

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, 2016

Commission file number: 001-35932

**Alcobra Ltd.**

(Exact name of Registrant as specified in its charter)

**State of Israel**

(Jurisdiction of incorporation or organization)

**Azrieli Triangle Building**

**132 Derech Menachem Begin, 39<sup>th</sup> Floor  
Tel Aviv 6701101 Israel**

(Address of principal executive offices)

**Dr. Yaron Daniely**

**Azrieli Triangle Building**

**132 Derech Menachem Begin, 39<sup>th</sup> Floor  
Tel Aviv 6701101 Israel**

**Tel: +972.72.220.4661**

(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.

27,562,795 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  No

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

Yes  No

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

Yes  No

Indicate by check mark whether the registrant has submitted electronically 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).

Yes  No

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

Large accelerated filer  Accelerated filer

Non-accelerated filer  (Do not check if a smaller reporting company)

Smaller reporting company

Emerging growth company  x

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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

U.S. GAAP

International 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

Unless otherwise indicated, all references to the “Company,” “we,” “our” and “Alcobra” refer to Alcobra Ltd. and its subsidiary, Alcobra Inc., a Delaware corporation. References to “U.S. dollars” and “\$” are to 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 prospects for consummating a strategic transaction or merger and acquisition, or M&A;
- FDA approval of, or other regulatory action in the United States and elsewhere with respect to, our drug candidate, Abuse-Deterrent Amphetamine Immediate-Release, or ADAIR, including the regulatory pathway to be designated to our product candidates;
- the commercial launch and future sales of ADAIR or any other future products or product candidates;
- our estimates regarding anticipated expenses, capital requirements, the sufficiency of our funds through 2018;
- the market potential of ADAIR or any other future products;
- the design, timing, duration and cost of clinical trials or whether such trials will be conducted at all;
- issuance of patents to us by the U.S. Patent and Trademark Office, or U.S. PTO, and other governmental patent agencies;
- our ability to protect our proprietary technology and enforce our intellectual property rights; 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 or other 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 herein 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 consolidated 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 consolidated financial information as of December 31, 2015 and 2016 and for the years ended December 31, 2014, 2015 and 2016 have been derived from, and should be read in conjunction with, the consolidated financial statements of Alcobra Ltd. and notes thereto appearing elsewhere in this annual report. The selected financial data as of December 31, 2012, 2013 and 2014 and for the years ended December 31, 2012 and December 31, 2013 have been derived from the audited financial statements of Alcobra Ltd. not included in this annual report.

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

#### **Consolidated Statement of Operations Data – Years Ended December 31** *(in thousands of U.S. dollars, except share and per share data)*

	2016	2015	2014	2013	2012
Research and development	\$ 18,391	\$ 13,461	\$ 25,105	\$ 7,066	\$ 818
Pre-commercialization	1,419	1,245	2,134	-	-
General and administrative	5,357	4,992	5,839	3,224	683
Operating loss	25,167	19,698	33,078	10,290	1,501
Financial expenses (income), net	(637)	(300)	(227)	197	78
Net loss before taxes	24,530	19,398	32,851	10,487	1,579
Taxes on income (tax benefit)	73	51	(17)	61	-
Net loss	\$ 24,603	\$ 19,449	\$ 32,834	\$ 10,548	\$ 1,579
Unrealized loss on available-for-sale marketable securities	6	-	-	-	-
Basic and diluted net loss per share	\$ (0.89)	\$ (0.9)	\$ (2.40)	\$ (1.04)	\$ (0.20)
Shares used in computing basic and diluted net loss per share	27,562,657	21,638,207	13,674,818	10,177,786	7,791,932

**Consolidated Balance Sheet Data – as of December 31**  
(in thousands of U.S. dollars, except for share data)

	2016		2015		2014		2013		2012
Working capital	\$ 46,959	\$	49,994	\$	19,751	\$	48,582	\$	(588)
Total assets	51,568		71,683		22,318		50,324		201
Shareholders' equity	\$ 47,228	\$	69,331	\$	19,943	\$	48,688	\$	(567)
Number of shares outstanding	27,562,795		27,560,920		13,702,772		13,636,709		7,794,256

**3.B. Capitalization and indebtedness**

Not applicable.

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

Not applicable.

**3.D. Risk factors**

In conducting our business, we face many risks that may interfere with our business objectives. Some of these risks could materially and adversely affect our business, financial condition and results of operations. In particular, we are subject to various risks resulting from inherent unknowns and uncertainties in the drug development process, as well as changing economic, political, industry, regulatory, business and financial conditions. The risks and uncertainties described below are not the only ones we face.

You should carefully consider the following factors and other information in this annual report before you decide to invest in our Ordinary Shares. If any of the negative events referred to below occur, our business, financial condition and results of operations could suffer. In any such case, the trading price of our Ordinary Shares could decline, and you may lose all or part of your investment.

**Risks Related to Our Financial Position and Need for Additional Capital**

***We are currently seeking business development and M&A opportunities to expand our product portfolio. There is intense competition for businesses/products suitable for a transaction of the type we are contemplating.***

There is currently a very competitive market for business opportunities, which could reduce the likelihood of consummating a successful transaction for acquisition of a business or technology. We anticipate that we will be a small participant in the pharmaceuticals M&A or joint ventures market with, or in the acquisition of, small private entities. A large number of established and well-financed entities, including small public companies, venture capital firms, and special purpose acquisition companies are active in M&A of companies that may be desirable target candidates for us. We have significantly less financial resources, technical expertise and managerial capabilities than many of these entities, and we may be unable to effectively compete with such entities in identifying possible business opportunities and successfully completing a transaction. These and other competitive factors may reduce the likelihood of our identifying and consummating a successful transaction.

***We may not be able to enter into a transaction of the type contemplated and if we complete such a transaction, we may need to raise additional capital.***

Even if we identify a successful target for a transaction, there can be no assurance that we (or the entity with which we combine) will be able to complete any such transaction. In the event that we complete such a transaction, we may need to raise substantial additional capital. In such event, we may need to rely on external sources of financing to meet any capital requirements and to obtain such funding through the debt and equity markets. We cannot provide any assurances regarding the availability of any such additional funding and, if available, regarding the terms thereof. If we fail to obtain such necessary funding, any such transaction may not be successful.

***Potential acquisitions of or investments in companies or technologies may negatively impact our financial condition and may not yield the expected returns.***

Even if we are able to make an acquisition or investment on reasonable terms, we have no prior experience in successfully completing acquisitions, and we could experience difficulties combining the two companies and/or in retaining and motivating key personnel from these businesses. We may also incur unanticipated liabilities. We cannot be certain that our actual cash requirements resulting from an acquisition, business combination or investment will not be greater than anticipated. Furthermore, there can be no assurance that we will be able to realize the anticipated benefits or synergies of any such acquisition, combination or investment. In that regard, we note that should we combine with, or invest in, any entity that is in the developmental stage, such as we were when we first went public, the ultimate success of such business will depend, in large part, on the combined company's ability to be successful with clinical trials and in obtaining any required regulatory approvals.

***Our Board of Directors has sole discretion to identify and evaluate transaction candidates and complete such transactions without approval of our shareholders.***

We are not obligated to follow any particular operating, financial, geographic or other criteria in evaluating candidates for a potential transaction. We will choose a technology or business that we believe will provide an opportunity for our shareholders potentially to receive long-term financial returns if the transaction is successful and our board will determine the purchase price and other terms and conditions of such transaction. Accordingly, there can be no assurance that any such transaction would be subject to shareholder review or approval. As a general matter, under Israeli law, there is no requirement for us to have an acquisition approved by our shareholders. Furthermore, under the NASDAQ Listing Rules, our status as a foreign private issuer enables us to take advantage of certain exemptions regarding NASDAQ Listing Rules, such as the NASDAQ shareholder approval requirement for an acquisition in which we would issue more than 20% of our existing share capital.

