in the case of genetic trials, special fertility trials and complex clinical trials, an additional authorization of the Ministry of Health's overseeing ethics committee. The institutional ethics committee must, among other things, evaluate the anticipated benefits that are likely to be derived from the project to determine if it justifies the risks and inconvenience to be inflicted on the human subjects, and the committee must ensure that adequate protection exists for the rights and safety of the participants as well as the accuracy of the information gathered in the course of the clinical testing. Since we perform a portion of the clinical studies on certain of our therapeutic candidates in Israel, we are required to obtain authorization from the ethics committee and general manager of each institution in which we intend to conduct our clinical trials, and in most cases, from the Israeli Ministry of Health.

4.C. Organizational structure

Our sole wholly owned subsidiary is BioBlast Pharma, Inc., incorporated in Delaware.

4.D. Property, plants and equipment

Our headquarters is currently located in Tel Aviv, Israel and consists of approximately 3,390 square feet of leased office space under a lease for a period of three years with an option to extend the lease period for two additional consecutive three-year periods. We may require additional space and facilities as our business expands.

We consider that our current office space is sufficient to meet our anticipated needs for the foreseeable future and is suitable for the conduct of our business.

ITEM 4A. UNRESOLVED STAFF COMMENTS

None.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

Overview

We are a development-stage biopharmaceutical company focused on the identification, licensing, acquisition, development and commercialization of drugs for rare and ultra-rare genetic and metabolic diseases. We seek to identify therapeutic platforms that offer solutions for several diseases that share a common pathophysiological mechanism. We focus on diseases with severe and debilitating manifestations, where the unmet medical need is clear, the biological mechanism of action is understood and for which there is no satisfactory treatment. Since our inception in 2012, we have developed and in-licensed potential treatments for six diseases, one of which is in a Phase 2/3 clinical trial which, if the results are positive, we believe could be a pivotal trial, another one which is in Phase 2 clinical studies and an additional one of which we expect will be in mid/late stage clinical studies by 2015. We believe, based on discussions with the FDA, that if the Phase 2/3 trial shows positive results, the data could be considered pivotal data, considering, among other things, the applicable FDA guidance for the industry called “Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products.”

Our current drug candidate pipeline has been either in-licensed from academic institutions or developed internally. Our strategy is based on risk diversification through multiple therapeutic platforms, diversified clinical and pre-clinical stages of our programs, and diversified diseases addressed. We use strict selection criteria of our pipeline platforms and cost-efficient drug development. This allows us to pursue multiple programs in parallel with the goal of promptly delivering safe and effective therapies to patients in dire need.

To date, we have not generated revenue from the sale of any product, and we do not expect to generate significant revenue unless and until we obtain marketing approval of, and commercialize our product candidates. As of December 31, 2014, we had an accumulated deficit of $8.4 million. Our financing activities are described below under “Liquidity and Capital Resources.”

Operating Expenses

Our current operating expenses consist of two components — research and development expenses, and general and administrative expenses.

Research and Development Expenses

Our research and development expenses consist primarily of the cost of third party clinical consultants and expenses related to conducting clinical and preclinical trials, salaries and related personnel expenses, share-based compensation expenses, travel expenses and other related research and development expenses.

The following table discloses the breakdown of research and development expenses:

(in thousands of U.S. dollars)	December 31, 2014	2013	2012
Cost of third party clinical consultants and expenses related to conducting clinical trials	$3,697	$470	$75
Salaries and related personnel expenses	561	171	34
Share-based compensation	83	44	-
Travel expenses	79	31	8
Other expenses	21	16	23
Total	$4,441	$732	$140

We expect that our research and development expenses will materially increase as we plan to initiate additional clinical activity for our product candidates and prepare to conduct clinical trials in the near future.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, share-based compensation expense, professional service fees for accounting, legal, bookkeeping, intellectual property and facilities, travel expenses and other general and administrative expenses.

The following table discloses the breakdown of general and administrative expenses:

(in thousands of U.S. dollars)	December 31, 2014	2013	2012
Share-based compensation	$654	$210	$ 9
Professional services	524	17	15
Intellectual property expenses	224	33	7
Rent and office related expenses	376	31	-
Salaries and related personnel expenses	655	103	55
Travel expenses	114	14	-
Other expenses	92	8	-
Total	$2,639	$416	$ 86

Comparison of the Year ended December 31, 2014 to the Year Ended December 31, 2013 to the Year Ended December 31, 2012

Results of Operations

(in thousands of U.S. dollars)	December 31, 2014	2013	2012
Research and development expenses	$4,441	$732	$140
General and administrative expenses	2,639	416	86
Operating loss	7,080	1,148	226
Financial Expense (income), net	(58)	(3)	3
Loss	7,022	1,145	229
Deemed dividend	-	26	-
Loss attributable to holders of Ordinary Shares	$7,022	$1,171	$229

Research and Development Expenses

Our research and development expenses for the year ended December 31, 2014 amounted to $4,441,000, representing an increase of $3,709,000, or 507%, compared to $732,000 for the year ended December 31, 2013. The increase was primarily attributable to an increase in third party clinical consultants expenses and expenses related to conducting clinical trials in an amount of $3,227,000, an increase of $390,000 in salaries and related personnel expenses, reflecting an increase in the number of employees and salary increases and an increase of $39,000 in share based compensation expenses.

Our research and development expenses for the year ended December 31, 2013 amounted to $732,000, representing an increase of $592,000, or 423%, compared to $140,000 for the year ended December 31, 2012. The increase was primarily attributable to an increase of expenses related to third party preclinical consultants and other expenses related to conducting preclinical trials in an amount of $395,000 and to an increase of salaries and related personnel expenses in an amount of $137,000, reflecting an increase in the number of employees engaged in research and development related activities from one to three, as well as an increase of stock-based compensation expenses of $44,000 in 2013 from $0 in 2012.

Research and development expenses by project

	December 31,		
(in thousands of U.S. dollars)	2014	2013	2012
Cabaletta projects:			
OPMD	$1,865	$407	$—
SCA3	141	39	—
SBMA	2	22	—
mPRT projects:			
Freiedrich’s Ataxia	276	75	64
OTC def	59	94	64
Read-through project:			
SMA	1,007	48	12
Other costs	347	47	—
Total	$3,697	$732	$140

Our research and development expense is highly dependent on the development phases of our projects and therefore fluctuates highly from year to year.

The variances in expense between the year ended December 31, 2014 and the corresponding period in 2013 and 2012 are mainly due to the following projects:

- *Cabaleta projects*. Our expenses related to OPMD, SCA3 and SBMA for the year ended December 31, 2014 amounted to $1,865,000, $141,000 and $2,000, respectively, compared to $407,000, $39,000 and $22,000, respectively, for the year ended December 31, 2013. These projects were initiated in 2013; therefore, there were no expenses in 2012.

- *mPRT projects*. Our expenses related to Freiedrich's Ataxia and OTC def for the year ended December 31, 2014 amounted to $276,000 and $59,000, respectively, compared to $75,000 and $94,000, respectively, for the year ended December 31, 2013, and $64,000 and $64,000, respectively, for the year ended December 31, 2012. The increase in 2014 was primarily attributable to growth in the preclinical trials and activities, and the increase in 2013 was primarily attributable to an increase in the number of employees involved in these projects from one to two and to an increase in the activity in these projects.

- *Read-through project*. Our expenses related to SMA for the year ended December 31, 2014 amounted to $1,007,000, compared to $48,000 for the year ended December 31, 2013, and $12,000 for the year ended December 31, 2012. The increase in 2014 was primarily attributable to growth in the preclinical trials and chemistry manufacturing control activities, and the increase in 2013 was primarily attributable to an increase in the number of employees involved in this project from one to two and to the initiation of pre-clinical trials.

General and administrative expenses

Our general and administrative expenses totaled $2,639,000 for the year ended December 31, 2014, an increase of $2,223,000, or 534%, compared to $416,000 for the year ended December 31, 2013. The increase resulted primarily from an increase of $444,000 in share-based compensation expenses, an increase of payroll in an amount of $552,000, reflecting an increase of payroll to our employees, an increase of $191,000 in intellectual property expenses, reflecting the progress in our IP portfolio, including the grant of a new patent application and the submission of an additional patent application, an increase of $345,000 in rent and office related expenses, primarily due to the our new offices, communication and information technology systems, and an increase of $507,000 in professional services for accounting, legal, bookkeeping, transfer agents and facilities, which increased after our August 2014 initial public offering.

Our general and administrative expenses totaled $416,000 for the year ended December 31, 2013, an increase of $330,000, or 384%, compared to $86,000 for the year ended December 31, 2012. The increase resulted primarily from an increase of $201,000 in share-based compensation expenses, an increase of payroll in an amount of $48,000, reflecting an increase of payroll to our employees, and an increase of $2,000 in professional services.

Operating loss

As a result of the foregoing, our operating loss for the year ended December 31, 2014 was $7,080,000, as compared to an operating loss of $1,148,000 for the year ended December 31, 2013, an increase of $5,932,000, or 517%.

Our operating loss for the year ended December 31, 2013 was $1,148,000, as compared to an operating loss of $226,000 for the year ended December 31, 2012, an increase of $922,000, or 408%.

Financial expense and income

Financial expense and income consist of bank fees and other transactional costs and exchange rate differences.

We recognized financial income of $58,000 for the year ended December 31, 2014, compared to financial income of $3,000 for the year ended December 31, 2013. The increase is primarily due to interest on bank deposits, offset by exchange rate differences during 2014.

We recognized financial income of $3,000 for the year ended December 31, 2013, compared to financial expenses of $3,000 for the year ended December 31, 2012. The increase is primarily due to interest on bank deposits.

Loss

As a result of the foregoing, our loss for the year ended December 31, 2014 was $7,022,000, as compared to $1,145,000 for the year ended December 31, 2013, an increase of $5,877,000 or 513%.

Our loss for the year ended December 31, 2013 was $1,145,000, as compared to $229,000 for the year ended December 31, 2012, an increase of $916,000 or 400%.

Critical Accounting Policies and Estimate

We describe our significant accounting policies more fully in Note 2b to our financial statements for the year ended December 31, 2014. We believe that the accounting policy below is critical in order to fully understand and evaluate our financial condition and results of operations.

We prepare our financial statements in accordance with accounting principles generally accepted in the United States, or U.S. GAAP. The preparation of the financial statements in conformity with U.S. GAAP requires management to make estimates, judgments and assumptions. Our management believes that the estimates, judgments and assumptions used are reasonable based upon information available at the time they are made. These estimates, judgments and assumptions can affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the dates of the financial statements, and the reported amounts of expenses during the reporting period. Actual results could differ from those estimates.

Stock-Based Compensation and Fair Value of Ordinary Shares

We account for stock-based compensation in accordance with ASC 718, “Compensation — Stock Compensation,”, or ASC 718, which requires companies to estimate the fair values of equity-based payments awards on the date of grant using an option-pricing model. The value of the stock options is recognized as an expense over the requisite service periods in our statement of operations. We recognize compensation expenses for the value of our awards granted based on the accelerated method over the requisite service period of each of the awards.

We selected the Black-Scholes-Merton, or Black-Scholes, option-pricing model as a fair value method for our options awards. The option-pricing model requires a number of assumptions:

Expected dividend yield - The expected dividend yield assumption is based on our historical experience and expectation of no future dividend payouts. We have historically not paid cash dividends and have no foreseeable plans to pay cash dividends in the future.

Volatility - Since the Company’s shares started trading on a stock exchange market only in July 2014, quoted prices data of our Ordinary Shares is limited. According to ASC 718-10-30-20, in case of insufficient historical data for a company, the expected volatility was based on similar companies' stock volatility.

Risk free interest rate - The risk free interest rate is based on the yield of U.S. Treasury bonds with equivalent terms.

Expected term - ASC 718 provides the factors to consider when estimating the expected term of an option: An option’s expected term must at least include the vesting period and the employees’ historical exercise and post-vesting employment termination behavior for similar grants. It also determines that if the amount of past exercise data is limited, that data may not represent a sufficiently large sample on which to base a robust conclusion on expected exercise behavior. In that circumstance, it may be appropriate to consider external data or the SEC staff’s “simplified” method for the expected term. Accordingly, we used the "simplified" method, meaning the expected life is set as the average of the vesting period for each vested tranche of options and the contractual term for those options.

Share price – Up until our initial public offering, because there had been no public market for our Ordinary Shares, the fair value of the Ordinary Shares underlying the options had been determined by our management, using the assistance of an independent valuation firm. Following our initial public offering, fair market value has been determined by NASDAQ Global Market quotes.

Options granted during 2014 were mostly granted at the initial public offering price or the last known closing price of our Ordinary Shares at the grant date.

During 2014, our Board of approved the grant by us of options to purchase 380,222 of our Ordinary Shares, subject to the terms and condition of our 2013 Incentive Option Plan.

Liquidity and Capital Resources

Overview

Since our inception through December 31, 2014, we have funded our operations principally with $38 million from the issuance of Ordinary Shares and preferred shares. As of December 31, 2014, we had $10.6 million in cash and cash equivalents, and an additional amount of $22 million in short-term bank deposits.

The table below presents our cash flows for the years 2014, 2013 and 2012:

	Years Ended December 31,		
	2014	2013	2012
	(in thousands of U.S. dollars)		
Operating activities	$ (4,409)	$ (865)	$ (149)
Investing activities	(22,063)	(2)	-
Financing activities	36,785	991	295
Net increase in cash and cash equivalents	$ 10,313	$ 124	$ 146

Operating Activities

Net cash used in operating activities of $4.4 million during the year ended December 31, 2014 was primarily used for payment of $2.3 million for clinical trials and other third party expenses and an aggregate of $1.2 million in salaries and related personnel expenses. The remaining amount of $0.9 million was for (travel, patent, rent) and other miscellaneous expenses.

Net cash used in operating activities of $0.9 million during the year ended December 31, 2013 was primarily used for payment of $0.6 million for clinical trials and other third party expenses and an aggregate of $0.2 million in salaries and related personnel expenses. The remaining amount of $0.1 million was for travel, patent, rent and other miscellaneous expenses. Net cash used in operating activities of $0.1 million during the year ended December 31, 2012 was primarily used for salary payments and for clinical trials and other third party expenses.

Investing Activities

Net cash used in investing activities of $22.1 million during 2014 primarily reflected investments of our cash in short term bank deposits.

Net cash used in investing activities during 2013 primarily reflected an increase in property and equipment. In 2012, we had no investment activity.

Financing Activities

Net cash provided by financing activities in the year ended December 31, 2014 consisted of approximately $36.8 million of net proceeds from issuance of Ordinary Shares. Net cash provided by financing activities in the year ended December 31, 2013 consisted of approximately $1 million of net proceeds from issuance of Ordinary Shares. Net cash provided by financing activities in the year ended December 31, 2012 consisted of approximately $0.3 million of net proceeds from issuance of Ordinary Shares.

Current Outlook

We have financed our operations to date primarily through proceeds from sales of our Ordinary Shares and preferred shares. We have incurred losses and generated negative cash flows from operations since inception. To date, we have not generated any revenue from the sale of products and we do not expect to generate revenues from sale of our products in the next few years.

As of December 31, 2014, our cash and cash equivalents including short-term bank deposits were $32.6 million. We expect that our existing cash, cash equivalents and short-term bank deposits will be sufficient to fund our current operations until the end of 2016 or early 2017; however, we expect that we will require substantial additional capital to obtain regulatory approval for, and to commercialize, our product candidates. In addition, our operating plans may change as a result of many factors that may currently be unknown to us, and we may need to seek additional funds sooner than planned. Our future capital requirements will depend on many factors, including:

- the progress and costs of our preclinical studies, clinical trials and other research and development activities;
- the costs of manufacturing of our drug candidates;
- the scope, prioritization and number of our clinical trials and other research and development programs;
- the costs and timing of obtaining regulatory approval for our drug candidates;
- the costs of filing, prosecuting, enforcing and defending patent claims and other intellectual property rights;
- the costs of, and timing for, strengthening our manufacturing agreements for production of sufficient clinical and commercial quantities of our drug candidates;
- the potential costs of contracting with third parties to provide marketing and distribution services for us or for building such capacities internally;
- the costs of acquiring or undertaking the development and commercialization efforts for additional, future therapeutic applications of our drug candidates;
- the magnitude of our general and administrative expenses; and
- any cost that we may incur under current and future in- and out-licensing arrangements relating to our drug candidates.

Until we can generate significant recurring revenues, we expect to satisfy our future cash needs through debt or equity financings, or by out-licensing applications of our drug candidates. We cannot be certain that additional funding will be available to us on acceptable terms, if at all. If funds are not available, we may be required to delay, reduce the scope of, or eliminate research or development plans for, or commercialization efforts with respect to, one or more applications of our drug candidates. This may raise substantial doubts about our ability to continue as a going concern.

5.E Off-Balance Sheet Arrangements

We currently do not have any off-balance sheet arrangements.

5.F Contractual Obligations

The following table summarizes our contractual obligations at December 31, 2014:

	Total	Less than 1 year	1-3 years	4-5 years	More than 5 years
	(in thousands of U.S. dollars)				
Operating leases:					
Facility	288	117	171	-	-
Motor vehicles	82	33	49	-	-

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

6.A. Directors and executive officers

The following table sets forth information regarding our executive officers, key employees and directors as of March 20, 2015:

Name	Age	Position
Fredric Price	69	Executive Chairman of the Board of Directors
Colin Foster	52	Chief Executive Officer, President and Director
Dr. Dalia Megiddo	63	Chief Development Officer, Director
Ehud (Udi) Gilboa	48	Chief Financial Officer, Senior Vice President of Operations and Director
Prof. Avizohar Argov	67	Chief Medical Officer
Michael Burshtine[(1)(2)]	51	Director
Gili Cohen[(1)(2)]	48	Director
Marlene Haffner	74	Director
Isaac Krymolowski[(1)(2)]	52	Director
Ran Nussbaum	42	Director

(1) Member of our Audit Committee.
(2) Member of our Compensation Committee.