***We have a limited operating history and we have incurred significant operating losses since our inception, and anticipate that we will incur continued losses for the foreseeable future.***

We are an emerging biopharmaceutical company with a limited operating history. We are in the development stage. To date, we have focused almost exclusively on developing our lead product candidates, MDX and ADAIR. We have funded our operations to date primarily through proceeds from the private placement and public offering of Ordinary Shares and convertible notes. We have only a limited operating history upon which you can evaluate our business and prospects. In addition, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the pharmaceutical industry. We have not generated any revenue from product sales to date. We have incurred losses in each year since our inception in February 2008. Our loss attributable to holders of our Ordinary Shares for the years ended December 31, 2015 and 2016 was approximately \$19.5 million, and \$24.6 million, respectively. As of December 31, 2016, we had an accumulated deficit of \$95.6 million. Substantially all of our operating losses resulted from costs incurred in connection with our development program and from general and administrative costs associated with our operations.

Our research and development expenses may increase in connection with our development plan. In addition, if we obtain marketing approval for MDX, ADAIR or any other product candidate, we will likely incur significant sales, marketing and outsourced manufacturing expenses, as well as continued research and development expenses. Furthermore, we incur and will continue to incur additional costs associated with operating as a public company, which are at least several hundred thousand dollars annually. As a result, we expect to continue to incur significant and potentially increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

***We have not generated any revenue from MDX, ADAIR or any other product candidate and may never be profitable.***

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from our development stage product candidates, MDX and ADAIR, and we do not know when, or if, we will generate any revenue. We do not expect to generate significant revenue from sales of our product candidates unless or until we obtain marketing approval of, and commercialize, MDX, ADAIR or any other product candidate. Our ability to generate revenue depends on a number of factors, including our ability to:

- obtain favorable results from and progress the clinical development of our product candidates;
- develop and obtain regulatory approval for registration studies protocols for our product candidates;
- subject to successful completion of registration, clinical trials and perhaps additional clinical trials of MDX, apply for and obtain marketing approval;
- contract for the manufacture of commercial quantities of our product candidates at acceptable cost levels if marketing approval is received; and

- establish sales and marketing capabilities, both internal and external, to effectively market and sell our product candidates in the United States and other countries.

Even if MDX, ADAIR, or any other product candidate is approved for commercial sale, it may not gain market acceptance or achieve commercial success. In addition, we anticipate incurring significant costs associated with commercialization. We may not achieve profitability soon after generating product revenue, if ever. If we are unable to generate product revenue, we will not become profitable and would be unable to continue operations without continued funding.

***We may need substantial additional capital in the future. If additional capital is not available, we will have to delay, reduce or cease operations.***

We may need to raise substantial additional capital (i) to fund our operations; (ii) to develop and commercialize MDX, ADAIR or any other product candidate; and/or (iii) in connection with an M&A transaction with another company. Our future capital requirements may be substantial and will depend on many factors including:

- our clinical trials results;
- the scope, progress, results and costs of researching and developing our current or future product candidates;
- the cost, timing and outcomes of seeking marketing approval of our product candidates;
- the cost of filing and prosecuting patent applications and the cost of defending our issued patents and future patents, if issued;
- the cost of prosecuting infringement actions against third parties;
- exploration and possible label expansion of our product candidates;
- the costs associated with commercializing our product candidates if we receive marketing approval, including the cost and timing of establishing sales, marketing and distribution capabilities to market and sell our product candidates;
- the cost of manufacturing our product candidates;
- the timing, receipt and amount of sales of, or royalties on, sales of our product candidates, if any;
- subject to receipt of marketing approval, revenue received from sales of approved products, if any, in the future;
- any product liability or other lawsuits related to our products;
- costs associated with the expansion of our product pipeline;
- the expenses needed to attract and retain skilled personnel; and
- the costs associated with being a public company.

Based on our current operating plan, we anticipate that our existing resources will be sufficient to enable us to maintain our currently planned operations, including our continued product development of ADAIR, through 2018. We believe these funds will enable us to fund ADAIR's development activities and to complete the NDA filing, which we currently expect at the end of 2018. Our operating plan may significantly change as a result of new clinical data or other considerations related to our development plan.

We will require significant additional funds to initiate and complete the FDA approval process. Changing circumstances may cause us to consume capital significantly faster than we currently anticipate. We have no committed external sources of funds. Additional financing may not be available when we need it or may not be available on terms that are favorable to us. If adequate funds are not available to us on a timely basis, or at all, we may be required to:

- delay, limit, reduce, or terminate development activities for MDX, ADAIR, or any other product candidate; or
- delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize any of our product candidates, if we obtain marketing approval.



In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

***Raising additional capital, or issuance of our ordinary shares as consideration in a merger or acquisition transaction would cause dilution to our existing shareholders, and may restrict our operations or require us to relinquish rights.***

We have in the past and may continue to seek additional capital through a combination of private and public equity offerings, debt financings and collaborations and strategic and licensing arrangements. Including our initial public offering in 2013, we have completed four underwritten public offerings to date. We may also in the future issue substantial number of our ordinary shares as consideration in connection with merger and acquisition transactions. To the extent that we raise additional capital through the sale of equity or convertible notes securities, or the issuance of securities as part of a merger and acquisition transaction 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 Product Development, Regulatory Approval and Commercialization**

***We currently depend on the success of our lead product candidate, Abuse-Deterrent Amphetamine Immediate-Release, or ADAIR, and we may not obtain regulatory approval to market this product or we may be unable to successfully commercialize it.***

Following the results of our MDX clinical studies in adult ADHD, we communicated our decision to explore strategic alternatives for MDX and withhold any additional significant investment of resources in MDX development. As a result, our current business strategy is dependent on our ability to complete the development of, obtain regulatory approval for, and successfully commercialize, ADAIR and/or any other product candidate we may develop in the future in a timely manner. The process to develop, obtain regulatory approval for, and commercialize our products is long, complex, costly and uncertain of outcome.

The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drugs are subject to extensive regulation by the FDA in the United States and other regulatory agencies in other countries. These regulations differ from country to country. We are not permitted to market ADAIR or any other product candidate in the United States until we receive approval of a NDA from the FDA, or in any foreign countries until we receive the requisite approval from regulatory agencies in such countries. We are required to conduct multiple additional pre-clinical and clinical trials to be able to submit an NDA to the FDA or comparable applications to other regulatory authorities in other countries. The results of additional pre-clinical and clinical trials may be unsatisfactory, and even if we believe those trials to be successful, there are many reasons why the FDA may not approve our NDA should we be in a position to file one.

Approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The marketing approval process in other countries may include all of the risks detailed above regarding FDA approval in the United States as well as other risks. In particular, in many countries outside the United States, it is required that a product receive pricing and reimbursement approval before the product can be commercialized. This can result in substantial delays in such countries. In other countries, product approval depends on showing superiority to an approved alternative therapy. This can result in significant expense for conducting complex clinical trials. Finally, we do not have any products approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be harmed.

Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in others. Failure to obtain marketing approval in other countries or any delay or setback in obtaining such approval would impair our ability to develop foreign markets for ADAIR and/or any other product candidate. This would reduce our target market and limit the full commercial potential of our products.

***If the FDA does not conclude that ADAIR, our product candidate in development, is sufficiently bioequivalent, or demonstrate comparable bioavailability to its respective listed drug, or if the FDA otherwise does not conclude that our product candidate satisfies the requirements for the Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, or FD&C Act, approval pathway, the approval pathway for this product candidate will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated, and the FDA may not approve this product candidate.***

A key element of our strategy is to seek FDA approval for our ADAIR product candidate through Section 505(b)(2) of the FD&C Act, or Section 505(b)(2), approval pathway. Section 505(b)(2) permits the filing of an NDA that contains full safety and efficacy reports but where at least some of the information required for approval comes from studies not conducted by or for the applicant. Such information could include the FDA's findings of safety and efficacy in the approval of a similar drug, and for which the applicant has not obtained a right of reference and/or published literature. Such reliance is typically predicated on a showing of bioequivalence or comparable bioavailability to an approved drug.

If the FDA does not allow us to pursue the Section 505(b)(2) approval pathway for ADAIR, or if we cannot demonstrate bioequivalence or comparable bioavailability of our product candidate to an approved product, we may need to conduct additional clinical trials, provide additional data and information, and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for this product candidate would increase. Moreover, our inability to pursue the Section 505(b)(2) approval pathway could result in new competitive products reaching the market sooner than our product candidate, which could have a material adverse effect on our competitive position and our business prospects. Even if we are allowed to pursue the Section 505(b)(2) approval pathway, we cannot assure you that ADAIR will receive the requisite approval for commercialization on a timely basis, if at all.

In addition, notwithstanding the approval of a number of products by the FDA under Section 505(b)(2) over the last few years, pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA's interpretation of Section 505(b)(2) is successfully challenged, the FDA may change its policies and practices with respect to the Section 505(b)(2) approval pathway, which could delay or even prevent the FDA from approving any NDA that we submit under Section 505(b)(2).

Even if our product candidate is approved under Section 505(b)(2), the approval may be subject to limitations on the indicated uses for which the product may be marketed or to other conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product, including additional preclinical studies and clinical trials.

***Our ADAIR product candidate contains a controlled substance, the manufacture, use, sale, importation, exportation and distribution of which are subject to regulation by state, federal and foreign law enforcement and other regulatory agencies.***

Our ADAIR product candidate contains, and our future product candidates, if any, may contain, controlled substances which are subject to state, federal, foreign laws and other regulations regarding their manufacturing, use, sale, importation, exportation and distribution. ADAIR's active ingredient, dextroamphetamine, is classified as a controlled substance under the Controlled Substances Act of 1970, or CSA, and regulations of the U.S. Drug Enforcement Administration, or DEA. A number of states also independently regulate these drugs as controlled substances. Controlled substances are classified by the DEA as Schedule I, II, III, IV or V substances, with Schedule I substances considered to present the highest risk of substance abuse and Schedule V substances the lowest risk. The active ingredient in our ADAIR product candidate, dextroamphetamine, is listed by the DEA as a Schedule II controlled substance under the CSA. For our current product candidate, and any potential future product candidates containing a controlled substance, we and our suppliers, manufacturers, contractors, customers and distributors are required to obtain and maintain applicable registrations from state, federal and foreign law enforcement and regulatory agencies and comply with their laws and regulations regarding the manufacturing, use, sale, importation, exportation and distribution of controlled substances. An example of such practice is that all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription. Furthermore, the amount of Schedule II substances that can be obtained for clinical trials and commercial distribution is limited by the CSA and DEA regulations. We may not be able to obtain sufficient quantities of these controlled substances in order to complete our clinical trials or meet commercial demand, if our product candidate is approved for marketing.

In addition, controlled substances are subject to regulations governing manufacturing, labeling, packaging, testing, dispensing, production and procurement quotas, recordkeeping, reporting, handling, shipment and disposal. These regulations increase the personnel needs and the expense associated with development and commercialization of product candidates that include controlled substances. The DEA and some states conduct periodic inspections of registered establishments that handle controlled substances.

Failure to obtain and maintain required registrations or to comply with any applicable regulations could delay or preclude us from developing and commercializing our product candidate that contains a controlled substance and subject us to enforcement action. The DEA may seek civil penalties, refuse to renew necessary registrations or initiate proceedings to revoke those registrations. In some circumstances, violations could lead to criminal proceedings. Because of their restrictive nature, these regulations could limit commercialization of our product candidates containing controlled substances.

If we, our drug products or the manufacturing facilities for our drug products fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw marketing approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications;
- suspend or impose restrictions on operations, including costly new manufacturing requirements;
- seize or detain products, refuse to permit the import or export of products or request that we initiate a product recall; or
- refuse to allow us to enter into supply contracts, including government contracts.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business.

***The FDA may not approve product labeling for our ADAIR product candidate that would permit us to market and promote our product in the United States by describing its abuse-deterrent features.***

We have invested resources conducting Laboratory Manipulation and Extraction Studies (Category 1), and may spend substantial additional resources conducting Pharmacokinetic Studies (Category 2) and Clinical Abuse Potential Studies (Category 3) to support ADAIR's abuse-deterrence characteristics, and we believe such studies are consistent with the April 2015 final FDA guidance on opioid medications, as no guidance exists on amphetamines. However, we have not yet received regulatory approval to market ADAIR and additional data may emerge that could change the FDA's position on the proposed product label, and there can be no assurance that ADAIR or our other current or any future product candidate will receive FDA-approved product labeling that describes abuse-deterrent features of such products given the current absence of specific FDA guidance on development of abuse-deterrent amphetamines. Our failure to achieve FDA approval of product labeling containing information on abuse-deterrence characteristics of ADAIR will prevent or substantially limit our promotion of the abuse-deterrent features of our product candidate. This type of limitation would make it difficult for us to differentiate ADAIR from other amphetamine-containing products, may cause us to lower the price of our product to the extent that there are competing products with abuse-deterrent claims on their product labels and as a result, our product would be less competitive in the market. The FDA closely regulates promotional materials and other promotional activities, even if the FDA initially approves product labeling that includes a description of the abuse-deterrent characteristics of our product candidate and therefore the FDA may object to our marketing claims and product advertising campaigns. This could lead to the issuance of warning letters or untitled letters, suspension or withdrawal of our product from the market, recalls, fines, disgorgement of money, operating restrictions, injunctions and civil or criminal prosecution. Any of these consequences would harm the commercial success of our products.

Even if any of our other product candidates are approved for marketing with certain abuse-deterrence claims, the April 2015 final FDA guidance on abuse-deterrent opioids may not apply to ADAIR, as the said guidance is not binding law and may be superseded or modified at any time. Also, if the FDA determines that our post-marketing data do not demonstrate that the abuse-deterrent properties result in reduction of abuse, or demonstrate a shift to routes of abuse that present a greater risk, the FDA may find that product labeling revisions are needed, and may require the removal of our abuse-deterrence claims.

***For ADAIR, we may need to comply with the requirements of the Drug Supply Chain Security Act, which outlines critical steps required to build an electronic, interoperable system to identify and trace certain prescription drugs as they are distributed in the United States.***

For ADAIR, we may need to comply with the requirements of the Drug Supply Chain Security Act, including those related to product tracing, verification, and authorized trading partners. Signed into law in 2013, the Drug Supply Chain Security Act, amended the Federal Food, Drug, and Cosmetic Act, and is being implemented over a 10-year period. The law's requirements include the ability to quarantine and promptly investigate a suspect product, such as a potentially counterfeit, diverted or stolen product, to determine if it is illegitimate, and notify our trading partners and the FDA of any illegitimate product. Such compliance may be time consuming and expensive to implement. Also, in the event that we fail to comply with these requirements, we may face regulatory actions that could affect our ability to commercialize ADAIR.