Fredric Price has been Executive Chairman of our Board of Directors since April 2014, having served as our Chairman of the Board of Directors from April 2012 until April 2014. Since 2013, Mr. Price has served as a member of the Advisory Board of FDNA Inc. From 2013 until 2014, he was Executive Chairman of the Board of Directors and from 2008 to 2013 Chairman of the Board of Directors and Chief Executive Officer of Chiasma, Inc. From 2004 to 2008, Mr. Price was Executive Chairman of the Board of Directors of Omrix Biopharmaceuticals, Inc., from 2006 to 2012 a member of the Board of Directors of Enobia Pharma Corp., from 2007 to 2010 a member of the Board of Directors of Pharmasset Inc., from 2007 to 2011 Executive Chairman of the Board of Directors of Peptimmune, Inc., from 2004 to 2005 Executive Chairman of the Board of Directors of Zymenex A/S, from 2000 to 2004 Chairman of the Board of Directors and Chief Executive Officer of BioMarin Pharmaceutical Inc., and from 1994 to 2000 Chief Executive Officer and a member of the Board of Directors of Applied Microbiology Inc. As chairman and/or chief executive officer, he has raised more than $600 million in a variety of securities transactions, led a total of 21 M&A and licensing transactions, built FDA approved facilities and had drugs approved in the United States as well as in international markets. His earlier experience includes having been Vice President of Finance and administration and Chief Financial Officer of Regeneron Pharmaceuticals, Inc., the founder of the strategy consulting firm RxFDP, and Vice President of Pfizer Pharmaceuticals with both line and staff responsibilities. Mr. Price is a co-inventor of 13 issued U.S. patents. He received a B.A. from Dartmouth College and an M.B.A. from the Wharton School of the University of Pennsylvania.

Colin Foster has been our President, Chief Executive Officer and a director since January 2015. Mr. Foster has extensive experience in leading therapeutic, diagnostic, and medical device companies in the United States and internationally, working across the R&D-to-commercial continuum. He was a founder of iSci Management LLC, a life sciences advisory firm, and served as its Chief Executive Officer from 2011 until 2015. In 2005, Mr. Foster co-founded Optherion, Inc., a venture backed biologics and diagnostics company targeting ultra-orphan diseases of the immune system and age-related macular degeneration, and served as its Chief Executive Officer from 2006 until 2012. Prior to that, and from 1994 until 2004, he held various senior executive positions at Bayer AG, including President and Chief Executive Officer of Bayer Pharmaceuticals Corporation USA and Region Head of the North American Pharmaceuticals business of Bayer AG. In 1988, Mr. Foster began his post-graduate career with Sandoz Canada Inc. before embarking on an international career with Bayer in Canada, the USA, and Europe. Mr. Foster currently serves as Chairman of Ivenix, Inc., and is a board member of Optherion, iSci Management LLC, and Vista Vocational & Life Skills Center. Mr. Foster has a B.Sc. in Zoology and Microbiology from the University of Toronto, and an M.B.A. from Western University in Canada. He is also an active member of The Jackson Laboratory National Council and Jackson Society.

Dr. Dalia Megiddo has been a director since our inception and currently serves as our Chief Development Officer. From our inception until February 2015, Dr. Megiddo was our Chief Executive Officer. Dr. Megiddo co-founded Alcobra Ltd., a NASDAQ traded company primarily focused on the development and commercialization of a proprietary drug, MG01CI, to treat Attention Deficit Hyperactivity Disorder in February 2008 and became a Director at that time. She is an entrepreneur and a medical doctor in family medicine. Since 2000, she has been a manager of InnoMed Ventures, an Israeli venture capital fund focused on life sciences. From 2006 to 2010, she was also a manager of 7 Health Ventures, a Israeli venture capital fund. She is also the founder of a number of life science companies. Dr. Megiddo received her M.D. degree from Hebrew University Hadassah Medical School and holds a specialist degree in Family Medicine, and also holds an M.B.A. from the Kellogg-Recanati School of Business.

Udi Gilboa has been a director, our Chief Financial Officer and our Senior Vice President of Operations since our inception. In addition, Mr. Gilboa co-founded Alcobra Ltd. in February 2008, became a director at that time and served as its Chief Financial Officer and Chief Accounting Officer until May 2014. From 2007 until 2014, Mr. Gilboa served as a director of Insuline Medical Ltd., a public company whose shares are listed for trading on the Tel Aviv Stock Exchange. Mr. Gilboa is the founder and managing partner of Top Notch Capital, a prominent Israeli life sciences investment bank. He is a director of Samson Neurosciences Ltd., and has founded a number of medical device and pharmaceutical companies. Mr. Gilboa holds a Bachelor's degree and M.B.A. from Tel Aviv University.

Prof. Avizohar Argov has been our Chief Medical Officer since June 1, 2014. Since 1991, Prof. Argov has been a professor of Neurology & Josephine Frank Kanrich Chair of Neuromuscular Diseases, Hadassah-Hebrew University Medical Center in Jerusalem, Israel, and since 1996, has been an adjunct professor in the Department of Neurology/Neurosurgery at the Neurological Institute at McGill University in Montreal, Canada. Since 2010, Prof. Argov has been a member of the executive committee of the World Muscle Society. From 2010 until 2011 he served as the President of the European Neurological Society and the Chairman of its subcommittee of Muscle & Neuromuscular Disorders. In addition, he has served as the Chairman of the Israeli Society of Neuromuscular Diseases. Prof. Argov's primary research fields include hereditary inclusion body myopathies, hereditary neuromuscular disorders, particularly in Jewish ethnic clusters, and latrogenic neuromuscular disorders, particularly drug-induced myasthenia. He received his M.D. from the Hebrew University-Hadassah Medical School in Jerusalem, Israel and was a Resident in Neurology at the Hadassah University Hospital in Jerusalem, Israel. He received training in neuromuscular diseases from the Muscular Dystrophy Association in Newcastle Upon Tyne, England and further training in biochemistry and biophysics from the University of Pennsylvania in the United States.

Michael Burshtine has been a director since October 30, 2014. Mr. Burshtine served as the president and Chief Executive Officer of Flight Medical Innovations Ltd., a med-tech company specializing in the development, manufacturing and marketing of portable ventilators, between 2009 and May 2014. Prior to that, between 2007 and 2009, he served as President and Chief Executive Officer of Recoly N.V., a bio-med company engaged in the research, development and commercialization of drug enhancement technologies. From 2004 to 2007, he served as the Chief Financial Officer of Omrix Biopharmaceuticals Inc., a public biotechnology company that develops, manufactures and commercializes plasma derivative products. Mr. Burshtine has been a certified CPA since 1994 and was a senior partner at Kesselman & Kesselman PricewaternhouseCoopers (PWC) auditing firm, until 2004. He holds an M.B.A. and a B.A. in economics and accounting, both from Tel Aviv University. Mr. Burshtine serves on our Audit Committee and our Compensation Committee.

Gili Cohen has been a director since July 30, 2014. Mr. Cohen has been a member of the Board of Directors of Harel Pension Funds Management Ltd. and Harel Atidit Provident Funds Ltd., which are both members of the Harel Insurance Investments and Financial Services Ltd. group, since March 2012. In addition, Mr. Cohen has been a member of Israel Land Development Co. Ltd., which deals in real estate and investments, since June 2012. He also currently serves as an independent financial consultant and is an economics professor at The College of Management Academic Studies. From 2000 to 2011, Mr. Cohen was the Chief Investments Officer and head of the Investments Department at Excellence Investments Ltd. Mr. Cohen has a degree in economics and geography and an M.B.A., both with honors, from the Hebrew University in Jerusalem. Mr. Cohen serves on our Audit Committee and our Compensation Committee.

Dr. Marlene Haffner has been a director since July 1, 2013. From 1986 until 2007, Dr. Haffner served as the Director of the Office of Orphan Products Development (OOPD) of the FDA. As OOPD Director she was responsible for the leadership and management of the FDA orphan products development program, the first Orphan Products program in the world. After leaving the FDA, and from 2007 until 2009, she served as Executive Director, Global Regulatory Policy and Intelligence at Amgen, Inc., and since 2009 has held the position of Chief Executive Officer at Orphan Solutions and Haffner Associates, services companies for the Orphan Drugs industry. In addition to her consulting activities, Since 2009, Dr. Haffner has been an Adjunct Professor at the Department of Preventive Medicine and Biometrics and a Clinical Professor at the Department of Medicine of the F. Edward Hébert School of Medicine, Uniformed Services University of the Health Sciences in Bethesda, Maryland. For 36 years she served in the United States Public Health Service beginning her career with the Indian Health Service in Gallup, New Mexico. She received her M.D. from the George Washington University School of Medicine where she then interned in Internal Medicine. She received further training in internal medicine, dermatology and hematology at the Presbyterian Hospital, New York and at the Albert Einstein College of Medicine, New York. She received an M.P.H. from the Johns Hopkins University Bloomberg School of Public Health. During her public health career, she rose to the rank of Rear Admiral in the United States Public Health Service.

Isaac Krymolowski has been a director since October 30, 2014. Mr. Krymolowski served as the Chairman of the Board of directors of Solcon Industries Ltd., a company focused on designing, developing and manufacturing industrial electronic systems from 2013 until 2015. From 2009 to 2011, he served as the global head of consulting and research of DTZ PLC, a professional services firm focused on commercial real estate. Prior to that, between 2006 and 2009, Mr. Krymolowski served as head of Barclays Group Strategy and Planning of Barclays PLC, a leading international bank. From 2004 to 2006, he served as a principal at Booz Allen Hamilton, a global management consulting firm. He holds an M.B.A. with distinction from Carnegie-Mellon University and a B.A. in Economics, cum laude, from Tel Aviv University. Mr. Krymolowski serves on our Audit Committee and our Compensation Committee.

Ran Nussbaum has been a director since July 1, 2013. Mr. Nussbaum is a managing partner and the co-founder of The Pontifax Group, which established three funds with over 30 portfolio companies. Over the past 10 years, Mr. Nussbaum has been co-managing The Pontifax Group. From 2006 to 2008 he also served as Chief Executive Officer of Biomedix Ltd. and Spearhead Ltd., as well as Chairman of the Board of Nasvax Ltd. Mr. Nussbaum’s experience in the life sciences arena coupled with a 10-year experience in the business intelligence field creates a unique blend of skills, enabling him to support companies from inception to commercialization. Mr. Nussbaum also serves on the Board of Directors of many of The Pontifax Group’s portfolio companies including, Kite pharma Inc., c-CAM Ltd., Insuline Ltd. (TASE: INSL), Eloxx Pharmaceuticals Ltd., Theracaot Ltd., CollPlant Ltd. (TASE: CLPT), Protab Ltd., Quiet Therapeutics Ltd., Fusimab Ltd. and as Chairman of the Board of Ocon Medical Ltd.

6.B. Compensation

The table below reflects the compensation granted to our five most highly compensated officers during or with respect to the year ended December 31, 2014. All amounts reported in the table reflect the cost to the Company, in U.S. Dollars, as recognized in our financial statements for the year ended December 31, 2014. Amounts paid in NIS are

translated into U.S. dollars at the rate of NIS 3.58= U.S.$1.00, based on the average representative rate of exchange between the NIS and the U.S. dollar as reported by the Bank of Israel in the year ended December 31, 2014.

Name and Position	Salary / Fees	Share-Based Payment (1)	Bonus	Total
Fredric Price, *Executive Chairman of the Board of Directors* (2)	$ 105,000	$ 542,921		$647,921
Dr. Dalia Megiddo, *Chief Development Officer* (3)	$ 200,432	-	$90,000	$290,432
Udi Gilboa, *Chief Financial Officer, Senior Vice President of Operations* (4)	$ 119,926	-	$150,000	$269,926
Professor Argov Avizohar, *Chief Medical Officer* (5)	$ 44,847 (6)	$ 14,010	$27,949	$97,618
Gili Cohen, *Director* (6)	$ 10,812	-	-	$10,278

(1) Represents the equity-based compensation expenses recorded in the Company's financial statements for the year ended December 31, 2014 based on the options' grant date fair value in accordance with accounting guidance for equity-based compensation.

(2) Mr. Price has been the Executive Chairman of the Board of Directors, since April, 2014, having served as our Chairman of the Board of Directors from April 2012 until April 2014.

(3) Until January 2015, Dr. Megiddo was the Company's Chief Executive Officer. Dr. Megiddo was engaged as a service provider during fiscal year 2014.

(4) Mr. Gilboa was engaged as a service provider during fiscal year 2014.

(5) Prof. Avizohar's engagement with the Company began in June 2014.

(6) Includes payment of mandatory and customary social benefits made by the Company on behalf of such officer.

(7) Mr. Cohen's engagement with the Company began in April 2014.

The aggregate amount of compensation paid or accrued to all of our directors and executive officers as a group with respect to the year ended December 31, 2014 was approximately $0.79 million. The amount does not include business travel, relocation, professional and business association due and expenses reimbursed to office holders, and other benefits commonly reimbursed or paid by companies in our industry.

In addition, stock based compensation in the amount of $0.56 million was accrued in 2014.

Employment Agreement with Mr. Colin Foster

Through our wholly owned subsidiary, BioBlast Pharma, Inc., we have entered into an employment agreement, dated January 29, 2015, with our Chief Executive Officer, Mr. Colin Foster. Pursuant to the terms of his agreement, Mr. Foster is entitled to a gross annual salary of $380,000. Mr. Foster is further entitled to participate in a benefits plan customary for chief executive officers in our industry. He is also entitled to a yearly bonus payment based on achievement of performance goals as shall be annually determined by our Board of Directors, subject to our Compensation Policy. The maximum bonus payable to Mr. Foster for fiscal year 2015 is an amount equal to 40% of his annual gross salary. We granted Mr. Foster an aggregate of 498,067 options to purchase our Ordinary Shares at an exercise price of $8.47, of which none have vested as of March 30, 2015.

Terms of Employment with Dalia Megiddo

Pursuant to the terms of her employment, and starting from January 29, 2015, our Chief Development Officer, Dr. Dalia Megiddo is entitled to a gross annual salary of $250,000. Dr. Megiddo is further entitled to benefits that are provided for by Israeli law or that are customary for senior executives in Israel, including the right to use (and all related fixed and variable costs in respect of) a leased car and cellular telephone. Dr. Megiddo is entitled to company contributions of her gross monthly salary towards certain pension, severance, disability and study funds. Dr. Megiddo is also entitled to a yearly bonus payment based on achievement of performance goals as shall be annually determined by our Board of Directors, subject to our Compensation Policy. The maximum bonus payable to Dr. Megiddo for fiscal year 2015 is an amount equal to 30% of her annual gross salary. In August 2014, Dr. Megiddo received, through her consulting company, a special bonus of $90,000 in recognition of efforts and contribution to consummate our initial public offering.

Services Agreement with Udi Gilboa through Top Notch Consultancy (2009) Ltd.

We have entered into an amended and restated service agreement, dated April 22, 2014, with our Chief Financial Officer, Mr. Udi Gilboa, through his wholly-owned company Top Notch Consultancy (2009) Ltd. for part time CFO services, effective as of August 1, 2013 and terminable by either party upon 60 days' prior written notice, and contains provisions standard for a company in our industry regarding non-competition, confidentiality of information and assignment of inventions. The monthly amount payable under the agreement is NIS 57,861 (approximately $12,857) plus Value Added Tax (currently at 18%). In August 2014, Top Notch Consultancy (2009) Ltd. received a special bonus of $80,000 in recognition of efforts and contribution to consummate our initial public offering. In addition, Top Notch Consultancy is entitled to an additional bonus of $70,000 with regards to services provided during 2014; such bonus was paid in 2015. In addition, effective as of September 10, 2013, we entered into an agreement with Top Notch Consultancy (2009) Ltd. to provide us with office space and services for a monthly fee of NIS 14,832 (approximately $4,250), plus Value Added Tax (currently at 18%). Either party may terminate the agreement on 30-days' notice. The office space and services were terminated in September 2014.

Engagement Letter with Fredric Price

Fredric Price, our Executive Chairman of the Board of Directors, has been appointed by us to our Board of Directors pursuant to an engagement letter agreement, effective April 24, 2012, as amended on April 22, 2014 and October 30, 2014. The annual amount payable under the agreement is $180,000 and may be terminable by either party upon 30 days prior written notice. In April 2013, we granted Mr. Price options to purchase an aggregate of 319,531 Ordinary Shares, at an exercise price of $0.0004 per share, all of which have vested as of March 30, 2015. In October 2014, we granted Mr. Price options to purchase an additional 206,702 Ordinary Shares at an exercise price of $11.00 per share, which options vest over a period of four quarters.

Engagement Letter with Marlene Haffner

Marlene Haffner, one of our directors, has been appointed to our Board of Directors pursuant to an engagement letter agreement, effective May 13, 2013, which is terminable by either party upon 30 days' prior written notice. We granted Mrs. Haffner an aggregate of 83,579 options to purchase our Ordinary Shares, of which 55,719 have vested as of March 30, 2015.

We do not have written agreements with any director providing for benefits upon the termination of his or her service to us.

In December 2012, an amendment to the Israeli Companies Law, or Amendment 20, became effective, requiring companies to appoint a Compensation Committee. Our existing Compensation Committee as detailed in Item 6.C. – "Board Practices – Board Committees – Compensation Committee" below meets this requirement.

Amendment 20 also requires us to adopt an office holder compensation policy no later than nine months from our initial public offering that will set forth company policy, or the Compensation Policy, regarding the terms of office and employment of office holders, including compensation, equity awards, severance and other benefits, exemption from liability and indemnification, referred to as the Terms of Office and Employment. The term "office holder," as defined in the Israeli Companies Law, includes directors, executive officers and any manager directly subordinate to the Chief Executive Officer.

The Compensation Policy must be approved by the Board of Directors, after considering the recommendations of the Compensation Committee. The Compensation Policy must also be approved by a majority of the company's shareholders, provided that (i) such majority includes at least a majority of the shareholders who are not controlling shareholders and who do not have a personal interest in the matter, present and voting (abstentions are disregarded), or (ii) the non-controlling shareholders and shareholders who do not have a personal interest in the matter who were present and voted against the policy hold two percent or less of the voting power of the company. The Compensation Policy must be approved by the Board of Directors and the shareholders every three years. If the Compensation Policy is not approved by the shareholders, the Compensation Committee and the Board of Directors may nonetheless approve the policy, following further discussion of the matter and for specified reasons.

Under Amendment 20, the "Terms of Office and Employment" of office holders require the approval of the Compensation Committee and the Board of Directors. The Terms of Office and Employment of directors and the Chief Executive Officer must also be approved by shareholders.

Changes to existing Terms of Office and Employment of office holders (other than directors) can be made with the approval of the Compensation Committee only, if the committee determines that the change is not substantially different from the existing terms.