***Following our announcements regarding the negative results from Phase 3 studies for MDX, we may not generate any future revenues from MDX or its underlying intellectual property.***

In October 2014, we announced that our Phase 3 study in adult ADHD, AL012, did not meet its primary endpoint. Following the results of this study, we introduced design and monitoring changes to our second Phase 3 trial, AL016, or MEASURE, with the goal of reducing variability and placebo response. In January 2017, we announced that despite our efforts, the MEASURE study also failed to show a positive statistical outcome on the primary efficacy endpoint. Following these clinical results, we may not generate any future revenues from MDX or its underlying intellectual property. We are not planning to invest additional significant capital in the development of MDX. Instead, we are currently exploring strategic alternatives for partnering or monetizing MDX for ADHD and other indications in various territories, but may not be able to complete such transactions due to limited demand or other reasons.

***The FDA placed MDX on full clinical hold, which could result in significant development delays, failure to obtain marketing approval for MDX, or limit our ability to monetize MDX or engage partners for MDX.***

In September 2016, the U.S. Food and Drug Administration, or FDA, placed a full clinical hold on our Investigational New Drug, or IND, applications for MDX in both ADHD and Fragile X. The full clinical hold currently prevents the conduct of any clinical efficacy studies in MDX and may prevent us or potential partners from gaining marketing approval for MDX in the United States. The FDA indicated that the clinical hold was due to adverse neurophysiological findings in long-term pre-clinical (animal) studies.

In order to consider a removal of the clinical hold, the FDA requested data from a six-month, Phase 1 clinical study to directly assess the potential relevance of adverse findings observed in long-term, pre-clinical (animal) studies of metadoxine with regard to human exposure. The FDA will review results from this safety study before considering the complete lifting of the full clinical hold currently in place on the MDX development programs. The safety study required by the FDA in response to the clinical hold may produce results that are not sufficient to lift the clinical hold. The full clinical hold could result in significant development delays, failure to obtain marketing approval for MDX, or limit our ability to monetize MDX or engage partners for MDX.

***We rely on limited sources of supply for our product candidates MDX and ADAIR, and any disruption in the chain of supply may impact production, and cause delays in developing and commercializing our product candidates.***

Any change to our manufacturing process, facilities or suppliers could require that we supplement any pending NDA. Also, because of our proprietary processes for manufacturing our product candidates, we cannot immediately transfer manufacturing activities for our product candidates to an alternate supplier. Any change to or in our manufacturing facilities would be a time-consuming and costly endeavor that would also require us to supplement or amend any future NDA filings to include the change regarding the manufacturing site.

Any changes to our manufacturing process would involve substantial costs and could result in a delay in our desired clinical and commercial timelines. We are also reliant on a limited number of suppliers for excipients, drug compounds, coating and other component substances of our final product candidates and products. If any of these single-source suppliers were to breach or terminate supply agreements, if any, with us or otherwise not supply us, we would need to identify an alternative source for the supply of component substances for our product candidates. Identifying an appropriately qualified source of alternative supply for any one or more of the component substances for our product candidates could be time consuming, and we may not be able to do so without incurring material delays in the development and commercialization of our product candidates, which could harm our financial position and commercial potential for our product candidates. The FDA, DEA or other regulatory agencies outside of the United States may also require additional studies if we enter into agreements with new suppliers for the manufacture of ADAIR that differ from the suppliers used for clinical development of such product candidates.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing them successfully. Furthermore, if our suppliers fail to deliver the required commercial quantities of components and active pharmaceutical ingredients on a timely basis and at commercially reasonable prices, including if our suppliers did not receive adequate DEA quotas for the supply of certain scheduled components, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, commercialization of our branded product candidates and clinical trials of future potential product candidates may be delayed or we could lose potential revenue and our business, financial condition, results of operation and reputation could be adversely affected.

***If third-party manufacturers fail to comply with manufacturing regulations, our financial results and financial condition will be adversely affected.***

Before third-party manufacturers can begin the commercial manufacturing of ADAIR, MDX or any other product, third-party manufacturers must obtain regulatory approval of their manufacturing facilities, processes and quality systems. In addition, pharmaceutical manufacturing facilities are continuously subject to inspection by the FDA and foreign regulatory authorities before and after product approval. Due to the complexity of the processes used to manufacture pharmaceutical products and product candidates, any potential third-party manufacturer may be unable to continue to pass or initially pass federal, state or international regulatory inspections in a cost-effective manner.

If a third-party manufacturer with whom we contract is unable to comply with manufacturing regulations, we may be subject to fines, unanticipated compliance expenses, recall or seizure of our products, total or partial suspension of production and/or enforcement actions, including injunctions, and criminal or civil prosecution. These possible sanctions would adversely affect our financial results and financial condition.

***We currently have no manufacturing, sales or distribution capabilities to market and sell ADAIR, MDX or any other product candidate. If we do not establish these capabilities, we will rely primarily on third parties to market and sell our products.***

While we have begun to implement pre-commercialization activities, we currently have no manufacturing, sales or distribution capabilities. To the extent we rely on third-parties to commercialize our product candidates, if marketing approval is obtained, we may receive less revenue than if we were to have commercialized the products ourselves. In addition, we would have less control over the sales efforts of any third-parties involved in our commercialization efforts. In the event that we are unable to collaborate with a third-party marketing and sales organization to commercialize our products, particularly for broader patient populations, our ability to generate revenue will be limited.

***The commencement and completion of clinical trials can be delayed or prevented for a number of reasons.***

We may not be able to commence or complete the clinical trials that would support our submission of an NDA to the FDA. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our clinical trials. Clinical trials can be delayed or prevented for a number of reasons, including:

- difficulties obtaining regulatory approval to commence or complete a clinical trial, or complying with conditions imposed by a regulatory authority regarding the scope or term of a clinical trial;
- delays in reaching or failing to reach agreement on acceptable terms with prospective contract research organizations, or CROs, contract manufacturing organizations, or CMOs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- failure of our third-party contractors, such as CROs and CMOs, or our investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner;
- insufficient or inadequate supply or quality of a product candidate or other materials necessary to conduct our clinical trials;
- difficulties obtaining institutional review board, or IRB, approval to conduct a clinical trial at a prospective site;
- the FDA requiring alterations to any of our study designs, our pre-clinical strategy or our manufacturing plans;
- challenges recruiting and enrolling subjects to participate in clinical trials for a variety of reasons, including size and nature of subject population, proximity of subjects to clinical sites, eligibility criteria for the trial, nature of trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications;
- difficulties in maintaining contact with subjects after treatment, which results in incomplete data;
- receipt by a competitor of marketing approval for a product targeting an indication that our product targets, such that we are not “first to market” with our product candidate;
- governmental or regulatory delays and changes in regulatory requirements, policy and guidelines; and
- varying interpretations of data by the FDA and similar foreign regulatory agencies.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRBs at the sites where the IRBs are overseeing a trial, or a data safety monitoring board overseeing the clinical trial at issue, or other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities;
- unforeseen safety issues, including serious adverse events associated with a product candidate, or lack of effectiveness; and
- lack of adequate funding to continue the clinical trial.

***Obtaining approval of an NDA even after clinical trials that are believed to be successful is an uncertain process.***

Even if we complete our planned clinical trials and believe the results to be successful, all of which are uncertain, obtaining approval of an NDA is an extensive, lengthy, expensive and uncertain process, and the FDA (and other regulatory agencies) may delay, limit or deny approval of ADAIR or any other product candidate for many reasons, including:

- we may not be able to demonstrate to the satisfaction of the FDA that the product candidate is safe and/or effective for any indication;
- we may not be able to demonstrate to the satisfaction of the FDA that the product candidate is bioequivalent to an approved listed drug, if applicable;
- we may observe different bioavailability of our product candidate as compared with an approved listed drug in a food effect study, which may result in our product candidate not being approved by the FDA or approved with certain relevant label language;
- clinical studies to demonstrate certain desirable label language (e.g., abuse-deterrent properties using a particular route) may not be feasible or practical, leading to an inability to obtain such desirable label language;
- the results of clinical trials may not meet the level of statistical significance or clinical significance required by the FDA for approval;
- the FDA may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the FDA may not find the data from pre-clinical studies and clinical trials sufficient to demonstrate that the product's clinical and other benefits outweigh its safety risks;
- the FDA may disagree with our interpretation of data from pre-clinical studies or clinical trials;
- the FDA may impose a Risk Evaluation and Mitigation Strategy, or REMS, program as part of the development program;
- the FDA may not accept data generated at our clinical trial sites;
- the data collected from pre-clinical studies and clinical trials may not be sufficient to support the submission of an NDA;
- the FDA may have difficulties scheduling an advisory committee meeting in a timely manner, or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional pre-clinical studies or clinical trials, limitations on approved labeling, or distribution and use restrictions, or may recommend against including some or all of the proposed labeling language proposed for the product;
- the FDA may require development of a risk evaluation and mitigation strategy as a condition of approval;
- the FDA may identify deficiencies in the manufacturing processes or facilities of third party manufacturers with which we enter into agreements for clinical and commercial supplies;
- the FDA may change its approval policies or adopt new regulations; and

- the FDA may require that an NDA application for ADHD also include other sub-populations, delaying an approval for our proposed sub-population.

Before we can submit an NDA to the FDA, we may be required to conduct multiple registration studies, which are trials intended to support FDA product registration. Registration studies frequently produce unsatisfactory results even if prior clinical trials were successful. Therefore, the results of the additional trials that we conduct may or may not be successful. The FDA may suspend all clinical trials or require that we conduct additional clinical, nonclinical, manufacturing validation or drug product quality studies and submit those data before it will consider or reconsider the NDA. Depending on the extent of these or any other studies, approval of any applications that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve the NDA. If any of these outcomes occur, we would not receive approval for our product candidates and may be forced to cease operations.

Even if we obtain FDA approval for our product candidates, the approval might contain significant limitations related to use restrictions for certain age groups, warnings, precautions or contraindications, or may be subject to significant post-marketing studies or risk mitigation requirements. If we are unable to successfully commercialize our product candidates, we may be forced to cease operations.

***Even if ADAIR or any other product candidate we may develop receives marketing approval, there could be adverse effects not discovered during development.***

Even if any of our product candidates receives marketing approval, we or others may later identify undesirable side-effects caused by the product or problems with our third-party manufacturers or manufacturing processes, and in either event a number of potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw their approval of the product;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications or distribution and use restrictions;
- regulatory authorities may require us to issue specific communications to healthcare professionals, such as “Dear Doctor” letters;
- regulatory authorities may issue negative publicity regarding the affected product, including safety communications;
- we may be required to change the way the product is administered, conduct additional pre-clinical studies or clinical trials or restrict the distribution or use of the product;
- 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 affected product candidate and could substantially increase commercialization costs or even force us to cease operations.

***Obtaining regulatory approval for conducting clinical trials in children, if needed, will be more difficult than obtaining such approvals for adult clinical trials since the requirements for regulatory approval to conduct pediatric clinical trials are more stringent.***

Pediatric drug development requires additional non-clinical work (such as animal studies in juvenile animals and additional reproductive toxicity work), as well as staged clinical work in determining safe dosing and monitoring. These additional tasks involve investment of significant additional resources beyond those needed for development of the drug for adults. Development of our drug for children may be significantly delayed due to these additional requirements.

***Changes in regulatory requirements and guidance or unanticipated events during our clinical trials may occur, which may result in necessary changes to clinical trial protocols, which could result in increased costs to us, delay our development timeline or reduce the likelihood of successful completion of our clinical trials.***

Changes in regulatory requirements and guidance or unanticipated events during our clinical trials may occur, as a result of which we may need to amend clinical trial protocols. Amendments may require us to resubmit our clinical trial protocols to IRBs for review and approval, which may impact the cost, timing or successful completion of a clinical trial. If we experience delays in completion of, or if we terminate, any of our clinical trials, the commercial prospects for our product candidates would be harmed and our ability to generate product revenue would be delayed, possibly materially.

***Current and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize MDX, ADAIR or any other product candidate that we develop and affect the prices we may set.***

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval for MDX, ADAIR or any other product candidate that we develop, restrict or regulate post-approval activities and affect our ability to profitably sell MDX, ADAIR or any other product candidate for which we obtain marketing approval.

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

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for drugs. In addition, this legislation authorized Medicare Part D prescription drug plans to limit the number of drugs that will be covered in any therapeutic class. As a result of this legislation and the expansion of federal coverage of drug products, we expect that there will be additional pressure to contain and reduce costs. These cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products and could seriously harm our business. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively PPACA, was enacted. The PPACA is a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and the health insurance industry, impose new taxes and fees on the healthcare industry and impose additional health policy reforms. This law revises the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states once the provision is effective. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may require us to modify our business practices with healthcare practitioners. While the U.S. Supreme Court upheld the constitutionality of most elements of the PPACA in June 2012, other legal challenges are still pending final adjudication in several jurisdictions. In addition, Congress has also proposed a number of legislative initiatives, including possible repeal of the PPACA. At this time, it remains unclear whether there will be any changes made to the PPACA, whether to certain provisions or its entirety. We can provide no assurance that the PPACA, as currently enacted or as amended in the future, will not adversely affect our business and financial results, and we cannot predict how future federal or state legislative or administrative changes relating to healthcare reform will affect our business.

***Even if ADAIR or any other product candidate that we develop receives marketing approval, we will continue to face extensive regulatory requirements and the product may still face future development and regulatory difficulties.***

Even if marketing approval is obtained, a regulatory authority may still impose significant restrictions on a product's indications, conditions for use, distribution or marketing or impose ongoing requirements for potentially costly post-market surveillance, post-approval studies or clinical trials. For example, any labeling ultimately approved by the FDA for ADAIR, if it is approved for marketing, may include restrictions on use. ADAIR will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, advertising, distribution, promotion, recordkeeping and submission of safety and other post-market information, including adverse events, and any changes to the approved product, product labeling, or manufacturing process. The FDA has significant post-market authority, including, for example, the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate serious safety risks related to the use of a drug. These risks include adverse drug interactions and concomitant therapy with other medications. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current Good Manufacturing Practice, or cGMP, and other regulations.