Under certain circumstances, the Compensation Committee and the Board of Directors may approve an arrangement that deviates from the Compensation Policy, provided that such arrangement is approved by the special majority of the company's shareholders mentioned above. Such shareholder approval will also be required with respect to determining the Terms of Office and Employment of a director or the Chief Executive Officer during the transition period until the company adopts a Compensation Policy. Notwithstanding the foregoing, a company may be exempted from receiving shareholder approval with respect to the Terms of Office and Employment of a candidate for Chief Executive Officer if such candidate meets certain independence criteria, the terms are in line with the Compensation Policy and the Compensation Committee has determined for specified reasons that shareholder approval would prevent the engagement.

Under the Israeli Companies Law and related regulations, the compensation payable to statutory independent directors and independent directors is subject to certain further limitations. See Item 6.C. – "Board Practices – External Directors" below.

6.C. Board practices

Board Practices

Board of Directors

Under the Israeli Companies Law, setting up our policy and oversight over our business 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 appointed by our Chief Executive Officer, 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 eleven directors, including at least two external directors required to be appointed under the Israeli Companies Law. Accordingly, at any time, the minimum number of directors (other than the external directors) may not fall below

three. Currently, our Board of Directors consists of eight directors, including two external directors. We have only one class of directors.

Other than external directors, for whom special election requirements apply under the Israeli Companies Law as detailed below, our directors are each elected at a general meeting of our shareholders and serve for a term of one year. Directors (other than external directors) shall nevertheless be removed prior to the end of their term by the majority of our shareholders at a general meeting of our shareholders or upon the occurrence of certain events, all in accordance with the Israeli Companies Law and our articles of association.

In addition, our articles of association allow our Board of Directors to appoint directors, other than external 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 directors whose offices 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” below.

In accordance with the exemption available to foreign private issuers under the Listing Rules of NASDAQ, we do not follow the NASDAQ requirements 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, or a certain number of directors serving thereon) is authorized to recommend to our shareholders director nominees for election. Under the Israeli Companies Law and our articles of association, nominations for directors may also be added to the agenda of future general meetings, which has yet to have been summoned, upon the request of any one or more shareholders holding at least one percent (1%) of our outstanding voting power. Furthermore, under the Israeli Companies Law either: (a)(i) two directors; or (ii) no less than one quarter of the directors in office; or (b) one or more shareholders holding, in the aggregate, either (i) 5% of our outstanding shares and 1% of our outstanding voting power; or (ii) 5% of our outstanding voting power, may request the Board of Directors to call a general meeting in order to nominate one or more persons for election as directors at a special meeting. However, any such shareholders may make such a nomination only if a written notice of such shareholder's intent to make such nomination has been given to our Chairman of the Board of Directors (or, if we have no Chairman, our Chief Executive Officer). Any such notice must include certain information we are required under the Israeli Companies Law to provide to our shareholders, 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.

In addition to its role in making director nominations, 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. Under applicable regulations, a director with accounting and financial expertise is a director who, by reason of his or her education, professional experience and skill, has a high level of proficiency in and understanding of business accounting matters and financial statements, sufficient to be able to thoroughly comprehend our financial statements and initiate debate regarding the manner in which financial information is presented. 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 our company and the scope and complexity of its operations. Our Board of Directors has determined that our company requires one director with such expertise and that Gili Cohen has such expertise.

External Directors

Under the Israeli Companies Law, the boards of directors of companies whose shares are publicly traded, including companies with shares listed on the NASDAQ Global Market, are required to include at least two members elected to serve as external directors. Accordingly, Gili Cohen and Isaac Krymolowski have been elected to serve as external directors.

The definitions of an external director under the Israeli Companies Law and independent director under the Listing Rules of NASDAQ are similar such that it would generally be expected that our two external directors will also comply with the independence requirement under the Listing Rules of NASDAQ. The definition of an external director includes a set of statutory criteria (which are described below) that must be satisfied and for which the

candidates must attest to the company, while the definition of an independent director requires a company's Board of Directors to consider any factor which would impair the ability of a director to exercise independent judgment. In addition, while external directors serve for a period of three years pursuant to the requirements of Israeli law, independent directors serve for one year pursuant to the provisions of our articles of association. External directors must be elected by a special majority of shareholders who are not controlling shareholders, while independent directors are elected by an ordinary majority.

The Israeli Companies Law provides that external directors must be elected by a majority vote of the shares present and voting at a shareholders meeting, provided that either:

- the majority voted in favor of election includes a majority of the shares held by non-controlling shareholders who 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 for such purpose any abstentions, which we refer to as a disinterested majority; or

- the total number of shares held by non-controlling disinterested shareholders (as described in the previous bullet-point) that voted against the election of the director does not exceed two percent (2%) of the aggregate voting rights in the company.

The term controlling shareholder is defined in the Israeli Companies Law as a shareholder with the ability to direct the activities of the company, other than by virtue of being an office holder. A shareholder is in any case deemed to be a controlling shareholder if the shareholder holds 50% or more of the means of control, which include the right to vote at a shareholders meeting and the right to appoint the directors of the company or its general manager. In connection with approval of certain extraordinary and interested party transactions as well as corporate approval of executive employment and compensation and private placements, by shareholders, any shareholder (or group of shareholders having interest in the same matter being brought for approval) who hold(s) in the aggregate 25% or more of the means of control if no other shareholder holds more than 50% of the voting rights, would be deemed a controlling shareholder.

After an initial term of three years, external directors may be reelected to serve in that capacity for up to two additional three year terms, provided that either (i) (1) his or her service for each such additional term is recommended by one or more shareholders holding in aggregate at least one percent (1%) of the company's voting rights and is approved at a shareholders meeting by a majority of the shares held by non-controlling shareholders who 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 for such purpose any abstentions, where the total number of shares held by non-controlling, disinterested shareholders voting for such reelection exceeds two percent (2%) of the aggregate voting rights in the company, and (2) the external director who has been nominated in such fashion by the shareholders is not a linked or competing shareholder, and does not have or has not had, on or within the two years preceding the date of such person's appointment to serve as another term as external director, any affiliation with a linked or competing shareholder. The term "linked or competing shareholder" means the shareholder(s) who nominated the external director for reappointment or a material shareholder of the company holding more than 5% of the shares in the company, provided that at the time of the reappointment, such shareholder(s) of the company, the controlling shareholder of such shareholder(s) of the company, or a company under such shareholder(s) of the company's control, has a business relationship with the company or are competitors of the company; the Israeli Minister of Justice, in consultation with the Israeli Securities Authority, may determine that certain matters will not constitute a business relationship or competition with the company; or (ii) his or her service for each such additional term is recommended by the Board of Directors and is approved at a shareholders meeting by the same disinterested 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 further extended, indefinitely, in increments of additional three-year terms, in each case provided that, in addition to reelection in such manner described above, (i) the Audit Committee and subsequently 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 is beneficial to the company, and (ii) prior to the approval of the reelection of the external director, the company's shareholders have been informed of the term previously served by such nominee and of the reasons why the Board of Directors and Audit Committee recommended the extension of such nominee's term. If an external director no longer complies with the applicable requirements, the external director must notify the company, and his term shall terminate upon such notification. Furthermore, where concerns regarding an external director's compliance with any requirements under Israeli Companies Law, or regarding an external director's breach of any fiduciary duty, have been brought to the Board of Directors' attention, the Board of Directors is required to discuss such concerns in its following meeting.

If the Board of Directors resolves that an external director no longer complies with any requirement for qualification as an external director, or that such external director has breached any fiduciary duty, a special general meeting shall be convened at which the termination of such external director's service shall be included in the agenda.

If an external directorship becomes vacant and there are less 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 possible to appoint a replacement external director.

Each committee of the Board of Directors that is authorized to exercise the powers of the Board of Directors must include at least one external director, except that the Audit Committee and Compensation Committee must each include all external directors then serving on the board of directors. Under the Israeli Companies Law, external directors of a company are prohibited from receiving, directly or indirectly, any compensation for their services as external directors, other than compensation and reimbursement of expenses pursuant to applicable regulations promulgated under the Israeli Companies Law. 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 serve as an external director if (i) the person is a relative of the 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 subject, 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 prohibited relationship with the company, with any person or entity who is a controlling shareholder of the company at the date of appointment or a relative of such person, or with any entity controlled, during the two years preceding the date of appointment as an external director, by the company or a controlling shareholder of the company; or (b) in the case of a company with no controlling shareholder, any affiliation or other prohibited relationship with a person serving, at the date of appointment as external director, as Chairman of the Board of Directors, Chief Executive Officer, a substantial shareholder or the most senior office holder in the company's finance department.

The term relative is defined as a spouse, sibling, parent, grandparent or descendant; spouse's sibling, parent or descendant; and the spouse of each of the foregoing persons. The term affiliation and the similar types of prohibited relationships include (subject to certain exemptions):

- 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 first offering of its shares to the public if such director was appointed as a director of the private company in order to be nominated to serve as an external director following the initial public offering.

The term office holder is defined under the Israeli Companies Law as the general manager (Chief Executive Officer), chief business manager, deputy general manager, vice general manager, any other person assuming the responsibilities of any of these positions regardless of that person's title, a director, or a 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 or 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 for his or her role as a director, other than compensation paid or given in accordance with Israeli Companies Law regulations or amounts paid pursuant to indemnification and/or exculpation contracts or commitments and insurance coverage. 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 with direct or indirect benefit by the company, its controlling shareholder or any entity under its controlling shareholder's control. This includes appointment as an office holder of the company or a company controlled by its controlling shareholder, employment as an employee, or receipt of professional services for consideration, either directly or indirectly, including through a corporation in his or her control. These restrictions extend 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 thereof, are of the same gender, the external director 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, 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). In addition, 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 Listing Rules of NASDAQ for membership on the Audit Committee, and (iii) has accounting and financial expertise as defined under Israeli law, then neither of our external directors is required to possess accounting and financial expertise as long as both possess other 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, in such a manner which allows him or her 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 service, (ii) an academic degree or has completed other higher education, in the main field of business of the company or a field relevant for the position, or (iii) at least five years of experience as one of the following, or at least five years accumulated experience as two or more of the following — (a) a senior officer in the business management of a company with a significant volume of business, (b) a senior public officer or senior position in the public service, and (c) a senior position in the company's main line of business.

Our Board of Directors has determined that both Gili Cohen and Isaac Krymolowski have accounting and financial expertise 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 Fredric Price to serve as Executive Chairman of the Board of Directors.

Role of Board in Risk Oversight Process

Risk assessment and oversight are an integral part of our governance and management processes. Our Board of Directors encourages management to promote a culture that incorporates risk management into our corporate strategy and day-to-day business operations. Management discusses strategic and operational risks at regular management meetings, and conducts specific strategic planning and review sessions during the year that include a focused discussion and analysis of the risks facing us. Throughout the year, senior management reviews these risks with the Board of Directors at regular board meetings as part of management presentations that focus on particular business

functions, operations or strategies, and presents the steps taken by management to mitigate or eliminate such risks.

Board Committees

Audit Committee

Under the Israeli Companies Law, the Board of Directors of a public company must appoint an Audit Committee. The Audit Committee must be 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 of Directors, any director employed by or otherwise providing services on a regular basis to the company, to a controlling shareholder or to any entity controlled by a controlling shareholder, any director whose main livelihood is dependent on a controlling shareholder, nor a controlling shareholder or a relative thereof.

Under the Israeli Companies Law, the Audit Committee of a publicly traded company must consist of a majority of unaffiliated directors. An “unaffiliated director” is defined as either an external director or as a director, classified as an “unaffiliated director” by the company, who meets the following criteria:

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

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 (i) 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 and amend such deficiencies — where material deficiencies have been revealed, at least one meeting of the Audit Committee is required to be convened, with the presence of our internal auditor or the independent auditor, and without the presence of any members of the Board of Directors who are not members of the Audit Committee (unless their presence is required for the purpose of presenting their position to matters under their responsibility); (ii) determining whether certain related party transactions (including transactions in which an office holder has a personal interest) should be deemed as material or extraordinary, and to approve such transactions (which may be approved according to certain criteria set out by our Audit Committee on an annual basis) (see Item 16G. – “Approval of Related Party Transactions under Israeli Law”), (iii) to establish procedures to be followed in respect of related party transactions with a controlling shareholder (where such are not extraordinary transactions), which may include, where applicable, the establishment of a competitive process for such transaction, under the supervision of the Audit Committee, or individual, or other committee or body selected by the Audit Committee, in accordance with criteria determined by the Audit Committee; (iv) to determine procedures for approving certain related party transactions with a controlling shareholder, which having been determined by the Audit Committee not to be extraordinary transactions, were also determined by the Audit Committee not to be negligible transactions; (v) where the Board of Directors approves the working plan of the internal auditor, to examine such working plan before its submission to the Board of Directors and propose amendments thereto, (vi) examining our internal controls and internal auditor’s performance, including whether the internal auditor has sufficient resources and tools to dispose of its responsibilities, (vii) 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 (viii) establishing procedures for the handling of employees’ complaints as to the management of our business and the protection to be provided to such employees. In compliance with regulations promulgated under the Israeli Companies Law, our Audit Committee will also approve our financial statements, thereby fulfilling the requirement that a board committee provides such approval. Our Audit Committee may not approve an action or a related party transaction, or take any other action required under the Israeli Companies Law, unless at the time of approval a majority of the committee’s members are present, which majority consists of unaffiliated directors including at least one external

director, and it further complies with the committee composition set forth above.

Audit Committee – Charter

Our Board of Directors has adopted an Audit Committee charter setting forth the responsibilities of the Audit Committee consistent with the rules of the SEC and the Listing Rules of NASDAQ, as well as subjecting the Audit Committee charter to the requirements under the Israeli Companies Law, as described below.

NASDAQ requirements

Under the Listing Rules of NASDAQ, we are required to maintain an Audit Committee consisting of at least three independent directors, all of whom are financially literate and one of whom has accounting or related financial management expertise.

Our Audit Committee consists of Mr. Isaac Krymolowski, who serves as the chairperson, Mr. Gili Cohen and Mr. Michael Burshtine. Our Board of Directors has determined that Gili Cohen is an Audit Committee financial expert as defined by the SEC rules and has the requisite financial experience as defined by the Listing Rules of NASDAQ. All of the members of our Audit Committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and the Listing Rules of NASDAQ.

Each member of the Audit Committee is required to be "independent" as such term is defined in Rule 10A-3(b)(1) under the Exchange Act, which is different from the general test for independence of board and committee members.

Compensation Committee

We chose to rely upon the exemption available to foreign private issuers under the Listing Rules of NASDAQ with respect to the determination of the compensation of our Chief Executive Officer and other executive officers in lieu of forming a Compensation Committee consisting entirely of independent directors (or the determination of such compensation solely by the independent members of our Board of Directors), and rather form a Compensation Committee in compliance with the Israeli Companies Law. See Item 16G. – "Corporate Governance." However, all of the current members of our compensation committee are independent.

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, which shall be a majority of the members of the compensation committee and one of whom must serve as Chairman of the committee. However, subject to certain exceptions, Israeli companies whose securities are traded on stock exchanges such as NASDAQ, and who do not have a controlling party, do not have to meet this majority requirement; provided, however, that the Compensation Committee meets other Israeli Companies Law composition requirements, as well as the requirements of the non-Israeli jurisdiction where the company's securities are traded. Other than the external directors, the rest of the members of the Compensation Committee shall be directors who will receive compensation for their role as directors only in accordance with Israeli Companies Law regulations or amounts paid pursuant to indemnification and/or exculpation contracts or commitments and insurance coverage.

The Compensation Committee may not include the Chairman of the Board of Directors, any director employed by or otherwise providing services on a regular basis to the company, to a controlling shareholder or to any entity controlled by a controlling shareholder, any director whose main livelihood is dependent on a controlling shareholder, nor a

controlling shareholder or a relative thereof.

Our Compensation Committee consists of Mr. Gili Cohen, who serves as the chairperson of the committee, Mr. Michael Burshtine and Mr. Isaac Krymolowski.

Under the Israeli Companies Law, our Compensation Committee is responsible for (i) proposing a Compensation Policy to the Board of Directors, (ii) propose necessary revisions to the Compensation Policy and examine its implementation, (iii) determining whether to approve transactions with respect to the terms of office and employment of office holders, and (iv) determining, in accordance with our Compensation Policy, whether to exempt an engagement with an unaffiliated nominee for the position of Chief Executive Officer from requiring shareholders' approval.

Under the Israeli Companies Law, our Compensation Policy must generally serve as the basis for corporate approvals with respect to the financial terms of employment or engagement of office holders, including exemption, insurance, indemnification or any monetary payment or obligation of payment in respect of employment or engagement. The Compensation Policy must relate to certain factors, including advancement of the company's objective, 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 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 and median 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 contributions 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 the long term performance and 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.

Under the amendment to the Israeli Companies Law, we are required to adopt a Compensation Policy no later than nine months following our initial public offering.

Compensation Committee — Charter

Our Board of Directors has adopted a Compensation Committee Charter setting forth the responsibilities of the Compensation Committee, pursuant to the Israeli Companies Law, as described above.

Nominating Committee

Our Board of Directors does not currently have a nominating committee, as director nominees are presented by our Board of Directors to our shareholders based upon the nominations made by the Board of Directors itself. We currently rely upon the exemption available to foreign private issuers under the Listing Rules of NASDAQ from the NASDAQ requirements related to independent director oversight of nominations to our Board of Directors and the adoption of a formal written charter or board resolution addressing the nominations process. See Item 16G. – "Corporate Governance."

Other than with Gili Cohen, Isaac Krymolowski and Michael Burshtine, we have service contracts or employment agreements with our directors, Colin Foster, Ehud Gilboa, Dr. Dalia Megiddo, Fredric Price, Marlene Haffner and with Pontifax (Cayman) III Limited Partnership and Pontifax (Israel) III Limited Partnership, who are affiliated with our director, Ran Nussbaum. All of the foregoing service contracts have been approved by our shareholders. Please see Item 6.B. – "Compensation" for additional information.

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 and nominated by the Board of Directors. An internal auditor may not be:

- a person (or a relative of a person) who holds more than 5% 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;
- 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 his or her behalf.

Guy Sapir from PriceWaterhouseCoopers (PWC) Israel was appointed as our internal auditor. The role of the internal auditor is to examine, among other things, our compliance with applicable law and orderly business procedures.