***If we obtain approval to commercialize ADAIR, MDX or any other product candidate outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.***

If MDX, ADAIR, or any other product candidate is approved for commercialization outside the United States, we will likely enter into agreements with third parties to market the product candidate outside the United States. We expect that we will be subject to additional risks related to entering into or maintaining international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- differing U.S. and foreign drug import and export rules;
- reduced protection for intellectual property rights in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- potential liability resulting from development work conducted by these distributors; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

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 revenues from our product candidates. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

***If we receive marketing approval for ADAIR, MDX or any other product candidate, sales will be limited unless the product achieves broad market acceptance.***

The commercial success of ADAIR, MDX or any other product candidate for which we obtain marketing approval from the FDA or other regulatory authorities will depend upon the acceptance of the product by the medical community, including physicians, patients and healthcare payors. The degree of market acceptance of any approved product will depend on a number of factors, including:

- demonstration of clinical safety and efficacy compared to other products;
- the relative convenience and ease of administration;
- the prevalence and severity of any adverse side effects;
- limitations or warnings contained in the product's approved labeling;
- distribution and use restrictions imposed by the FDA or agreed to by us as part of a mandatory or voluntary risk management plan;

- availability of alternative treatments, or competitive products already approved or expected to be commercially launched in the near future;
- pricing and cost effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- our ability to obtain sufficient third-party coverage or reimbursement; and
- the willingness of patients to pay for drugs out of pocket in the absence of third-party coverage.

If MDX, ADAIR or any other product candidate, is approved but does not achieve an adequate level of acceptance by physicians, healthcare payors and patients, we may not generate sufficient revenue from the product, and we may not become or remain profitable. In addition, our efforts to educate the medical community and third-party payors on the benefits of the product may require significant resources and may never be successful.

***The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have improperly promoted off-label uses, we may become subject to significant liability.***

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. In particular, any labeling approved by the FDA for ADAIR, MDX or any other product candidate may include restrictions on use, such as limitations on how the indication is defined and diagnosed, limiting the use to a specific population, such as a defined age group, or limiting the product to second-line or concomitant therapy. The FDA may impose further requirements or restrictions on the distribution or use of the product as part of a mandatory plan, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. If we receive marketing approval for one of our product candidates, physicians may nevertheless prescribe the product to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

***It will be difficult for us to profitably sell ADAIR, MDX or any other product candidate if reimbursement for the product is limited.***

Market acceptance and sales of ADAIR, MDX or any other product candidate will depend on reimbursement policies and may be affected by healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that reimbursement will be available for our products and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product for which we obtain marketing approval. In addition, third-party payors are likely to impose strict requirements for reimbursement in order to limit off label use of a higher priced drug. Reimbursement by a third-party payor may depend upon a number of factors including the third-party payor's determination that use of a product candidate is:

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

Obtaining coverage and reimbursement approval for a product candidate from a government or other third-party payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical, and cost effectiveness data for the use of our product candidates to the payor. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our product candidates. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize certain of our product candidates profitably, or at all, even if approved.

***Our market is subject to intense competition. If we are unable to compete effectively, ADAIR, MDX or any other product candidate that we develop may be rendered noncompetitive or obsolete.***

There are a number of existing treatments for ADHD currently on the market, all of which are marketed by pharmaceutical companies that are far larger and more experienced than we are. The FDA has not approved any drugs specifically for the treatment of Fragile X or its symptoms, although there are several pharmaceutical companies with compounds to treat Fragile X in late stage clinical development. Patients and doctors are often unwilling to change medications, and this factor will make it difficult for ADAIR, MDX or any other product candidates to penetrate the market. Further, our industry is highly competitive and subject to rapid and significant technological change. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. All of these competitors currently engage in, have engaged in or may engage in the future in the development, manufacturing, marketing and commercialization of new pharmaceuticals, some of which may compete with ADAIR, MDX or other product candidates we may have in the future. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. These companies may have products in development that are superior to our product candidates. Key competitive factors affecting the commercial success of ADAIR, MDX and any other product candidates that we may develop in the future are likely to be efficacy, time of onset, safety and tolerability profile, reliability, convenience of dosing, price and reimbursement.

Many of our potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of drug candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Established competitors may invest heavily to quickly discover and develop novel compounds that could make ADAIR, MDX or other product candidates we may develop obsolete. Accordingly, our competitors may be more successful than we may be in obtaining FDA and other marketing approvals for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render ADAIR, MDX or any other product candidate that we develop obsolete or non-competitive before we can recover the expenses of developing and commercializing the product. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. Finally, the development of new treatment methods for the diseases we are targeting could render ADAIR, MDX or any other product candidate that we develop non-competitive or obsolete.

***We face potential product liability exposure, and, if claims are brought against us, we may incur substantial liability.***

The use of ADAIR, MDX or other drugs exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers or others selling or otherwise coming into contact with our products. If we cannot successfully defend ourselves against product liability claims, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for ADAIR, MDX or any other product candidate for which we obtain marketing approval;
- impairment of our business reputation and exposure to adverse publicity;
- increased warnings on product labels;
- withdrawal of clinical trial participants;
- costs of related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- loss of revenue; and
- the inability to successfully commercialize ADAIR, MDX or any other product candidate for which we obtain marketing approval.

***If product liability lawsuits are successfully brought against us, our insurance may be inadequate.***

We expect to obtain insurance before we conduct clinical trials. However, our insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, the insurance market experiences significant changes from year to year due to various factors including the international claims record and general reinsurance terms. Therefore, coverage may become more expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for ADAIR, MDX or any other product candidate, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain this product liability insurance on commercially reasonable terms. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial. A successful product liability claim or series of claims brought against us could cause our share price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

The product liability insurance we will need to obtain in connection with the commercial sales of our product candidates if and when they receive regulatory approval may be unavailable in meaningful amounts or at a reasonable cost. If we are the subject of a successful product liability claim that exceeds the limits of any insurance coverage we obtain, we would incur substantial charges that would adversely affect our earnings and require the commitment of capital resources that might otherwise be available for the development and commercial launch of our product programs.

### **Risks Related to Our Reliance on Third Parties**

***We have no manufacturing capacity and may choose to rely on third-party manufacturers for our products.***

We do not currently operate manufacturing facilities for clinical production of MDX, ADAIR or any other product candidate. We do not intend to develop facilities for the manufacture of products for clinical trials or commercial purposes in the foreseeable future. We will rely on third-party manufacturers to produce bulk drug products required for our clinical trials on a timely basis. We plan to continue to rely upon CMOs and, potentially, collaboration partners to manufacture commercial quantities of our drug product candidates if and when approved for marketing by the applicable regulatory authorities. If the third-party manufacturing sources we rely on cease to be available to us on commercially reasonable terms or on a timely basis, we may not be able to complete development, production and marketing of MDX, ADAIR or any other product candidate.

In June 2015, we entered into a Development and Clinical Manufacture Services Agreement, or the Services Agreement, with M.W. Encap Limited, or Encap, pursuant to which Encap provides formulation development and clinical manufacturing services of ADAIR to Alcobra. The term of the Services Agreement is for the longer of two years or the completion or termination of the services provided pursuant to the Services Agreement. In February 2016, and pursuant to the provision of the Services Agreement, we entered into a term sheet with Capsugel US, LLC, or Capsugel, an affiliate of Encap, in connection with commercial manufacturing of the pharmaceutical product, or the Product, containing the active pharmaceutical ingredient forming ADAIR.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including reliance on the third party for regulatory compliance and quality assurance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control (including a failure to synthesize and manufacture our product candidates in accordance with our product specifications) and the possibility of termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or damaging to us. We will be dependent on the ability of these third-party manufacturers to produce supplies of drug product adequate to support our clinical development programs and future commercialization of our products.

***Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our current and potential future product candidates.***

We may seek collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of our current and potential future product candidates. We may enter into these arrangements on a selective basis depending on the merits of retaining commercialization rights for ourselves as compared to entering into selective collaboration arrangements with other pharmaceutical or biotechnology companies for each product candidate, both in the United States and internationally. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements should we so choose to enter into such arrangements. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations.

Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision making authority.

Even with respect to certain other programs that we intend to commercialize ourselves, we may enter into agreements with collaborators to share in the burden of conducting clinical trials, manufacturing and marketing our product candidates or products. In addition, our ability to apply our proprietary technologies to develop proprietary compounds will depend on our ability to establish and maintain licensing arrangements or other collaborative arrangements with the holders of proprietary rights to such compounds. We may not be able to establish such arrangements on acceptable terms or at all.

Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

***We currently depend on third parties to conduct our clinical trials.***

We rely on third parties, such as CROs, medical institutions, clinical investigators and contract laboratories to oversee some of the operations of our clinical trials and to perform data collection and analysis. If we are unable to maintain or enter into agreements with these third parties on acceptable terms, or if any such agreement is terminated, we may be unable to enroll patients on a timely basis or otherwise conduct our trials in the manner we anticipate. Even if we are able to maintain or enter into such agreements, we may face additional delays outside of our control if these parties do not perform their obligations in a timely fashion or in accordance with regulatory requirements. If these third parties do not successfully carry out their contractual duties or obligations and 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 or for other reasons, our financial results and the commercial prospects for MDX, ADAIR or any other potential product candidates could be harmed, our costs could increase and our ability to obtain regulatory approval and commence product sales could be delayed.

**Risks Related to Our Intellectual Property**

***We have filed multiple patent applications and have four issued patents by the U.S. PTO, and 11 issued patents in other jurisdictions. There can be no assurance that any of our other patent applications will result in issued patents. As a result, we may have limited protection of our proprietary technology in the marketplace.***

We have filed patent applications in many countries worldwide. These applications cover a range of areas including: different formulations of metadoxine, uses of metadoxine for cognitive impairments, new molecular derivatives of metadoxine, and methods for determining responsiveness to metadoxine treatment. Additionally, we have recently filed patent applications directed to Abuse-Deterrent Amphetamine Immediate-Release (ADAIR) for ADHD. As of December 31, 2016, we have four issued U.S. patents, covering the composition of the sustained release form of MDX, the use of metadoxine for ADHD, and new molecular derivatives of metadoxine. We also have eight issued patents in Australia, Canada, Japan, India, Israel, Mexico, Russia and Europe that cover the composition of the sustained release form of MDX. The European patent includes the following territories: Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czech Republic, Germany, Denmark, Estonia, Spain, Finland, France, United Kingdom, Greece, Croatia, Hungary, Ireland, Iceland, Italy, Lithuania, Latvia, Luxembourg, Monaco, Malta, Netherlands, Norway, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia and Turkey. Additionally, we have eight issued patents in Australia, China, Eurasia, Hong Kong, Israel, Japan, Mexico and New Zealand that cover the use of metadoxine for ADHD. The Eurasian patent includes the following territory: Russian Federation. Unless and until other pending applications issue, their additional protective scope is impossible to determine.

It is impossible to predict whether or how many of these additional applications will result in issued patents. Even if pending applications issue, they may issue with claims significantly narrower than those we currently seek. The patent position of biotechnology and pharmaceutical companies is generally uncertain because it involves complex legal and factual considerations. The standards applied by the U.S. PTO and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. Consequently, patents may not issue from our pending patent applications. As such, we do not know the degree of future protection that we will have on our proprietary products and technology.

***The patent positions of pharmaceutical products are complex and uncertain and therefore we cannot predict the scope and extent of patent protection for MDX with respect to our issued patents, or any patents we may be issued in the future.***

The patents we were issued as well as any additional patents that may in the future issue to us will not ensure the protection of our intellectual property for a number of reasons, including without limitation the following:

- any issued patents may not be broad or strong enough to prevent competition from other products including identical or similar products;
- if we are not issued additional patents or if issued patents expire, there would be no protections against competitors making generic equivalents;
- there may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim;
- there may be other patents existing in the patent landscape for MDX that will affect our freedom to operate;
- if our issued patents or future patents, if issued, are challenged, a court could determine that they are not valid or enforceable;
- a court could determine that a competitor's technology or product does not infringe our issued patents or future patents, if issued;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- our issued patents and future patents, if issued, could irretrievably lapse due to failure to pay fees or otherwise comply with regulations, or could be subject to compulsory licensing; and
- if we encounter delays in our development or clinical trials, the period of time during which we could market our products under patent protection would be reduced.

***We may not be able to enforce our intellectual property rights throughout the world. This risk is exacerbated for us because metadoxine is manufactured and used in a number of foreign countries in other applications.***

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. This risk is exacerbated for us because metadoxine is manufactured and used in a number of foreign countries in other applications and is generally available. The manufacture of metadoxine and its use in other indications will not infringe our intellectual property rights, and will make it more difficult to monitor and enforce any patent rights that may be issued to us.

The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of any in-licensed patents we may acquire or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain adequate protection for our technology and the enforcement of intellectual property.

***We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our products.***

Our commercial success depends significantly on our ability to operate without infringing the patents and other intellectual property rights of third parties. For example, there could be issued patents of which we are not aware that our products infringe. There also could be patents that we believe we do not infringe, but that we may ultimately be found to infringe. Moreover, patent applications are in some cases maintained in secrecy until patents are issued. The publication of discoveries in the scientific or patent literature frequently occurs substantially later than the date on which the underlying discoveries were made and patent applications were filed. Because patents can take many years to issue, there may be currently pending applications of which we are unaware that may later result in issued patents that our products infringe. For example, pending applications may exist that provide support or can be amended to provide support for a claim that results in an issued patent that our product infringes.

Third parties may assert that we are employing their proprietary technology without authorization. If a court held that any third-party patents are valid, enforceable and cover our products or their use, the holders of any of these patents may be able to block our ability to commercialize our products unless we obtained a license under the applicable patents, or until the patents expire. We may not be able to enter into licensing arrangements or make other arrangements at a reasonable cost or on reasonable terms. Any inability to secure licenses or alternative technology could result in delays in the introduction of our products or lead to prohibition of the manufacture or sale of products by us. Even if we or any future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing one or more of our products or be forced to cease some aspect of our business operations if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. This could harm our business significantly.

***We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.***

We rely on trade secrets to protect our proprietary know-how and technological advances, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights. Failure to obtain or maintain trade secret protection could enable competitors to use our proprietary information to develop products that compete with our products or cause additional, material adverse effects upon our competitive business position.

***Under applicable employment laws, we may not be able to enforce covenants not to compete and therefore may be unable to prevent our competitors from benefiting from the expertise of some of our former employees.***

We generally enter into non-competition agreements with our employees and certain key consultants. These agreements prohibit our employees and certain key consultants, if they cease working for us, from competing directly with us or working for our competitors or clients for a limited period of time. We may be unable to enforce these agreements under the laws of the jurisdictions in which our employees work and it may be difficult for us to restrict our competitors from benefitting from the expertise our former employees or consultants developed while working for us. For example, Israeli courts have required employers seeking to enforce non-compete undertakings of a former employee to demonstrate that the competitive activities of the former employee will harm one of a limited number of material interests of the employer which have been recognized by the courts, such as the secrecy of a company's confidential commercial information or the protection of its intellectual property. If we cannot demonstrate that such interests will be harmed, we may be unable to prevent our competitors from benefiting from the expertise of our former employees or consultants and our ability to remain competitive may be diminished.