6.D. Employees

As of March 30, 2015, our staff included 12 persons, comprised of 11 full time employees and one officer, who engaged with us as a service provider. Our management consists of our Chief Executive Officer, our Chief Financial Officer, our Chief Development Officer, our Chief Medical Officer and our VP Finance. We believe that we maintain good relations with all of them.

6.E. Share ownership

As of March 20, 2015, each of our executive officers and directors, other than Mr. Price, Mr. Foster, Mr. Gilboa, Dr. Megiddo and Mr. Nussbaum, beneficially owned less than 1% of our Ordinary Shares.

For information regarding the share ownership of Mr. Gilboa, Dr. Megiddo and Mr. Nussbaum, see Item 7.A. "Major Shareholders."

As of March 20, 2015, Mr. Price owns 131,752 Ordinary Shares, or approximately 1% of our outstanding Ordinary Shares. In addition, Mr. Price and Mr. Foster each own options to purchase our Ordinary Shares as set forth in the table below.

	NUMBER OUTSTANDING	EXERCISE PRICE PER SHARE	EXPIRATION DATE
Fredric Price	319,531	$ 0.0004	April 2023
	206,702	$ 11.00	October 2024
Colin Foster	498,067	$ 8.47	March 2025

2013 Incentive Option Plan

We maintain one equity incentive plan — our 2013 Incentive Option Plan, or our 2013 Plan. As of March 30, 2015, 30,269 Ordinary Shares remained available for issuance under our 2013 Plan. In addition, options to purchase 1,325,399 Ordinary Shares were issued and outstanding. Of such outstanding options, options to purchase 501,795 Ordinary Shares were vested as of that date, with a weighted average exercise price of $6.072 per share.

Our 2013 Plan, which was adopted by our Board of Directors on November 13, 2013, provides for the grant of options to our and our affiliates' respective directors, employees, office holders, service providers and consultants.

The 2013 Plan is administered by our Board of Directors, which shall determine, subject to Israeli law, the grantees of awards and various terms of the grant. The 2013 Plan provides for granting options in compliance with Section 102 of the Israeli Income Tax Ordinance, 1961, or the Ordinance.

Options granted under the 2013 Plan to Israeli employees have been granted under the capital gains track of Section 102 of the Ordinance. Section 102 of the Ordinance allows employees, directors and officers, who are not controlling shareholders and are considered Israeli residents, to receive favorable tax treatment for compensation in the form of shares or options. Our Israeli non-employee service providers and controlling shareholders may only be granted options under Section 3(9) of the Ordinance, which does not provide for similar tax benefits. 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, the most favorable tax treatment for grantees, permits the issuance to a trustee under the "capital gains track." However, under this track we are not allowed to deduct an expense with respect to the issuance of the options or shares. In order to comply with the terms of the capital gains track, all options granted under the 2013 Plan pursuant and subject to the provisions of Section 102 of the Ordinance, as well as the Ordinary Shares issued upon exercise of these options and other shares received subsequently following any realization of rights with respect to such options, such as share dividends and share splits, must be granted to a trustee for the benefit of the relevant employee, director or officer and should be held by the trustee for at least two years after the date of the grant.

Options granted under the 2013 Plan will generally vest over four years commencing on the date of grant such that 25% vest after one year and an additional 6.25% vest at the end of each subsequent three-month period thereafter for 36 months. Options that are not exercised within ten years from the grant date expire, unless otherwise determined by the Board of Directors or its designated committee, as applicable. In case of termination for reasons of disability or death, the grantee or his legal successor may exercise options that have vested prior to termination within a period of six months 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 30 days 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 subsequent to which we shall no longer exist as a legal entity, or a sale of all, or substantially all, of our shares or assets or other transaction having a similar effect on us, then any outstanding option shall be assumed, or an equivalent option shall be substituted, by such successor corporation or an affiliate thereof or, in case the successor corporation refuses to assume or substitute the option, our Board of Directors or its designated committee may (a) provide the grantee with the opportunity to exercise the option as to all or part of the shares, vested or otherwise, and (b) specify a period of time, no less than 7 days, following which all outstanding options shall terminate.

Item 7. Major Shareholders and Related Party Transactions

7.A. Major shareholders

The following table sets forth information regarding the beneficial ownership by each person or entity known to beneficially own more than 5% of our Ordinary Shares as of March 20, 2015, or a different date, if so provided in the table below or footnotes thereof.

According to our transfer agent, as March 20, 2015, there were 21 record holders of our Ordinary Shares, among whom are 13 U.S. holders who beneficially owns less than 5% of our Ordinary Shares. None of our shareholders has different voting rights from other shareholders.

We are not owned or controlled, directly or indirectly, by another corporation or by any foreign government. We are not aware of any arrangement that may, at a subsequent date, result in a change of control of our company.

Except as indicated in footnotes to this table, we believe that the shareholders named in this table have sole voting and investment power with respect to all Ordinary Shares shown to be beneficially owned by them, based on information provided to us by such shareholders. Unless otherwise noted below, each beneficial owner's address is: c/o BioBlast Pharma Ltd., 37 Dereh Menachem Begin St., Tel Aviv 6522042, Israel.

Name	Ordinary Shares Beneficially Owned Number	Percentage	
Udi Gilboa (1)	3,320,512	23.3	%
Dr. Dalia Megiddo	3,311,421	23.3	%
Ran Nussbaum (2)	2,529,008	17.8	%
Visium Asset Management, LP (3)	844,160	5.9	%

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(1) Based solely on a Schedule 13G filed with the SEC on February 17, 2015, and which reflects holdings as of December 31, 2014.

(2) Comprised of Pontifax (Cayman) III Limited Partnership that holds 804,909 Ordinary Shares and Pontifax (Israel) III Limited Partnership that holds 1,724,099 Ordinary Shares. These two entities are under common control of, and are affiliated with, our director, Ran Nussbaum. The address of Ran Nussbaum is 14 Shenkar St. Herzliya, 46140, Israel.

(3) Comprised of Visium Asset Management, LP, JG Asset, LLC, Jacob Gottlieb and Visium Balanced Master Fund, Ltd, of 888 Seventh Avenue, New York, NY 10019. Based solely on a Schedule 13G filed with the SEC on February 13, 2015, and which reflects holdings as of December 31, 2014.

7.B. Related party transactions

For a description of the compensation to our directors and officers and agreements related thereto, see Item 6.B –"Compensation".

Indemnification Agreements

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. We have entered into indemnification agreements with each of our directors and other office holders, undertaking to indemnify them to the fullest extent permitted by Israeli law. We have also obtained directors and officers insurance for each of our officers and directors.

7.C. Interests of experts and counsel

Not applicable.

Item 8. Financial Information

8.A. Financial statements and other financial information

See Item 18 – Financial Statements.

Legal Proceedings

From time to time, we are involved in various routine legal proceedings incidental to the ordinary course of our business. We do not currently believe that the outcome of these legal proceedings have had in the recent past, or will have (with respect to any pending proceedings), significant effects on our financial position or profitability.

Dividends

We have never declared or paid any cash dividends on our Ordinary Shares and do not anticipate paying any cash dividends in the foreseeable future. Payment of cash dividends, if any, in the future will be at the discretion of our Board of Directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our Board of Directors may deem relevant.

The Israeli Companies Law imposes further restrictions on our ability to declare and pay dividends. See Item 10.B. – "Articles of Association – Rights, Preferences and Restrictions – Dividend and Liquidation Rights" for additional information.

Payment of dividends may be subject to Israeli withholding taxes. See Item 10.E. – "Taxation" below for additional information.

8.B. Significant changes

Except as disclosed elsewhere in this annual report, there have been no other significant changes since December 31, 2014, until the date of the filing of this annual report.

Item 9. The Offer and Listing

9.A. Offer and listing details

Our Ordinary Shares have been listed on the NASDAQ Global Market under the symbol "ORPN" since July 31, 2014. Prior to that date, there was no public trading market for our Ordinary Shares. Our initial public offering was priced at $11.00 per share on July 30, 2014. The following table sets forth for the periods indicated the high and low sales prices per ordinary share as reported on the NASDAQ Global Market:

	Low	High
Annual Information:		
2014	4.53	9.79

Quarterly Information:		
Third Quarter 2014	6.90	9.79
Fourth Quarter 2014	4.53	7.78
First Quarter 2015 (through March 27, 2015)	5.81	8.85
Monthly Information:		
September 2014	7.27	9.12
October 2014	5.25	7.40
November 2014	4.53	7.78
December 2014	5.71	7.78
January 2015	6.61	8.47
February 2015	6.46	8.37
March 2015 (through March 27, 2015)	5.90	7.70

9.B. Plan of distribution

Not applicable.

9.C. Market for Ordinary Shares

Our Ordinary Shares have been quoted on the Nasdaq Global Market since July 31, 2014 under the symbol ORPN.

9.D. Selling shareholders

Not applicable.

9.E. Dilution

Not applicable.

9.F. Expenses of the issue

Not applicable.

Item 10. Additional information

10.A. Share capital

Not applicable.

10.B. Articles of Association

Securities Register

We are registered with the Israeli Registrar of Companies. Our registration number is 51-471648-9. Section 1.2 of our articles of association provides that we may engage in any type of lawful business.

Board of Directors

The Israeli Companies Law requires that certain transactions, actions and arrangements be approved as provided for in a company's articles of association and in certain circumstances by the Audit Committee, the Compensation Committee, by the Board of Directors itself and by the shareholders. The vote required by the Audit Committee, Compensation Committee and the Board of Directors for approval of such matters, in each case, is a majority of the disinterested directors participating in a duly convened meeting. If, however, a majority of the members participating in such meeting have a personal interest in the approval of such matter, then all directors may participate in the discussions and the voting on approval thereof and in such case the matter shall be subject to further shareholder approval.

The Israeli Companies Law requires that an office holder promptly disclose to the Board of Directors any personal interest that he or she may have concerning any existing or proposed transaction with a company, as well as any substantial information or document with respect thereof. 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 one'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 interest of the office holder with respect to his or her vote on behalf of the shareholder for whom he or she holds a proxy even if such shareholder itself has no personal interest in the approval of the matter. An office holder is not, however, obliged to disclose a personal interest if it derives solely from the personal interest of a relative of such office holder 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:

- transaction other than in the ordinary course of business;

- transaction that is not on market terms; or

- 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, 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 duty of loyalty. However, a company may not approve a transaction or action that is adverse to the company's interest or that is not performed by the office holder in good faith. Approval first by the company's Audit Committee and subsequently by the Board of Directors is required for an extraordinary transaction in which an office holder has a personal interest. Arrangements regarding the compensation, indemnification or insurance of an office holder require the approval of the Compensation Committee, Board of Directors and, in certain circumstances, the shareholders, in that order.

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 controlling shareholder or an officer who is a controlling shareholder of the company, a controlling shareholder also includes any shareholder who holds 25% or more of the voting rights if no other shareholder holds more than 50% of the voting rights. Two or more shareholders with a personal interest in the approval of the same transaction are deemed to be a single shareholder and may be deemed a controlling shareholder for the purpose of approving such transaction. Extraordinary transactions, including private placement transactions, with a controlling shareholder or in which a controlling shareholder has a personal interest, and engagements with a controlling shareholder or his or her relative, directly or indirectly, including through a corporation in his or her control, require the approval of the Audit Committee, the Board of Directors and the shareholders of the company, in that order. In addition, the shareholder approval must fulfill one of the following requirements:

- a disinterested majority; or

- the votes of shareholders who have no personal interest in the transaction and who are present and voting, in person, by proxy or by voting deed at the meeting, and who vote against the transaction may not represent more than two percent (2%) of the voting rights of 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 the Audit Committee determines that the duration of the transaction is reasonable given the circumstances related thereto.

Arrangements regarding the terms of engagement and compensation of a controlling shareholder who is an office holder, and the terms of employment of a controlling shareholder who is an employee of the company, require the approval of the Compensation Committee, Board of Directors and, generally, the shareholders, in that order.

Our articles of association provide that, all actions done bona fide at any meeting of the Board of Directors or by a committee thereof or by any person(s) acting as director(s) will, notwithstanding that it may afterwards be discovered that there was some defect in the appointment of the participants in such meeting or any of them or any person(s) acting as aforesaid, or that they or any of them were disqualified, be as valid as if there were no such defector disqualification.

- Pursuant to Israeli law, a director who has a personal interest in an extraordinary transaction which is brought for discussion before our Board of Directors or our Audit Committee shall neither vote in nor attend discussions concerning the approval of such transaction. If the director did vote or attend as aforesaid, the approval given to the aforesaid activity or arrangement will be invalid.

- Our articles of association provide that, subject to the Israeli Companies Law, our Board of Directors may delegate its authority, in whole or in part, to such committees of the Board of Directors as it deems appropriate, and it may from time to time revoke such delegation. To the extent permitted by the Israeli Companies Law, our Board of Directors may from time to time confer upon and delegate to a President, Chief Executive Officer, Chief Operating Officer or other executive officer then holding office, such authorities and duties of the Board of Directors as it deems fit, and they may delegate such authorities and duties for such period and for such purposes and subject to such conditions and restrictions which they consider in our best interests, without waiving the authorities of the Board of Directors with respect thereto.

- Arrangements regarding compensation of directors require the approval of the Compensation Committee, our Board of Directors and the shareholders.

Rights, Preferences and Restrictions of Shares

- General. Our share capital is NIS 500,000, divided into 50,000,000 Ordinary Shares NIS 0.01 par value per share.

- The Ordinary Shares do not have cumulative voting rights in the election of directors. As a result, the holders of Ordinary Shares that represent more than 50% of the voting power have the power to elect all the Directors.

Dividend and liquidation rights. Our Board of Directors may declare a dividend to be paid to the holders of our Ordinary Shares according to their rights and interests in our profits and may fix the record date for eligibility and the time for payment. The directors may from time to time pay to the shareholders on account of the next forthcoming dividend such interim dividends as, in their judgment, our position justifies. All dividends unclaimed for one year after having been declared may be invested or otherwise used by the directors for our benefit until claimed. No unpaid dividend or interest shall bear interest as against us. Our Board of Directors may determine that a dividend may be paid, wholly or partially, by the distribution of certain of our assets or by a distribution of paid up shares, debentures or debenture stock or any of our securities or of any other companies or in any one or more of such ways in the manner and to the extent permitted by the Israeli Companies Law.

Transfer of shares; record dates. Fully paid up Ordinary Shares may be freely transferred pursuant to our articles of association unless such transfer is restricted or prohibited by another instrument or securities laws. Each shareholder who would be entitled to attend and vote at a General Meeting of shareholders is entitled to receive notice of any such meeting. For purposes of determining the shareholders entitled to notice and to vote at such meeting, the Board of Directors will fix a record date.

Voting; annual general and extraordinary meetings. Subject to any rights or restrictions for the time being attached to any class or classes of shares, each shareholder shall have one vote for each share of which he or she is the holder, whether on a show of hands or on a poll. Our articles of association do not permit cumulative voting and it is not mandated by Israeli law. Votes may be given either personally or by proxy. A proxy need not be a shareholder. If any shareholder is without legal capacity, he may vote by means of a trustee or a legal custodian, who may vote either personally or by proxy. If two or more persons are jointly entitled to a share then, in voting upon any question, the vote of the senior person who tenders a vote, whether in person or by proxy, shall be accepted to the exclusion of the votes of the other registered holders of the share and, for this purpose seniority shall be determined by the order in which the names stand in the shareholder register.

Quorum for general meetings.The quorum required for our general meetings of shareholders consists of at least two shareholders present in person, by proxy or written ballot who holds or represent between them at least one-third 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/date if so specified in the summons or notice of the meeting. At the reconvened meeting, any two or more shareholders present in person or by proxy shall constitute a lawful quorum.

- Notice of general meetings. Unless a longer period for notice is prescribed by the Israeli Companies Law, at least 10 days and not more than 60 days' notice of any general meeting shall be given, specifying the place, the day and the hour of the meeting and, in the case of special business, the nature of such business, shall be given in the manner hereinafter mentioned, to such shareholders as are under the provisions of our articles of association, entitled to receive notices from us. Only shareholders of record as reflected on our share register at the close of business on the date fixed by the Board of Directors as the record date determining the then shareholders who will be entitled to vote, shall be entitled to notice of, and to vote, in person or by proxy, at a general meeting and any postponement or

adjournment thereof.

Annual; agenda; calling a general meeting. General Meetings are held at least once in every calendar year at such time (within a period of 15 months after the holding of the last preceding General Meeting), and at such time and place as may be determined by the Board of Directors. At a General Meeting, decisions shall be adopted only on matters that were specified on the agenda. The Board of Directors is obligated to call extraordinary general meeting of the shareholders upon a written request in accordance with the Israeli Companies Law. The Israeli Companies Law provides that an extraordinary general meeting of shareholder may be called by the Board of Directors or by a request of two directors or 25% of the directors in office, or by shareholders holding at least 5% of the issued share capital of the company and at least 1% of the voting rights, or of shareholders holding at least 5% of the voting rights of the company.

- Majority vote. Except as otherwise provided in the articles of association, any resolution at a General Meeting shall be deemed adopted if approved by the holders of a majority of our voting rights represented at the meeting in person or by proxy and voting thereon. In the case of an equality of votes, the chairman of the meeting shall not be entitled to a further vote.

- Discrimination against shareholders. According to our articles of association, there are no discriminating provisions against any existing or prospective holders of our shares as a result of a shareholder holding a substantial number of shares.

Modification of Class Rights

If, at any time, the share capital is divided into different classes of shares, the rights attached to any class (unless otherwise provided by the terms of issuance of the shares of that class) may be varied with the consent in writing of the holders of all the issued shares of that class, or with the sanction of a majority vote at a meeting of the shareholders passed at a separate meeting of the holders of the shares of the class. The provisions of our articles of association relating to general meetings shall apply, mutatis mutandis, to every such separate general meeting. Any holder of shares of the class present in person or by proxy may demand a secret poll.

Unless otherwise provided by the conditions of issuance, the enlargement of an existing class of shares, or the issuance of additional shares thereof, shall not be deemed to modify or abrogate the rights attached to the previously issued shares of such class or of any other class. These conditions provide for the minimum shareholder approvals permitted by the Israeli Companies Law.

Restrictions on Shareholders Rights to Own Securities

Our articles of association and the laws of the State of Israel do not restrict in any way the ownership or voting or our shares by non-residents of Israel, except with respect to subjects of countries which are in a state of war with Israel.

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 or of the issued and outstanding share capital of a certain class of shares 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 or of all of the issued and outstanding shares of the same class.

If the shareholders who do not respond to or accept the offer hold less than 5% of the issued and outstanding share capital of the company or of the applicable class of the shares, and more than half of the shareholders who do not have a personal interest in the offer accept the offer, all of the shares that the acquirer offered to purchase will be transferred to the acquirer by operation of law. However, a tender offer will be accepted if the shareholders who do not accept it hold less than 2% of the issued and outstanding share capital of the company or of the applicable class of the shares.

Upon a successful completion of such a full tender offer, any shareholder that was an offeree in such tender offer, whether such shareholder accepted the tender offer or not, may, within six months from the date of acceptance of the tender offer, petition the Israeli court to determine whether the tender offer was for less than fair value and that the fair value should be paid as determined by the court. However, under certain conditions, the offeror may determine in the terms of the tender offer that an offeree who accepted the offer will not be entitled to petition the Israeli court as described above.

If the shareholders who did not respond or accept the tender offer hold at least 5% of the issued and outstanding share capital of the company or of the applicable class, the acquirer may not acquire shares of the company that will increase its holdings to more than 90% of the company's issued and outstanding share capital or of the applicable class from shareholders who accepted the tender offer.

Special tender offer

The Israeli Companies Law provides that an acquisition of shares of an Israeli public company must be made by means of a special tender offer if as a result of the acquisition the purchaser would become a holder of at least 25% of the voting rights in the company. This rule does not apply if there is already another holder of at least 25% of the voting rights in the company.

Similarly, the Israeli Companies Law provides that an acquisition of shares 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.

These requirements do not apply if the acquisition (i) occurs in the context of a private offering, on the condition that the shareholders meeting approved the acquisition as a private offering whose purpose is to give the acquirer at least 25% of the voting rights in the company if there is no person who holds at least 25% of the voting rights in the company, or as a private offering whose purpose is to give the acquirer 45% of the voting rights in the company, if there is no person who holds 45% of the voting rights in the company; (ii) was from a shareholder holding at least 25% of the voting rights in the company and resulted in the acquirer becoming a holder of at least 25% of the voting rights in the company; or (iii) was from a holder of more than 45% of the voting rights in the company and resulted in the acquirer becoming a holder of more than 45% of the voting rights in the company.

The special tender offer may be consummated only if (i) at least 5% of the voting power attached to the company's outstanding shares will be acquired by the offeror and (ii) the special tender offer is accepted by a majority of the votes of those offerees who gave notice of their position in respect of the offer; in counting the votes of offerees, the votes of a holder of control in the offeror, a person who has personal interest in acceptance of the special tender offer, a holder of at least 25% of the voting rights in the company, or any person acting on their or on the offeror's behalf, including their relatives or companies under their control, are not taken into account.

In the event that a special tender offer is made, a company's Board of Directors is required to express its opinion on the advisability of the offer or shall abstain from expressing any opinion if it is unable to do so, provided that it gives the reasons for its abstention.

An office holder in a target company who, in his or her capacity as an office holder, performs an action the purpose of which is to cause the failure of an existing or foreseeable special tender offer or is to impair the chances of its acceptance, is liable to the potential purchaser and shareholders for damages resulting from his acts, unless such office holder acted in good faith and had reasonable grounds to believe he or she was acting for the benefit of the company.

However, office holders of the target company may negotiate with the potential purchaser in order to improve the terms of the special tender offer, and may further negotiate with third parties in order to obtain a competing offer.

If a special tender offer was accepted by a majority of the shareholders who announced their stand on such offer, then shareholders who did not respond to the special offer or had objected to the special tender offer may accept the offer within four days of the last day set for the acceptance of the offer.

In the event that a special tender offer is accepted, then the purchaser or any person or entity controlling it and any corporation controlled by them shall refrain from making a subsequent tender offer for the purchase of shares of the target company and may not execute a merger with the target company for a period of one year from the date of the offer, unless the purchaser or such person or entity undertook to effect such an offer or merger in the initial special tender offer.

Merger

The Israeli Companies Law permits merger transactions if approved by each party's Board of Directors and, unless certain requirements described under the Israeli Companies Law are met, a majority of each party's shareholders, by a majority of each party's shares that are voted on the proposed merger at a shareholders' meeting.

The Board of Directors of a merging company is required pursuant to the Israeli Companies Law to discuss and determine whether in its opinion there exists a reasonable concern that as a result of a proposed merger, the surviving company will not be able to satisfy its obligations towards its creditors, taking into account the financial condition of the merging companies. If the Board of Directors has determined that such a concern exists, it may not approve a proposed merger. Following the approval of the Board of Directors of each of the merging companies, the Boards of Directors must jointly prepare a merger proposal for submission to the Israeli Registrar of Companies.

For purposes of the shareholder vote, unless a court rules otherwise, the merger will not be deemed approved if a majority of the shares voting at the shareholders meeting (excluding abstentions) that are held by parties other than the other party to the merger, any person who holds 25% or more of the means of control of the other party to the merger or any one on their behalf including their relatives or corporations controlled by any of them, vote against the merger.

If the transaction would have been approved but for the separate approval of each class of shares or the exclusion of the votes of certain shareholders as provided above, a court may still rule that the company has approved the merger upon the request of holders of at least 25% of the voting rights of a company, if the court holds that the merger is fair and reasonable, taking into account the appraisal of the merging companies' value and the consideration offered to the shareholders.

Under the Israeli Companies Law, each merging company must send a copy of the proposed merger plan to its secured creditors. Unsecured creditors are entitled to receive notice of the merger, as provided by the regulations promulgated under the Israeli Companies Law. Upon the request of a creditor of either party to the proposed merger, the court may delay or prevent the merger if it concludes that there exists a reasonable concern that, as a result of the merger, the surviving company will be unable to satisfy the obligations of the target company. The court may also give instructions in order to secure the rights of creditors.

In addition, a merger may not be completed unless at least 50 days have passed from the date that a proposal for approval of the merger was filed with the Israeli Registrar of Companies and 30 days from the date that shareholder approval of both merging companies was obtained.

Potential Issues that Could Delay a Merger

Certain provisions of Israeli corporate and tax law may have the effect of delaying, preventing or making more difficult any merger or acquisition of us.

Requirement of Disclosure of Shareholder Ownership

There are no provisions of our articles of association governing the ownership threshold above which shareholder ownership must be disclosed. We are subject, however, to U.S. securities rules that require beneficial owners of more than 5% of our Ordinary Shares to make certain filings with the SEC.

Changes in Capital

Our articles of association do not impose any conditions governing changes in capital that are more stringent than required by the Israeli Companies Law.

10.C. Material contracts

For a description of the agreements related to our directors and officers, see Item 6.B –"Compensation".

10.D. Exchange controls

There are currently no Israeli currency control restrictions on payments of dividends or other distributions with respect to our Ordinary Shares or the proceeds from the sale of our Ordinary Shares, except for the obligation of Israeli residents to file reports with the Bank of Israel regarding certain transactions. However, legislation remains in effect pursuant to which currency controls can be imposed by administrative action at any time.

Non-residents of Israel who purchase our securities with non-Israeli currency will be able to repatriate dividends (if any), liquidation distributions and the proceeds of any sale of such securities, into non-Israeli currencies at the rate of exchange prevailing at the time of repatriation, provided that any applicable Israeli taxes have been paid (or withheld) on such amounts.

Neither our articles of association nor the laws of the State of Israel restrict in any way the ownership or voting of our Ordinary Shares by non-residents of Israel, except with respect to citizens of countries that are in a state of war with Israel.

10.E. Taxation

The following is a summary of the current tax structure, which is applicable to companies in Israel, with special reference to its effect on us. The following also contains a discussion of material Israeli and U.S. tax consequences to persons purchasing our Ordinary Shares and government programs from which we and some of our group companies benefit. To the extent that the discussion is based on new tax legislation, which has yet to be subject to judicial or administrative interpretation, there can be no assurance that the views expressed in the discussion will accord with any such interpretation in the future. The discussion is not intended and should not be construed as legal or professional tax advice and is not exhaustive of all possible tax considerations. An Israeli company that is subject to Israeli taxes on the income of its non-Israeli subsidiaries will receive a credit for income taxes paid/withheld or that will be paid/withheld by the subsidiary in its country of residence, according to the terms and conditions determined in the Israeli Tax Ordinance.

The following summary is included herein as general information only and is not intended as a substitute for careful tax planning. Accordingly, each investor should consult his or her own tax advisor as to the particular tax consequences to such investor of the purchase, ownership or sale of an Ordinary Share, including the effect of applicable state, local, foreign or other tax laws and possible changes in tax laws.

Israeli Tax Considerations

The following is a summary of the material Israeli income tax laws applicable to us. This section also contains a discussion of material Israeli income tax consequences concerning the ownership and disposition of our Ordinary Shares. This summary does not discuss all the aspects of Israeli income 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 this kind of investor 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. This summary is based on

laws and regulations in effect as of the date of this annual report and does not take into account possible future amendments which may be under consideration.

General corporate tax structure in Israel

Israeli resident companies, such as us, are generally subject to corporate tax at the rate of 26.5% as of 2014.

Capital gains derived by an Israeli resident company are generally subject to tax at the same rate as the corporate tax rate. Under Israeli tax legislation, a corporation will be considered as an “Israeli Resident” if it meets one of the following: (a) it was incorporated in Israel; or (b) the control and management of its business are exercised in Israel.

Taxation of our Israeli individual shareholders on receipt of dividends

Israeli residents who are individuals are generally subject to Israeli income tax for dividends paid on our Ordinary Shares (other than bonus shares or share dividends) at a rate of 25%, or 30% if the recipient of such dividend is a “substantial shareholder” (as defined below) at the time of distribution or at any time during the preceding 12-month period.

As of January 1, 2015, an additional income tax at a rate of 2% is imposed on high earners whose annual income or gain exceeds NIS 810,720.

A "substantial Shareholder" is generally a person who alone, or together with his relative or another person who collaborates with him on a regular 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 officer, receive assets upon liquidation, or instruct someone who holds any of the aforesaid rights regarding the manner in which he or she is to exercise such right(s), and all regardless of the source of such right.

The term "Israeli Resident" is generally defined under Israeli tax legislation with respect to individuals as a person whose center of life is in Israel. The Israeli Tax Ordinance New Version, 1961 (the "Israeli Tax Ordinance") provides that in order to determine the center of life of an individual, account will be taken of the individual's family, economic and social connections, including: (a) place of permanent home; (b) place of residential dwelling of the individual and the individual's immediate family; (c) place of the individual's regular or permanent occupation or the place of his permanent employment; (d) place of the individual's active and substantial economic interests; (e) place of the individual's activities in organizations, associations and other institutions. The center of life of an individual will be presumed to be in Israel if: (a) the individual was present in Israel for 183 days or more in the tax year; or (b) the individual was present in Israel for 30 days or more in the tax year, and the total period of the individual's presence in Israel in that tax year and the two previous tax years is 425 days or more. The presumption in this paragraph may be rebutted either by the individual or by the assessing officer.

Taxation of Israeli Resident Corporations on Receipt of Dividends

Israeli resident corporations are generally exempt from Israeli corporate income tax with respect to dividends paid on our Ordinary Shares as long as the profits from which the dividends were distributed were derived in Israel.

Capital Gains Taxes Applicable to Israeli Resident Shareholders

The income tax rate applicable to Real Capital Gain derived by an Israeli individual from the sale of shares which had been purchased after January 1, 2012, whether listed on a stock exchange or not, is 25%. However, if such shareholder is considered a "Substantial Shareholder" (as defined above) at the time of sale or at any time during the preceding 12-month period, such gain will be taxed at the rate of 30%. As of January 1, 2015, an additional tax at a rate of 2% is imposed on high earners whose annual income or gains exceed NIS 810,720.

Moreover, capital gains derived by a shareholder who is a dealer or trader in securities, or to whom such income is otherwise taxable as ordinary business income, are taxed in Israel at ordinary income rates (26.5% as of 2014 for corporations and up to 50% for individuals).

Taxation of Non-Israeli Shareholders on Receipt of Dividends

Non-Israeli residents are generally subject to Israeli income tax on the receipt of dividends paid on our Ordinary Shares at the rate of 25% (or 30% for individuals, if such person is a "substantial shareholder" at the time receiving the dividend or on any date in the 12 months preceding such date), which tax will be withheld at source, unless a lower tax rate is provided in a tax treaty between Israel and the shareholder's country of residence.

A non-Israeli resident who receives dividends from which tax was withheld is generally exempt from the duty to file returns in Israel in respect of such income; provided such income was not derived from a business conducted in Israel by the taxpayer, and the taxpayer has no other taxable sources of income in Israel.

For example, under the Convention Between the Government of the United States of America and the Government of Israel with Respect to Taxes on Income, as amended (the "U.S.-Israel Tax Treaty"), Israeli withholding tax on dividends paid to a U.S. resident for treaty purposes may not, in general, exceed 25%, or 15% in the case of dividends paid out of the profits of a Benefited Enterprise, subject to certain conditions. Where the recipient is a U.S. corporation owning 10% or more of the voting shares of the paying corporation during the part of the paying corporation's taxable year which precedes the date of payment of the dividend and during the whole of its prior taxable year (if any) and the dividend is not paid from the profits of a Benefited Enterprise, the Israeli tax withheld may not exceed 12.5%, subject to certain conditions.

Capital gains income taxes applicable to non-Israeli shareholders.

Non-Israeli resident shareholders are generally exempt from Israeli capital gains tax on any gains derived from the sale, exchange or disposition of our Ordinary Shares, provided that such gains were not derived from a permanent establishment or business activity of such shareholders in Israel. However, non-Israeli corporations will not be entitled to the foregoing exemptions if an Israeli resident (i) has a controlling interest of more than 25% in such non-Israeli corporation or (ii) is the beneficiary of or is entitled to 25% or more of the revenues or profits of such non-Israeli corporation, whether directly or indirectly.

Regardless of whether shareholders may be liable for Israeli income tax on the sale of our Ordinary Shares, the payment of the consideration may be subject to withholding of Israeli tax at the source. Accordingly, 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.

Estate and gift tax

Israeli law presently does not impose estate or gift taxes.

United States Federal Income Tax Consequences

THE FOLLOWING SUMMARY IS INCLUDED HEREIN FOR GENERAL INFORMATION AND IS NOT INTENDED TO BE, AND SHOULD NOT BE CONSIDERED TO BE, LEGAL OR TAX ADVICE. EACH U.S. HOLDER SHOULD CONSULT WITH HIS OR HER OWN TAX ADVISOR AS TO THE PARTICULAR U.S. FEDERAL INCOME TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND SALE OF ORDINARY SHARES, INCLUDING THE EFFECTS OF APPLICABLE STATE, LOCAL, FOREIGN OR OTHER TAX LAWS

AND POSSIBLE CHANGES IN THE TAX LAWS.

U.S. Federal Income Taxation

Subject to the limitations described in the next paragraph, the following discussion summarizes the material U.S. federal income tax consequences to a “U.S. Holder” arising from the purchase, ownership and sale of the Ordinary Shares. For this purpose, a “U.S. Holder” is a holder of Ordinary Shares that is: (1) an individual citizen or resident of the United States, including an alien individual who is a lawful permanent resident of the United States or meets the substantial presence residency test under U.S. federal income tax laws; (2) a corporation (or other entity treated as a corporation for U.S. federal income tax purposes) or a partnership (other than a partnership that is not treated as a U.S. person under any applicable U.S. Treasury Regulations) created or organized in or under the laws of the United States or the District of Columbia or any political subdivision thereof; (3) an estate, the income of which is subject to U.S. federal income tax regardless of source; (4) a trust if a court within the United States is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust; (5) a trust that has a valid election in effect to be treated as a U.S. person to the extent provided in U.S. Treasury regulations; or (6) any person otherwise subject to U.S. federal income tax on a net income basis in respect of the Ordinary Shares, if such status as a U.S. Holder is not overridden pursuant to the provisions of an applicable tax treaty.

This summary is for general information purposes only and does not purport to be a comprehensive description of all of the U.S. federal income tax considerations that may be relevant to a decision to purchase or hold our Ordinary Shares. This summary generally considers only U.S. Holders that will own our Ordinary Shares as capital assets. Except to the limited extent discussed below, this summary does not consider the U.S. federal tax consequences to a person that is not a U.S. Holder, nor does it describe the rules applicable to determine a taxpayer's status as a U.S. Holder. This summary is based on the provisions of the Internal Revenue Code of 1986, as amended, or the Code, final, temporary and proposed U.S. Treasury Regulations promulgated thereunder, administrative and judicial interpretations thereof, and the U.S./Israel Income Tax Treaty, all as in effect as of the date hereof and all of which are subject to change, possibly on a retroactive basis, and all of which are open to differing interpretations. We will not seek a ruling from the U.S. Internal Revenue Service, or the IRS, with regard to the U.S. federal income tax treatment of an investment in our Ordinary Shares by U.S. Holders and, therefore, can provide no assurances that the IRS will agree with the conclusions set forth below.

This discussion does not address all of the aspects of U.S. federal income taxation that may be relevant to a particular shareholder based on such shareholder's particular circumstances and in particular does not discuss any estate, gift, generation-skipping, transfer, state, local or foreign tax considerations. In addition, this discussion does not address the U.S. federal income tax treatment of a U.S. Holder who is: (1) a bank, life insurance company, regulated investment company, or other financial institution or "financial services entity"; (2) a broker or dealer in securities or foreign currency; (3) a person who acquired our Ordinary Shares in connection with employment or other performance of services; (4) a U.S. Holder that is subject to the U.S. alternative minimum tax; (5) a U.S. Holder that holds our Ordinary Shares as a hedge or as part of a hedging, straddle, conversion or constructive sale transaction or other risk-reduction transaction for U.S. federal income tax purposes; (6) a tax-exempt entity; (7) real estate investment trusts; (8) a U.S. Holder that expatriates out of the United States or a former long-term resident of the United States; or (9) a person having a functional currency other than the U.S. dollar. This discussion does not address the U.S. federal income tax treatment of a U.S. Holder that owns, directly or constructively, at any time, Ordinary Shares representing 10% or more of our voting power. Additionally, the U.S. federal income tax treatment of persons who hold Ordinary Shares through a partnership or other pass-through entity are not considered.

You are encouraged to consult your own tax advisor with respect to the specific U.S. federal and state income tax consequences to you of purchasing, holding or disposing of our Ordinary Shares, including the effects of applicable state, local, foreign or other tax laws and possible changes in the tax laws.

Distributions on Ordinary Shares

Subject to the discussion under the heading "Passive Foreign Investment Companies" below, a U.S. Holder will be required to include in gross income as ordinary income the amount of any distribution paid on Ordinary Shares (including the amount of any Israeli tax withheld on the date of the distribution), to the extent that such distribution does not exceed our current and accumulated earnings and profits, as determined for U.S. federal income tax purposes. The amount of a distribution which exceeds our earnings and profits will be treated first as a non-taxable return of capital, reducing the U.S. Holder's tax basis for the Ordinary Shares to the extent thereof, and then capital gain. Corporate holders generally will not be allowed a deduction for dividends received. For noncorporate U.S. Holders, to the extent that their total adjusted income does not exceed applicable thresholds, the maximum federal income tax rate for "qualified dividend income" and long-term capital gains is generally 15%. For those noncorporate U.S. Holders whose total adjusted income exceeds such income thresholds, the maximum federal income tax rate for "qualified dividend income" and long-term capital gains is generally 20%. For this purpose, "qualified dividend income" means, *inter alia*, dividends received from a "qualified foreign corporation." A "qualified foreign corporation" is a corporation that is entitled to the benefits of a comprehensive tax treaty with the United States which includes an exchange of information program. The IRS has stated that the Israel/U.S. Tax Treaty satisfies this requirement and we believe we are eligible for the benefits of that treaty.

In addition, our dividends will be qualified dividend income if our Ordinary Shares are readily tradable on NASDAQ or another established securities market in the United States. Dividends will not qualify for the preferential rate if we are treated, in the year the dividend is paid or in the prior year, as a PFIC. A U.S. Holder will not be entitled to the

preferential rate: (1) if the U.S. Holder has not held our Ordinary Shares or ADRs for at least 61 days of the 121 day period beginning on the date which is 60 days before the ex-dividend date, or (2) to the extent the U.S. Holder is under an obligation to make related payments on substantially similar property. Any days during which the U.S. Holder has diminished its risk of loss on our Ordinary Shares are not counted towards meeting the 61-day holding period. Finally, U.S. Holders who elect to treat the dividend income as “investment income” pursuant to Code section 163(d)(4) will not be eligible for the preferential rate of taxation.

The amount of a distribution with respect to our Ordinary Shares will be measured by the amount of the fair market value of any property distributed, and for U.S. federal income tax purposes, the amount of any Israeli taxes withheld therefrom. (See discussion above under “Israeli Tax Considerations - Taxation of Our Shareholders – Dividends.”) Cash distributions paid by us in NIS will be included in the income of U.S. Holders at a U.S. dollar amount based upon the spot rate of exchange in effect on the date the dividend is includible in the income of the U.S. Holder, and U.S. Holders will have a tax basis in such NIS for U.S. federal income tax purposes equal to such U.S. dollar value. If the U.S. Holder subsequently converts the NIS, any subsequent gain or loss in respect of such NIS arising from exchange rate fluctuations will be U.S. source ordinary exchange gain or loss.

Distributions paid by us will generally be foreign source income for U.S. foreign tax credit purposes. Subject to the limitations set forth in the Code, U.S. Holders may elect to claim a foreign tax credit against their U.S. income tax liability for Israeli income tax withheld from distributions received in respect of the Ordinary Shares. In general, these rules limit the amount allowable as a foreign tax credit in any year to the amount of regular U.S. tax for the year attributable to foreign source taxable income. This limitation on the use of foreign tax credits generally will not apply to an electing individual U.S. Holder whose creditable foreign taxes during the year do not exceed $300, or $600 for joint filers, if such individual's gross income for the taxable year from non-U.S. sources consists solely of certain passive income. A U.S. Holder will be denied a foreign tax credit with respect to Israeli income tax withheld from dividends received with respect to the Ordinary Shares if such U.S. Holder has not held the Ordinary Shares for at least 16 days out of the 31-day period beginning on the date that is 15 days before the ex-dividend date or to the extent that such U.S. Holder is under an obligation to make certain related payments with respect to substantially similar or related property. Any day during which a U.S. Holder has substantially diminished his or her risk of loss with respect to the Ordinary Shares will not count toward meeting the 16-day holding period. A U.S. Holder will also be denied a foreign tax credit if the U.S. Holder holds the Ordinary Shares in an arrangement in which the U.S. Holder's reasonably expected economic profit is insubstantial compared to the foreign taxes expected to be paid or accrued. The rules relating to the determination of the U.S. foreign tax credit are complex, and U.S. Holders should consult with their own tax advisors to determine whether, and to what extent, they are entitled to such credit. U.S. Holders that do not elect to claim a foreign tax credit may instead claim a deduction for Israeli income taxes withheld, provided such U.S. Holders itemize their deductions.

Disposition of Shares

Except as provided under the PFIC rules described below, upon the sale, exchange or other disposition of our Ordinary Shares, a U.S. Holder will recognize capital gain or loss in an amount equal to the difference between such U.S. Holder's tax basis in the sold Ordinary Shares and the amount realized on the disposition of such Ordinary Shares (or its U.S. dollar equivalent determined by reference to the spot rate of exchange on the date of disposition, if the amount realized is denominated in a foreign currency). The gain or loss realized on the sale or exchange or other disposition of Ordinary Shares will be long-term capital gain or loss if the U.S. Holder has a holding period of more than one year at the time of the disposition.

In general, gain realized by a U.S. Holder on a sale, exchange or other disposition of Ordinary Shares will generally be treated as U.S. source income for U.S. foreign tax credit purposes. A loss realized by a U.S. Holder on the sale, exchange or other disposition of Ordinary Shares is generally allocated to U.S. source income. However, U.S. Treasury Regulations require such loss to be allocated to foreign source income to the extent specified dividends were received by the taxpayer within the 24-month period preceding the date on which the taxpayer recognized the loss. The deductibility of a loss realized on the sale, exchange or other disposition of Ordinary Shares is subject to limitations.

Tax on Net Investment Income

U.S. Holders who are individuals, estates or trusts will generally be required to pay a 3.8% tax on their net investment income (including dividends on and gains from the sale or other disposition of our Ordinary Shares), or in the case of estates and trusts on their net investment income that is not distributed. In each case, the 3.8% Medicare tax applies only to the extent the U.S. Holder's total adjusted income exceeds applicable thresholds.

Passive Foreign Investment Companies

Special U.S. federal income tax laws apply to a U.S. Holder who owns shares of a corporation that was (at any time during the U.S. Holder's holding period) a PFIC. We would be treated as a PFIC for U.S. federal income tax purposes for any tax year if, in such tax year, either:

- 75% or more of our gross income (including our pro rata share of gross income for any company, U.S. or foreign, in which we are considered to own 25% or more of the shares by value), in a taxable year is passive (the "Income Test"); or
- At least 50% of our assets, averaged over the year and generally determined based upon value (including our pro rata share of the assets of any company in which we are considered to own 25% or more of the shares by value), in a taxable year are held for the production of, or produce, passive income (the "Asset Test").

For this purpose, passive income generally consists of dividends, interest, rents, royalties, annuities and income from certain commodities transactions and from notional principal contracts. Cash is treated as generating passive income.

If we are or become a PFIC, each U.S. Holder who has not elected to treat us as a qualified electing fund by making a "QEF election", or who has not elected to mark the shares to market (as discussed below), would, upon receipt of certain distributions by us and upon disposition of our Ordinary Shares at a gain, be liable to pay U.S. federal income tax at the then prevailing highest tax rates on ordinary income plus interest on such tax, as if the distribution or gain had been recognized ratably over the taxpayer's holding period for the Ordinary Shares. In addition, when shares of a PFIC are acquired by reason of death from a decedent that was a U.S. Holder, the tax basis of such shares would not receive a step-up to fair market value as of the date of the decedent's death, but instead would be equal to the decedent's basis if lower, unless all gain were recognized by the decedent. Indirect investments in a PFIC may also be subject to special U.S. federal income tax rules.

The PFIC rules would not apply to a U.S. Holder who makes a QEF election for all taxable years that such U.S. Holder has held the Ordinary Shares while we are a PFIC, provided that we comply with specified reporting requirements. Instead, each U.S. Holder who has made such a QEF election is required for each taxable year that we are a PFIC to include in income such U.S. Holder's *pro rata* share of our ordinary earnings as ordinary income and such U.S. Holder's *pro rata* share of our net capital gains as long-term capital gain, regardless of whether we make any distributions of such earnings or gain. In general, a QEF election is effective only if we make available certain required information. The QEF election is made on a shareholder-by-shareholder basis and generally may be revoked only with the consent of the IRS. U.S. Holders should consult with their own tax advisors regarding eligibility, manner and advisability of making a QEF election if we are treated as a PFIC.

A U.S. Holder of PFIC shares which are traded on qualifying public markets, including the NASDAQ, can elect to mark the shares to market annually, recognizing as ordinary income or loss each year an amount equal to the difference as of the close of the taxable year between the fair market value of the PFIC shares and the U.S. Holder's adjusted tax basis in the PFIC shares. Losses are allowed only to the extent of net mark-to-market gain previously included income by the U.S. Holder under the election for prior taxable years.

Based on the nature of our business, the projected composition of our income and the projected composition and estimated fair market values of our assets, we cannot rule out a PFIC designation. In particular, in light of the complexity of PFIC rules, we cannot assure you that we have not been a PFIC in prior years or are not a PFIC or will avoid becoming a PFIC in the future. U.S. Holders who hold Ordinary Shares during a period when we are a PFIC will be subject to the foregoing rules, even if we cease to be a PFIC, subject to specified exceptions for U.S. Holders who made a QEF or mark-to-market election. U.S. Holders are strongly urged to consult their tax advisors about the PFIC rules, including tax return filing requirements and the eligibility, manner, and consequences to them of making a QEF or mark-to-market election with respect to our Ordinary Shares in the event we that qualify as a PFIC.

Information Reporting and Withholding

A U.S. Holder may be subject to backup withholding (at a rate of 28%) with respect to cash dividends and proceeds from a disposition of Ordinary Shares. In general, back-up withholding will apply only if a U.S. Holder fails to comply with specified identification procedures. Backup withholding will not apply with respect to payments made to designated exempt recipients, such as corporations and tax-exempt organizations. Backup withholding is not an additional tax and may be claimed as a credit against the U.S. federal income tax liability of a U.S. Holder, provided that the required information is timely furnished to the IRS.

Under the Hiring Incentives to Restore Employment Act of 2010 (the "HIRE Act"), some payments made to "foreign financial institutions" in respect of accounts of U.S. stockholders at such financial institutions may be subject to withholding at a rate of 30%. U.S. Treasury Regulations provide that such withholding will only apply to distributions paid on or after January 1, 2014, and to other "withholdable payments" (including payments of gross proceeds from a sale or other disposition of our Ordinary Shares) made on or after January 1, 2017. U.S. Holders should consult their tax advisors regarding the effect, if any, of the HIRE Act on their ownership and disposition of our Ordinary Shares. See "Non-U.S. Holders of Ordinary Shares" below.

Non-U.S. Holders of Ordinary Shares

Except as provided below, an individual, corporation, estate or trust that is not a U.S. Holder generally will not be subject to U.S. federal income or withholding tax on the payment of dividends on, and the proceeds from the disposition of, our Ordinary Shares.

A non-U.S. Holder may be subject to U.S. federal income or withholding tax on a dividend paid on our Ordinary Shares or the proceeds from the disposition of our Ordinary Shares if: (1) such item is effectively connected with the conduct by the non-U.S. Holder of a trade or business in the United States or, in the case of a non-U.S. Holder that is a resident of a country which has an income tax treaty with the United States, such item is attributable to a permanent establishment or, in the case of gain realized by an individual non-U.S. Holder, a fixed place of business in the United States; (2) in the case of a disposition of our Ordinary Shares, the individual non-U.S. Holder is present in the United States for 183 days or more in the taxable year of the sale and other specified conditions are met; (3) the non-U.S. Holder is subject to U.S. federal income tax pursuant to the provisions of the U.S. tax law applicable to U.S. expatriates.

In general, non-U.S. Holders will not be subject to backup withholding with respect to the payment of dividends on our Ordinary Shares if payment is made through a paying agent, or office of a foreign broker outside the United States. However, if payment is made in the United States or by a U.S. related person, non-U.S. Holders may be subject

to backup withholding, unless the non-U.S. Holder provides on an applicable Form W-8 (or a substantially similar form) a taxpayer identification number, certifies to its foreign status, or otherwise establishes an exemption. A U.S. related person for these purposes is a person with one or more current relationships with the United States.

The amount of any backup withholding from a payment to a non-U.S. Holder will be allowed as a credit against such holder's U.S. federal income tax liability and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

The HIRE Act may impose withholding taxes on some types of payments made to “foreign financial institutions” and some other non-U.S. entities. Under the HIRE Act, the failure to comply with additional certification, information reporting and other specified requirements could result in withholding tax being imposed on payments of dividends and sales proceeds to U.S. Holders that own Ordinary Shares through foreign accounts or foreign intermediaries and specified non-U.S. Holders. The HIRE Act imposes a 30% withholding tax on dividends on, and gross proceeds from the sale or other disposition of, Ordinary Shares paid from the United States to a foreign financial institution or to a foreign nonfinancial entity, unless (1) the foreign financial institution undertakes specified diligence and reporting obligations or (2) the foreign nonfinancial entity either certifies it does not have any substantial U.S. owners or furnishes identifying information regarding each substantial U.S. owner. In addition, if the payee is a foreign financial institution, it generally must enter into an agreement with the U.S. Treasury that requires, among other things, that it undertake to identify accounts held by specified U.S. persons or U.S.-owned foreign entities, annually report certain information about such accounts, and withhold 30% on payments to other specified account holders. U.S. Treasury Regulations provide that such withholding will only apply to distributions paid on or after January 1, 2014, and to other “withholdable payments” (including payments of gross proceeds from a sale or other disposition of our Ordinary Shares) made on or after January 1, 2017. You should consult your tax advisor regarding the HIRE Act.

10.F. Dividends and paying agents

Not applicable.

10.G. Statement by experts

Not applicable.

10.H. Documents on display

We are subject to certain of the information reporting requirements of the Exchange Act. As a foreign private issuer, we are exempt from the rules and regulations under the Exchange Act prescribing 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, with respect to their purchase and sale of our Ordinary Shares. In addition, we are not required to file 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 four months after the end of each fiscal year, an annual report on Form 20-F containing financial statements audited by an independent accounting firm. We publish unaudited interim financial information after the end of each quarter. We furnish this quarterly financial information to the SEC under cover of a Form 6-K.

You may read and copy any document we file with the SEC at its public reference facilities at 100 F Street, NE, 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, NE, Washington, D.C. 20549. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address of this website is http://www.sec.gov. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

10.I. Subsidiary information

Not applicable.

item 11. Quantitative and Qualitative Disclosures About Market Risk

In the ordinary course of our operations, we are exposed to certain market risks, primarily changes in foreign currency exchange rates and interest rates.

Quantitative and Qualitative Disclosure About Market Risk

We are exposed to market risks in the ordinary course of our business. Market risk represents the risk of loss that may impact our financial position due to adverse changes in financial market prices and rates. Our current investment policy is to invest available cash in bank deposits with banks that have a credit rating of at least A-minus. Accordingly, a substantial majority of our cash and cash equivalents is held in deposits that bear interest. Given the current low rates of interest we receive, we will not be adversely affected if such rates are reduced. Our market risk exposure is primarily a result of NIS/U.S. dollar exchange rates, which is discussed in detail in the following paragraph.

Foreign Currency Exchange Risk

Our results of operations and cash flow are subject to fluctuations due to changes in NIS/U.S. dollar currency exchange rates. The vast majority of our liquid assets is held in U.S. dollars, and a certain portion of our expenses is denominated in NIS. For instance, in 2014, approximately 23% of our expenses were denominated in NIS. Changes of 5% and 10% in the U.S. Dollar / NIS exchange rate will increase/decrease our operating expenses by 1.7% and 3.5%, respectively. However, these historical figures may not be indicative of future exposure, as we expect that the percentage of our NIS denominated expenses will materially decrease in the near future, therefore reducing our exposure to exchange rate fluctuations.

We do not hedge our foreign currency exchange risk. In the future, we may enter into formal currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rates of our principal operating currencies. These measures, however, may not adequately protect us from the material adverse effects of such fluctuations.

Item 12. Description of Securities other than Equity Securities

We do not have any outstanding American Depositary Shares or American Depositary Receipts.

Part two

Item 13. Defaults, dividend arrearages and delinquencies

None.

Item 14. Material modifications to the rights of security holders and use of proceeds

None.

Item 15. CONTROLS AND PROCEDURES

(a) Disclosure Controls and Procedures

Our management, with the participation of 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, 2014, or the Evaluation Date. Based on such evaluation, those officers have concluded that, as of the Evaluation Date, our disclosure controls and procedures are effective in recording, processing, summarizing and reporting, on a timely basis, information required to be included in periodic filings under the Exchange Act and that such information is accumulated and communicated to management, including our principal executive and financial officers, as appropriate to allow timely decisions regarding required disclosure.

(b) Management's Annual Report on Internal Control over Financial Reporting

This annual report does not include a report of management’s assessment regarding internal control over financial reporting due to a transition period established by rules of the SEC for newly public companies.

(c) Attestation Report of the Registered Public Accounting Firm

This annual report does not include an attestation report of our registered public accounting firm due to a transition period established by rules of the SEC for newly public companies and because we are an emerging growth company.

(d) Changes in Internal Control over Financial Reporting

During the year ended December 31, 2014, there were no changes in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 16A. Audit Committee Financial Expert

Our Board of Directors has determined that Gili Cohen, a member of our Audit Committee, is an audit committee financial expert, as defined under the rules under the Exchange Act, and are independent in accordance with applicable Exchange Act rules and Nasdaq rules.

ITEM 16B. Code of Ethics

We have adopted a written code of ethics that applies to our officers and employees, including our principal executive officer, principal financial officer, principal controller and persons performing similar functions as well as our directors. Our Code of Business Conduct and Ethics is posted on our website at www.bioblast-pharma.com.

ITEM 16C. Principal Accountant Fees and Services

Kost Forer Gabbay & Kasierer (a Member of EY Global), has served as our principal independent registered public accounting firm for each of the two years ended December 31, 2014 and 2013.

The following table provides information regarding fees paid by us to Kost Forer Gabbay & Kasierer and/or other member firms of EY Global for all services, including audit services, for the years ended December 31, 2014 and 2013:

	Year Ended December 31,	
	2014	2013
Audit fees [1]	$49,000	$60,000
Audit-related fees [2]	-	240,000
Tax fees [3]	8,000	2,000
All other fees	-	-
Total	$57,000	$302,000

(1) Includes professional services rendered in connection with the audit of our annual financial statements and the review of our interim financial statements.

(2) Includes fees for our initial public offering.

(3) Includes professional fees related to tax returns and other tax related services.

Pre-Approval of Auditors' Compensation

Our Audit Committee has adopted a pre-approval policy for the engagement of our independent registered public accounting firm to perform certain audit and non-audit services. Pursuant to this policy, which is designed to assure that such engagements do not impair the independence of our auditors, the Audit Committee pre-approves annually a catalog of specific audit and non-audit services in the categories of audit services, audit-related services and tax services that may be performed by our independent registered public accounting firm. If a type of service, that is to be provided by our auditors, has not received such general pre-approval, it will require specific pre-approval by our Audit Committee. The policy prohibits retention of the independent registered public accounting firm to perform the prohibited non-audit functions defined in applicable SEC rules. All of the fees in the table above were either pre-approved according to this policy, or otherwise pre-approved by our Audit Committee or Board of Directors.

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

The Sarbanes-Oxley Act, as well as related rules subsequently implemented by the SEC, require foreign private issuers, such as us, to comply with various corporate governance practices. In addition, we are required to comply with the Listing Rules of NASDAQ. Under those Listing Rules, we may elect to follow certain corporate governance practices permitted under the Israeli Companies Law in lieu of compliance with corresponding corporate governance requirements otherwise imposed by the Listing Rules of NASDAQ for U.S. domestic issuers.

In accordance with Israeli law and practice and subject to the exemption set forth in Rule 5615 of the Listing Rules of NASDAQ, we have elected to follow the provisions of the Israeli Companies Law, rather than the Listing Rules of NASDAQ, with respect to the following requirements:

- *Distribution of periodic reports to shareholders; proxy solicitation.* As opposed to the Listing Rules of NASDAQ, which require listed issuers to make such reports available to shareholders in one of a number of specific manners, Israeli law does not require us to distribute periodic reports directly to shareholders, and the generally accepted business practice in Israel is not to distribute such reports to shareholders but to make such reports available through a public website. In addition to making such reports available on a public website, we currently make our audited financial statements available to our shareholders at our offices and will only mail such reports to shareholders upon request. As a foreign private issuer, we are generally exempt from the SEC's proxy solicitation rules.

- *Nomination of our directors.* With the exception of our 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. See Item 6.C. – "Board Practices – Board of Directors." 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 by a majority of independent directors, as required under the Listing Rules of NASDAQ. Nominations may also be made by one or more of our shareholders, as provided under the Israeli Companies Law.

- *Compensation of officers.* Israeli law and our articles of association do not require that the independent members of our Board of Directors (or a Compensation Committee composed solely of independent members of our Board of Directors) determine an executive officer's compensation, as is generally required under the Listing Rules of NASDAQ with respect to the Chief Executive Officer and all other executive officers. Instead, compensation of executive officers is determined and approved by our Board of Directors, our Compensation Committee, and in some events, our shareholders, either in consistency with our Compensation Policy or, in special circumstances, taking into account certain considerations stated in the Israeli Companies Law.

Shareholder approval is generally required in the event (i) approval by our Board of Directors and our Compensation Committee is not consistent with our office holders Compensation Policy, or (ii) compensation required to be approved is that of Our Chief Executive officer or an executive officer who is also the controlling shareholder of us (including an affiliate thereof). Such shareholder approval shall require a majority vote of the shares present and voting at a shareholders meeting, provided either (i) such majority includes a majority of the shares held by non-controlling shareholders who do not have a personal interest in the compensation arrangement that are voted at the meeting, excluding for such purpose any abstentions disinterested majority, or (ii) the total shares held by non-controlling disinterested shareholders voted against the arrangement does not exceed two percent (2%) of the voting rights in us.

Additionally, approval of the compensation of an executive officer, who is also a director, shall require a simple majority vote of the shares present and voting at a shareholders meeting, if consistent with our office holders

Compensation Policy or a special majority as set forth above if the proposed compensation for the director is not consistent with our Compensation Policy. Our Compensation Committee and Board of Directors may, in special circumstances, approve the compensation of an executive officer (other than a director or a controlling shareholder) despite shareholders' objection, based on specified arguments and taking shareholders' objection into account. Our Compensation Committee may exempt an engagement with a nominee for the position of Chief Executive Officer, who meets the non-affiliation requirements set forth for an external director, from requiring shareholders' approval, if such engagement is consistent with our office holders Compensation Policy and our Compensation Committee determines based on specified arguments that presentation of such engagement to shareholders' approval is likely to prevent such engagement. 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.

A director or executive officer may not be present when the Compensation Committee or Board of Directors of a company discusses or votes upon the terms of his or her compensation, unless the Chairman of the Compensation Committee or Board of Directors (as applicable) determines that he or she should be present to present the transaction that is subject to approval.

Independent directors. Israeli law does not require that a majority of the directors serving on our Board of Directors be "independent," as defined under NASDAQ Listing Rule 5605(a)(2), and rather requires we have at least two external directors who meet the requirements of the Israeli Companies Law, as described above under Item 6.C. – "Board Practices – External Directors." We are required, however, to ensure that all members of our Audit Committee are "independent" under the applicable NASDAQ and SEC criteria for independence (as we cannot exempt ourselves from compliance with that SEC independence requirement, despite our status as a foreign private issuer), and we must also ensure that a majority of the members of our Audit Committee are "unaffiliated directors" as defined in the Israeli Companies Law. Furthermore, Israeli law does not require, nor do our independent directors conduct, regularly scheduled meetings at which only they are present, which the Listing Rules of NASDAQ otherwise require.

Shareholder approval. We will seek shareholder approval for all corporate actions requiring such approval under the requirements of the Israeli Companies Law, rather than seeking approval for corporation actions in accordance with NASDAQ Listing Rule 5635. In particular, under this NASDAQ rule, shareholder approval is generally required for: (i) an acquisition of shares/assets of another company that involves the issuance of 20% or more of the acquirer's shares or voting rights or if a director, officer or 5% shareholder has greater than a 5% interest in the target company or the consideration to be received; (ii) the issuance of shares leading to a change of control; (iii) adoption/amendment of equity compensation arrangements; and (iv) issuances of 20% or more of the shares or voting rights (including securities convertible into, or exercisable for, equity) of a listed company via a private placement (and/or via sales by directors/officers/5% shareholders) if such equity is issued (or sold) at below the greater of the book or market value of shares. By contrast, under the Israeli Companies Law, shareholder approval is required for, among other things: (i) transactions with directors concerning the terms of their service or indemnification, exemption and insurance for their service (or for any other position that they may hold at a company), for which approvals of the Compensation Committee, Board of Directors and shareholders are all required, (ii) extraordinary transactions with controlling shareholders of publicly held companies, which require the special approval described below under "Approval of Related Party Transactions under Israeli Law — Disclosure of personal interests of controlling shareholders", and (iii) terms of employment or other engagement of the controlling shareholder of the company or such controlling shareholder's relative, which require the special approval described below under "Approval of Related Party Transactions under Israeli Law — Disclosure of personal interests of controlling shareholders". In addition, under the Israeli Companies Law, a merger requires approval of the shareholders of each of the merging companies.

Approval of Related Party Transactions under Israeli Law

Disclosure of personal interests of a controlling shareholder and approval of transactions

The Israeli Companies Law also requires that a controlling shareholder promptly disclose to the company any personal interest that he or she may have and all related material information or documents relating to any existing or proposed transaction by the company. A controlling shareholder'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. Extraordinary transactions with a controlling shareholder or in which a controlling shareholder has a personal interest, including a private placement in which a controlling shareholder has a personal interest, and the terms of engagement of the company, directly or indirectly, with a controlling shareholder or a controlling shareholder's relative (including through a corporation controlled by a controlling shareholder), regarding the company's receipt of services from the controlling shareholder, and if such controlling shareholder is also an office holder of the company, regarding his or her terms of employment, require the approval of each of (i) the Audit Committee or the Compensation Committee with respect to the terms of the engagement of the company, (ii) the Board of Directors and (iii) the shareholders, in that order. In addition, the shareholder approval must fulfill one of the following requirements:

- a majority of the shares held by shareholders who have no personal interest in the transaction and are voting at the meeting must be voted in favor of approving the transaction, excluding abstentions; or

- the shares voted by shareholders who have no personal interest in the transaction who vote against the transaction represent no more than 2.0% of the voting rights in the company.

In addition, any extraordinary transaction with a controlling shareholder or in which a controlling shareholder has a personal interest with a term of more than three years requires the abovementioned approval every three years, however, such transactions not involving the receipt of services or compensation can be approved for a longer term, provided that the Audit Committee determines that such longer term is reasonable under the circumstances.

The Israeli Companies Law requires that every shareholder that participates, in person, by proxy or by voting instrument, in a vote regarding a transaction with a controlling shareholder, must indicate in advance or in the ballot whether or not that shareholder has a personal interest in the vote in question. Failure to so indicate will result in the invalidation of that shareholder's vote.

ITEM 16H. Mine Safety Disclosure

Not applicable.

Part Three

Item 17. Financial statements

Not applicable.

Item 18. Financial statements

The following financial statements, and the related notes thereto, and the Reports of Independent Public Accountants are filed as a part of this annual report.

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Item 19. Exhibits

EXHIBIT INDEX

EXHIBIT NUMBER	DESCRIPTION OF DOCUMENT
1.1	Articles of Association of the Company, filed as Exhibit 3.2 to Form F-1/A filed on July 8, 2014 (File No. 333-193824) and incorporated herein by reference.
4.1	Amended and Restated Services Agreement between the Company and Top-Notch Consultancy 2009 Ltd., dated April 22, 2014, filed as Exhibit 10.2 to Form F-1/A filed on July 15, 2014 (File No. 333-193824) and incorporated herein by reference.

4.2	BioBlast Pharma Ltd. 2013 Incentive Option Plan, filed as Exhibit 10.3 to Form F-1/A filed on March 17, 2014 (File No. 333-193824) and incorporated herein by reference.
4.3	Form of Indemnification Agreement, filed as Exhibit 10.4 to Form F-1/A filed on April 8, 2014 (File No. 333-193824) and incorporated herein by reference.
4.4	Engagement Letter between the Company and Fredric Price dated April 24, 2012, filed as Exhibit 10.8 to Form F-1/A filed on July 15, 2014 (File No. 333-193824) and incorporated herein by reference.
4.5	Engagement Letter between the Company and Fredric Price dated April 22, 2014, filed as Exhibit 10.6 to Form F-1/A filed on July 15, 2014 (File No. 333-193824) and incorporated herein by reference.
4.6	Engagement Letter between the Company and Marlene Haffner dated May 13, 2013, filed as Exhibit 10.7 to Form F-1/A filed on March 17, 2014 (File No. 333-193824) and incorporated herein by reference.

12.1	Certification of the Chief Executive Officer pursuant to rule 13a-14(a) of the Securities Exchange Act of 1934
12.2	Certification of the Chief Financial Officer pursuant to rule 13a-14(a) of the Securities Exchange Act of 1934
13.1	Certification of the Chief Executive Officer pursuant to 18 U.S.C. 1350, furnished herewith
13.2	Certification of the Chief Financial Officer pursuant to 18 U.S.C. 1350, furnished herewith
101	The following materials from our Annual Report on Form 20-F for the year ended December 31, 2014 formatted in XBRL (eXtensible Business Reporting Language) are furnished herewith: (i) the Balance Sheets, (ii) the Statements of Comprehensive Loss, (iii) the Statements of Changes in Shareholders' Equity, (iv) the Statements of Cash Flows and (v) the Notes to Financial Statements, tagged as blocks of text and in detail.

SIGNATURES

BioBlast Pharma Ltd. 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.

BioBlast PharMa LTD.

By: /s/ Colin Foster
Colin Foster
Chief Executive Officer and President
Date: March 30, 2015

BIOBLAST PHARMA LTD.

FINANCIAL STATEMENTS

AS OF DECEMBER 31, 2014

U.S. DOLLARS IN THOUSANDS

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACOUNTING FIRM

To the Shareholders and Board of Directors of

BIOBLAST PHARMA LTD.

We have audited the accompanying balance sheets of BioBlast Pharma Ltd. ("the Company") as of December 31, 2014 and 2013, and the related statements of operations, changes in shareholders' equity and cash flow for each of the three years in the period ended December 31, 2014. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances 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. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by the and management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of the Company and its subsidiary as of December 31, 2014 and 2013, and the consolidated results of their operations and their cash flows for each of the three years in ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

Tel-Aviv, Israel /s/ KOST FORER GABBAY & KASIERER
March 31, 2015 A Member of EY Global

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BIOBLAST PHARMA LTD.

BALANCE SHEETS

U.S. dollars in thousands

	December 31,	
	2014	2013
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$10,583	$270
Short-term bank deposits	22,028	-
Receivables and prepaid expenses	274	29
Total current assets	32,885	299
LONG-TERM ASSETS:		
Long-term deposit	9	5
Property and equipment, net	60	2
Total long-term assets	69	7
TOTAL ASSETS	$32,954	$306
LIABILITIES AND SHAREHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Trade payables	$1,285	$46
Other accounts payable	995	85
Total current liabilities	2,280	131
SHAREHOLDERS' EQUITY:		
Ordinary shares of NIS 0.01 par value - 50,000,000 and 16,613,139 shares authorized at December 31, 2014 and 2013, respectively; 14,230,480 and 9,182,867 issued and outstanding shares at December 31, 2014 and 2013, respectively;	39	24
Additional paid- in capital	39,057	1,551
Accumulated deficit	(8,422)	(1,400)
Total shareholders' equity	30,674	175
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	$32,954	$306

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

BIOBLAST PHARMA LTD.

STATEMENTS OF OPERATIONS

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

	Year ended December 31,		
	2014	2013	2012
Research and development expenses	$4,441	$732	$140
General and administrative expenses	2,639	416	86
Operating loss	7,080	1,148	226
Financial expenses (income), net	(58)	(3)	3
Loss	$7,022	$1,145	$229
Deemed dividend	-	26	-
Loss attributable to holders of Ordinary shares	$7,022	$1,171	$229
Basic and diluted loss per share	(0.57)	(0.14)	(0.03)
Weighted average number of Ordinary shares used in computing basic and diluted loss per share	12,259,600	8,423,018	7,551,427

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

BIOBLAST PHARMA LTD.

STATEMENTS OF CHANGES IN SHAREHOLDERS' EQUITY

U.S. dollars in thousands, except share data

	Ordinary shares		Preferred A shares		Additional paid-in	Accumulated	Total shareholders'
	Number	Amount	Number	Amount	capital	deficit	equity
Balance as of January 22, 2012 (date of inception)	-	-	-	-	-	-	-
Issuance of Ordinary shares to founders	7,551,427	20	-	-	(20)	-	-
Issuance of Preferred A shares, net ($0.53 per share)	-	-	566,357	1	294	-	295
Share based compensation	-	-	-		9	-	9
Loss	-	-	-	-	-	(229)	(229)
Balance as of December 31, 2012	7,551,427	20	566,357	1	283	(229)	75
Conversion of Preferred A shares into Ordinary shares	566,357	1	(566,357)	(1)	-	-	-
Deemed Dividend	-	-	-	-	26	(26)	-
Issuance of Ordinary shares, net ($0.95 per share)	1,065,083	3	-	-	988	-	991
Share based compensation	-	-	-	-	254	-	254
Loss	-	-	-	-	-	(1,145)	(1,145)
Balance as of December 31, 2013	9,182,867	24	-	-	1,551	(1,400)	175
Issuance of Ordinary shares, net ($0.95 per share)	1,065,076	3	-	-	1,009	-	1,012
Issuance of Ordinary shares upon private placement, net ($6.07 per share)	782,537	3	-	-	4,365	-	4,368
Issuance of Ordinary shares upon initial public offering, net ($11 per share)	3,200,000	9	-	-	31,396	-	31,405
Share based compensation	-	-	-	-	736	-	736
Loss	-	-	-	-	-	(7,022)	(7,022)
Balance as of December 31, 2014	14,230,480	$ 39	-	$ -	$ 39,057	$ (8,422)	$ 30,674

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

BIOBLAST PHARMA LTD.

STATEMENTS OF CASH FLOWS

U.S. dollars in thousands, except share data

	Year ended December 31,		
	2014	2013	2012
Cash flows from operating activities			
Loss	$(7,022)	$(1,145)	$(229)
Adjustments to reconcile loss to net cash used in operating activities:			
Depreciation	5	- *)	-
Stock based compensation	736	254	9
Interest on short-term bank deposits	(28)	-	-
Changes in operating assets and liabilities:			
Receivables and prepaid expenses	(245)	(19)	(10)
Long-term deposit	(4)	(5)	-
Trade payables	1,239	(28)	74
Other accounts payables	910	78	7
Net cash used in operating activities	(4,409)	(865)	(149)
Cash flows from investing activities			
Short-term bank deposits	(22,000)	-	-
Purchase of property and equipment	(63)	(2)	-
Net cash used in investing activities	(22,063)	(2)	-
Cash flows from financing activities			
Issuance of shares, net	36,785	991	295
Net cash provided by financing activities	36,785	991	295
Increase in cash and cash equivalents	10,313	124	146
Cash and cash equivalents at the beginning of the year	270	146	-
Cash and cash equivalents at the end of the year	$10,583	$270	$146

*) Represents an amount lower than $1.

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

BIOBLAST PHARMA LTD.

NOTES TO FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

NOTE 1:- GENERAL

a. BioBlast Pharma Ltd. (the "Company") was incorporated in Israel and commenced its operations on January 22, 2012. The Company is a clinical-stage biotechnology company committed to developing clinically meaningful therapies for patients with rare and ultra-rare genetic diseases. The Company is rapidly building a diverse portfolio of product candidates with the potential to address unmet medical needs for incurable diseases. The Company's platforms are based on deep understanding of the disease-causing biological processes, and potentially offer solutions for several diseases that share the same biological pathology. The Company seeks to identify therapeutic platforms that offer solutions for several diseases that share a common pathophysiological mechanism. The Company's objective is to conduct additional clinical trials for its drugs (the "Drugs") and, if those trials are successful, seek marketing approval from the U.S. Food and Drug Administration (the "FDA") and other worldwide regulatory bodies.

b. The Company is engaged in the research and development of products in the biopharmaceutical field, has not generated revenue from the sale of any product, and does not expect to generate significant revenue unless and until the obtaining of marketing approval, and commercializing its Drugs. The Company has incurred losses in the amount of $7,022 during the year ended December 31, 2014.

c. During August 2014, the Company completed an Initial Public Offering ("IPO") in United States in which it issued 3,200,000 Ordinary shares in consideration of approximately $31,405, net and its Ordinary shares began trading on the "NASDAQ Capital Market".

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES

The financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP").

a. Use of estimates:

The preparation of the financial statements in conformity with U.S. GAAP requires management to make estimates, judgments and assumptions. The Company's management believes that the estimates, judgments and assumptions used are reasonable based upon information available at the time they are made. These estimates, judgments and

assumptions can affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the dates of the financial statements, and the reported amounts of expenses during the reporting period. Actual results could differ from those estimates.

BIOBLAST PHARMA LTD.

NOTES TO FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

b. New accounting pronouncements:

In June 2014 the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 10-2014 ("ASU 10-2014") regarding development stage entities. The ASU removes the definition of development stage entity, as was previously defined under U.S. GAAP, from the accounting standards codification, thereby removing the financial reporting distinction between development stage entities and other reporting entities from U.S. GAAP. In addition, the ASU eliminates the requirements for development stage entities to (i) present inception-to-date information in the statement of income, cash flow and stockholders' equity, (ii) label the financial statements as those of a development stage entity, (iii) disclose a description of the development stage activities in which the entity is engaged, and (iv) disclose in the first year in which the entity is no longer a development stage entity that in prior years it had been in the development stage. The amendments to ASU 10-2014 are effective for annual reporting periods beginning after December 15, 2014. The Company has applied the ASU in these financial statements.

In 2014, the FASB issued ASU 15-2014, Presentation of Financial Statements-Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern, which defines management’s responsibility to assess an entity’s ability to continue as a going concern, and to provide related footnote disclosures if there is substantial doubt about its ability to continue as a going concern. The pronouncement is effective for annual reporting periods ending after December 15, 2016 with early adoption permitted. The Company is currently evaluating the effect, if any, that the adoption of this guidance will have on the Company’s financial statements.

c. Financial statements in U.S. dollars:

The Company finances its operation in U.S. dollars. The majority of the Company's operations are currently conducted in Israel, a significant part of the Company's expenses are denominated and determined in U.S. dollars. The Company's management believes that the dollar is the currency of the primary economic environment in which the Company operates and expects to continue to operate in the foreseeable future. Thus, the functional currency of the Company is the U.S. dollar.

The Company's transactions and balances denominated in U.S. dollars are presented at their original amounts. Non-dollar transactions and balances have been remeasured to U.S. dollars in accordance with Accounting Standards Codification ("ASC") 830, "Foreign Currency Matters", of the FASB. All transaction gains and losses from remeasurement of monetary balance sheet items denominated in non-dollar currencies are reflected in the

statements of operations as financial income or expenses, as appropriate.

d. Cash equivalents:

Cash equivalents are short-term highly liquid investments that are readily convertible to cash with original maturities of three months or less at acquisition.

BIOBLAST PHARMA LTD.

NOTES TO FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

e. Short-term bank deposits:

Short-term bank deposits are deposits with maturities of more than three months but less than one year. Short–term bank deposits are presented at their cost, including accrued interest, which approximates fair value. As of December 31, 2014, the Company's bank deposits were in U.S. dollars and bore interest at a weighted average interest rate of 0.66%.

f. Property and equipment, net:

Property and equipment are stated at cost, net of accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets at the following rates:

	%
Computers and software	33
Electronic equipment	15
Office furniture and equipment	6

The Company's property and equipment are reviewed for impairment in accordance with ASC 360, "Property, Plant, and Equipment," whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to the future undiscounted cash flows expected to be generated by the assets. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the assets exceeds the fair value of the assets. Assets to be disposed of are reported at the lower of the carrying amount or fair value less costs to sell. In 2014, 2013 and 2012 no impairment losses have been identified.

g. Long-term deposits:

Long-term deposits include long-term deposits for motor vehicles under operating leases, presented at their cost.

h. Research and development costs:

Research and development costs are expensed as incurred. Those expenses includes payments to third party clinical consultants, expenses related to conducting clinical trials, salaries and related personnel expenses, travel expenses, and share based compensation expenses related to research and development employees.

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BIOBLAST PHARMA LTD.

NOTES TO FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

i. Income taxes:

The Company accounts for income taxes in accordance with ASC 740, "Income Taxes". This topic prescribes the use of the liability method whereby deferred tax assets and liability account balances are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company provides a valuation allowance to reduce deferred tax assets to the amount that is more likely than not to be realized.

The Company implements a two-step approach to recognize and measure uncertain tax positions. The first step is to evaluate the tax position taken or expected to be taken in a tax return by determining if the weight of available evidence indicates that it is more likely than not that, on an evaluation of the technical merits, the tax position will be sustained on audit, including resolution of any related appeals or litigation processes. The second step is to measure the tax benefit as the largest amount that is more than 50% (cumulative basis) likely to be realized upon ultimate settlement. As of December 31, 2014 and 2013, the Company has not recorded a liability for uncertain tax positions.

j. Concentrations of credit risk:

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash and cash equivalents.

Cash and cash equivalents are invested in major banks in Israel. Management believes that the financial institutions that hold the Company's investments are financially sound and, accordingly, minimal credit risk exists with respect to these investments.

The Company has no off-balance-sheet concentration of credit risk such as foreign exchange contracts, option contracts or other foreign hedging arrangements.

k. Fair value of financial instruments:

The Company has no financial instruments that are measured at fair value.

The carrying amounts of cash and cash equivalents, short-term bank deposits, accounts receivable and accounts payable, approximate their fair value due to the short-term maturities of such instruments.

l. Basic and diluted loss per share:

Basic net loss per share is computed based on the weighted average number of Ordinary shares outstanding during each year. Diluted loss per share is computed based on the weighted average number of Ordinary shares outstanding during each year plus dilutive potential equivalent Ordinary shares considered outstanding during the year, in accordance with ASC 260, "Earnings per Share."

BIOBLAST PHARMA LTD.

NOTES TO FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

For the years ended December 31, 2014, 2013 and 2012, all outstanding options have been excluded from the calculation of the diluted net loss per share since their effect was anti-dilutive.

m. Accounting for stock-based compensation:

The Company accounts for stock-based compensation in accordance with ASC 718, "Compensation - Stock Compensation" ("ASC 718") that requires the measurement and recognition of compensation expense based on estimated fair values for all share-based payment awards made to employees and directors. ASC 718 requires companies to estimate the fair value of equity-based payment awards on the date of grant using an option-pricing model. The value of the option award is recognized as an expense over the requisite service periods in the Company's statements of operations based on the accelerated method.

The Company selected the Black-Scholes-Merton ("Black-Scholes") option-pricing model as the fair value method for of its stock-options awards. The option-pricing model requires a number of assumptions as noted below:

Expected dividend yield - The expected dividend yield assumption is based on the Company's historical experience and expectation of no future dividend payouts. The Company has historically not paid cash dividends and has no foreseeable plans to pay cash dividends in the future.

Volatility - Since the Company's shares started trading on NASDAQ in July 2014, sufficient quoted prices of the Company's share are unavailable. Due to insufficient historical data for the Company, the expected volatility determination was based on similar companies' stock volatility.

Risk free interest rate - The risk free interest rate is based on the yield of U.S. Treasury bonds with equivalent terms.

Expected term - ASC 718 provides the factors to consider when estimating the expected term of an option: an option's expected term must at least include the vesting period and the employees' historical exercise and post-vesting employment termination behavior for similar grants. It also determines that if the amount of past exercise data is limited, that data may not represent a sufficiently large sample on which to base a robust conclusion on expected exercise behavior. In that circumstance, it may be appropriate to consider external data or the SEC staff's "simplified"

method for the expected term. Accordingly, the Company used the "simplified" method, meaning the expected life can be set as the average of the vesting period for each vested tranche of options and the contractual term for those options.

BIOBLAST PHARMA LTD.

NOTES TO FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

NOTE 3:- RECEIVABLES AND PREPAID EXPENSES

	December 31, 2014	2013
Government authorities	$93	$ 26
Prepaid expenses	181	3
	$274	$ 29

NOTE 4:- PROPERTY AND EQUIPMENT, NET

	December 31, 2014	2013
Cost:		
Computers and software	$ 19	$ 2
Electronic equipment	14	-
Office furniture and equipment	32	-
	65	2
Accumulated depreciation:		
Computers and software	3	*)
Electronic equipment	1	-
Office furniture and equipment	1	-
Depreciated cost	$ 60	$ 2

*) Represents an amount lower than $ 1.

Depreciation expenses for the years ended December 31, 2014, 2013 and 2012 were $5, less than $1 and $0, respectively.

NOTE 5:- OTHER ACCOUNTS PAYABLE

	December 31,	
	2014	2013
Employees and payroll accruals	$ 235	$ 26
Accrued expenses	760	59
	$ 995	$ 85

BIOBLAST PHARMA LTD.

NOTES TO FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

NOTE 6:- INCOME TAXES

a. Tax laws applicable to the Company:

Taxable income of Israeli companies is subject to tax at the rate of 25% in 2012 and 2013 and a rate of 26.5% in 2014 and afterwards.

b. Net operating losses carry forward:

The Company has accumulated losses for tax purposes as of December 31, 2014 in the amount of $684, which may be carried forward and offset against taxable income in the future for an indefinite period.

c. Deferred income taxes:

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets are as follows:

	December 31,	
	2014	2013
Operating loss carry forward	$181	$166
Research and development expenses	923	142
Issuance expenses	671	-
Other	16	4
Net deferred tax asset before valuation allowance	1,791	312
Valuation allowance	(1,791)	(312)
Net deferred tax asset	$-	$-

Management currently believes that since the Company has a history of losses it is more likely than not that the deferred tax regarding the loss carry forward and other temporary differences will not be realized in the foreseeable future.

d. No liability for uncertain tax positions was recorded as of December 31, 2014 and 2013.

e. The main reconciling item between the statutory tax rate of the Company and the effective tax rate is the recognition of valuation allowances in respect of deferred taxes due to the uncertainty of the realization of such deferred taxes.

BIOBLAST PHARMA LTD.

NOTES TO FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

NOTE 7:- CONTINGENT LIABILITIES AND COMMITMENTS

a. The Company is engaged in an operating lease agreement for its office facilities. The rent expenses for the years ended December 31, 2014, 2013 and 2012 amounted to $88, $14 and $0. Future minimum payments under the lease are as follows:

Year ended December 31,	Total
2015	$117
2016	117
2017	54
	$288

The Company has provided bank guarantees in the amount of $25 as security for the performance of its lease agreement.

b. During 2014 the Company entered into a new operating lease agreement for its vehicles until 2017. Future minimum payments under the lease are $8. The lease expenses for the years ended December 31, 2014, 2013 and 2012 amounted to $25, $11 and $0.

c. License agreement:

(i) The Company entered into a Research and Exclusive License Agreement with Yissum Research Development Company of the Hebrew University in Jerusalem Ltd., for the use, development and commercialization of TAT-MTS- Protein for protein replacement in mitochondrial diseases. The consideration to Yissum is composed of a tiered low single digit royalties on net sales and a sublicense fee that will not exceed the mid-high ten to twenty percent range of the sublicense consideration, but, if the sublicense arises from the sales of a product, the sublicense fee shall not be less than a low single digit percent of the gross sales of such product.

(ii) The Company entered into an Exclusive License Agreement with Ramot at Tel Aviv University Ltd. for the use, development and commercialization of our read-through platform. The consideration to Ramot is composed of a

tiered low single digit royalties on net sales and a sublicense fee that will not exceed the mid to high single digit percent range of payments or other consideration that the Company receives in connection with a sublicense.

NOTE 8:- SHAREHOLDERS' EQUITY

a. General:

All Ordinary shares, options, per share data and exercise price included in these financial statements for all periods presented have been retroactively adjusted to reflect the issuance on January 26, 2014 of 6.55-to-one bonus shares (equivalent to a 7.55-for-1 stock split).

BIOBLAST PHARMA LTD.

NOTES TO FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

NOTE 8:- SHAREHOLDERS' EQUITY (Cont.)

b. Share capital:

The Ordinary shares confer upon their holders the right to participate and vote in general shareholders meetings of the Company and to share in the distribution of dividends, if any, declared by the Company.

c. Issuances of share:

1. On January 22, 2012 (inception day), the Company issued 7,551,427 Ordinary shares in consideration of their par value.

2. In February 2012, the Company entered into an investment agreement, according to which the Company issued 471,964 Preferred A shares in consideration of $250. In addition, in August 2012, the Company issued 94,393 Preferred A shares in consideration of $50. The issuance expenses amounted to $5.

3. In June 2013, the Company entered into a share purchase agreement according to which, the Company issued a total of 2,130,159 Ordinary shares in consideration of $2,024, in two equal installments in 2013 and January 2014.

Prior to the closing of the share purchase agreement above and as a condition to it, the Company affected an equity restructuring, under which, all of the Company's Preferred shares (566,357 Preferred A shares) were converted into Ordinary shares at a 1:1 ratio. As a result and in accordance with ASC 718-20-35-6, the Company recorded compensation expense in the amount of $183 and a deemed dividend in the amount of $26 in the year ended December 31, 2013.

4. On February 6, 2014, the Company issued 782,537 Ordinary shares to private placement investors in consideration of $4,368, net.

5.

On August 5, 2014, the Company completed a successful IPO of 3,200,000 Ordinary shares at a price of $11.00 per share generating net proceeds of $31,405, after deducting underwriting discounts and commissions and other issuance expenses.

d. 2013 Incentive option plan:

In December 2013, the Company authorized through its 2013 incentive option plan (the "2013 Plan") the grant of options to officers, directors, advisors, management and other key employees. The options granted have a graded vesting schedule of generally four years and expire ten years after the grant date.

BIOBLAST PHARMA LTD.

NOTES TO FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

NOTE 8:- SHAREHOLDERS' EQUITY (Cont.)

A summary of the Company's options activity (for employees and directors) under the 2013 Plan is as follows:

	Year ended December 31,			
	2014		2013	
	Number of options	Weighted average exercise price	Number of options	Weighted average exercise price
Outstanding at beginning of year	403,110	$ 0.0004	319,531	$ 0.0004
Granted	380,222	9.21	83,579	0.0004
Outstanding at end of year	783,332	4.47	403,110	$ 0.0004
Vested and expected to vest	783,332	$ 4.47	403,110	$ 0.0004
Options exercisable at the end of the year	429,589	$ 1.33	134,370	$ 0.0004

As of December 31, 2014, the weighted-average remaining contractual term of the outstanding and exercisable options is 5.6 years and 2.3 years; the aggregated intrinsic value of the outstanding and exercisable options is $2,664 and $2,174. As of December 31, 2014, the unrecognized compensation cost is $889 to be recognized through 2017.

e. Options granted to service providers:

The Company granted options to certain service providers and accounted for these options in accordance with ASC 505-50, "Equity-Based payment to non-employees".

The outstanding options granted to the Company's service providers are as follows:

Grant date	Number of options	Exercise price	Expiration date
December 2, 2014	20,000	7.78	December 2, 2024

*) All options were fully vested on the grant date.

f. Share-based payment:

The share based expense recognized in the financial statements is as follows:

	Year ended December 31,		
	2014	2013	2012
Research and development	$83	$44	$ -
General and administrative expenses	653	210	9
	$736	$254	$ 9

BIOBLAST PHARMA LTD.

NOTES TO FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

NOTE 9:- RELATED PARTY BALANCES AND TRANSACTIONS

Balances with related parties:

	December 31,	
	2014	2013
Trade payable (d)	$2	$ 1
Other accounts payable (a) (b) (c)	$123	$ 36

Related parties' expenses:

	Year ended December 31,		
	2014	2013	2012
Amounts charged to: *)			
Research and development expense (c)	$145	$99	$ 34
General and administrative expense (a) (b) (c) (d)	$467	$257	$ 55

a. In August, 2012, the Company signed an agreement with a consultant, who is also one of the Company's shareholders and a director, to render management, finance and operation services. The Company pays the consultant an amount of approximately $6 per month. During August 2014, the monthly fee was increased to an amount of $15 effective immediately. In August 2014, the Company granted the consultant bonus in the amount of $80 in connection with the consummation of the IPO. The Company granted an additional bonus in the amount of $70 with regards to services provided during 2014.

b. The Company signed an agreement with a company owned by one of its related parties. Under the agreement, the related company renders the Company with office services and an office lease for a monthly fee in the amount of approximately $4 since September 10, 2013. The parties terminated the agreement on September 1, 2014.

c. An agreement was signed on August 20, 2013 between the Company and one of its shareholders, as a consultant to render management, finance and operation services for an amount of approximately $15 per month. During August 2014, the monthly fee was increased to an amount of $19 effective immediately. In August 2014, the Company granted the consultant a bonus in the amount of $90 in connection with the consummation of the IPO.

d. On July 1, 2013, the Company signed an agreement with a consultant, who is also one of the Company's shareholders, to render advisory services. The Company pays the consultant an amount of $1 per month.

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BIOBLAST PHARMA LTD.

NOTES TO FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

NOTE 10:- FINANCIAL EXPENSES (INCOME), NET

	Year ended December 31,		
	2014	2013	2012
Financial expenses:			
Interest expense	$*)	$ 2	$ *)
Bank fees	6	-	-
Exchange rate	21	-	3
	27	2	3
Financial income:			
Interest income	85	-	-
Exchange rate	-	5	-
	85	5	-
	$(58)	$ (3)	$ 3

*) Represents an amount lower than $1.

NOTE 11:- SUBSEQUENT EVENTS

1. During January 2015, a wholly-owned subsidiary was established in the state of Delaware named BioBlast Pharma Inc.

2. On February 2, 2015, the Company appointed a new President and Chief Executive Officer and a member of its board of directors. As part of the agreement the new CEO was granted 498,067 options to purchase Ordinary shares with exercise price of $8.47 per share.

3. On February 16, 2015, the Company's board of directors resolved to issue 24,000 options to employees with an exercise price of $7.17 per share.

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