***Any lawsuits relating to infringement of intellectual property rights necessary to defend ourselves or enforce our rights will be costly and time consuming.***

Our ability to defend our intellectual property may require us to initiate litigation to enforce our rights or defend our activities in response to alleged infringement of a third party. In addition, we may be sued by others who hold intellectual property rights who claim that their issued patents are infringed by MDX or any future products or product candidates. These lawsuits can be very time consuming and costly. There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries generally.

In addition, our patents and patent applications, or those of our licensors, could face other challenges, such as interference proceedings, opposition proceedings, and re-examination proceedings. Any of these challenges, if successful, could result in the invalidation of, or in a narrowing of the scope of, any of our patent and patent applications subject to challenge. Any of these challenges, regardless of their success, would likely be time consuming and expensive to defend and resolve and would divert our management's time and attention.

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

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity. Therefore, obtaining and enforcing pharmaceutical 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. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening 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 decisions by the U.S. Congress, the federal courts, and the U.S. PTO, 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.

***Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.***

The U.S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

***Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our ordinary shares to decline.***

During the course of any patent litigation, there could be public announcements of the results of hearings, rulings on motions and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our products, programs or intellectual property could be diminished. Accordingly, the market price of our ordinary shares may decline.

#### **Risks Related to Our Business Operations and Industry**

***We are a clinical-stage company with no approved products, which makes it difficult to assess our future viability.***

We are a clinical-stage biopharmaceutical company with a limited operating history. We have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan, we will need to successfully:

- execute product candidate development activities;
- obtain required regulatory approvals for the development and commercialization of our product candidates;
- maintain, leverage and expand our intellectual property portfolio;
- build and maintain robust sales, distribution and marketing capabilities, either on our own or in collaboration with strategic partners;
- gain market acceptance for our products;
- develop and maintain any strategic relationships we elect to enter into; and
- manage our spending as costs and expenses increase due to drug discovery, pre-clinical development, clinical trials, regulatory approvals and commercialization.

If we are unsuccessful in accomplishing these objectives, we may not be able to develop product candidates, raise capital, expand our business or continue our operations.



***We manage our business through a small number of employees and key consultants. We depend on them even more than similarly-situated companies.***

Our key employees include our Chief Executive Officer, Dr. Yaron Daniely, who has been with us since 2010, our Chief Financial Officer and Chief Operating Officer, Dr. Tomer Berkovitz, who has been with us since 2014, our Chief Medical Officer, Dr. Jonathan Rubin, who has been with us since 2013, our Chief Commercial Officer, Mr. David Baker, who has been with us since 2014, our Senior Director CMC (chemistry, manufacturing and controls), Mr. David Siner, who has been with us since 2014, our Vice President of Finance, Ms. Irena Katsman, who has been with us since 2015, our Senior Vice President of Preclinical Development, Dr. Johanna Schumann, who has been with us since 2013, and our Director of Regulatory Affairs, Mr. Elad Ben David, who has been with us since 2015. Our future growth and success depend on our ability to recruit, retain, manage and motivate our employees and key consultants. The loss of the services of our Chief Executive Officer, our Chief Financial Officer or any of our key employees or the inability to hire or retain experienced management personnel could adversely affect our ability to execute our business plan and harm our operating results. Although we have employment agreements in place with management, these agreements are terminable at will with minimal notice.

Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific and technical consultants. In particular, the loss of one or more of our senior executive officers or key consultants could be detrimental to us if we cannot recruit suitable replacements in a timely manner. We do not currently carry “key person” insurance on the lives of members of senior management. The competition for qualified personnel in the pharmaceutical field is intense. Due to this intense competition, we may be unable to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel.

***If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, our shareholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our Ordinary Shares.***

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our Ordinary Shares.

We are required to disclose changes made in our internal controls and procedures on an annual basis and our management is required to assess the effectiveness of these internal controls annually. However, for as long as we are an “emerging growth company” under the Jumpstart our Business Startups Act of 2012, or the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act. We could be an emerging growth company for up to five years from our initial public offering in 2013. An independent assessment of the effectiveness of our internal controls could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

***Our relationships with customers and third-party payors in the United States and elsewhere will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal, state and foreign healthcare laws and regulations include the following:

- the Medicare-Medicaid Anti-Fraud and Abuse Act, as amended, or the Anti-Kickback Statute, prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government and also includes provisions allowing for private, civil whistleblower or “qui tam” actions;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program. HIPAA and HITECH also regulate the use and disclosure of identifiable health information by health care providers, health plans and health care clearinghouses, and impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of identifiable health information as well as requiring notification of regulatory breaches. HIPAA and HITECH violations may prompt civil and criminal enforcement actions as well as enforcement by state attorneys general;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Health Care Reform Law requires manufacturers of drugs, devices, biologics and medical supplies to report to the U.S. Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests;
- analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures; and
- analogous anti-kickback, fraud and abuse and healthcare laws and regulations in foreign countries may also apply.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

***If our employees commit fraud or other misconduct, including noncompliance with regulatory standards and requirements and insider trading, our business may experience serious adverse consequences.***

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state healthcare fraud and abuse laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

In addition, during the course of our operations, our directors, executives and employees may have access to material, nonpublic information regarding our business, our results of operations or potential transactions we are considering. Despite the adoption of an Insider Trading Policy, we may not be able to prevent a director, executive or employee from trading in our Ordinary Shares on the basis of, or while having access to, material, nonpublic information. If a director, executive or employee was to be investigated, or an action was to be brought against a director, executive or employee for insider trading, it could have a negative impact on our reputation and our stock price. Such a claim, with or without merit, could also result in substantial expenditures of time and money, and divert attention of our management team from other tasks important to the success of our business.

***Our business may be affected by macroeconomic conditions.***

A deterioration in global economic conditions and uncertainties may have an adverse effect on our business. Interest rates and the ability to access credit markets could adversely affect the ability of patients and distributors to purchase, pay for and effectively distribute our products. Similarly, these macroeconomic factors could affect the ability of our CMOs, sole-source or single-source suppliers to remain in business or otherwise manufacture or supply product. Failure by any of them to remain a going concern could affect our ability to manufacture products.

#### **Risks Related to Our Ordinary Shares**

***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 shares may not be sustained. It may be difficult for you to sell your shares at all or without depressing the market price for the 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 has been and is likely to continue 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 our products;
- 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;
- any major changes in our Board of Directors or management;
- actions of investors and shareholders, including proxy contests;
- legislation in the United States relating to the sale or pricing of pharmaceuticals; or
- future substantial sales of our Ordinary Shares.

In addition, the stock market in general, and NASDAQ Stock Market 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.

***We are subject to the continued listing criteria of the NASDAQ Global Market, and our failure to satisfy these criteria (in particular, the minimum bid price requirement) may result in the delisting of our Ordinary Shares.***

For a period of time, since the start of 2017 (which followed our announcements of the failure of our Phase 3 clinical trial for MDX), the closing price of our Ordinary Shares on the NASDAQ Global Market fell below \$1.00 per share. Under NASDAQ Listing Rule 5550(a)(2), we are required to maintain a minimum bid price of \$1.00 per share in order to maintain compliance with the continued listing qualifications. We are currently in compliance as our Ordinary Shares achieved a minimum bid closing price of at least \$1.00 per share for a minimum of ten consecutive business days. We intend to monitor the bid price for our Ordinary Shares, and we will consider all available options to resolve any potential deficiency and regain compliance with the NASDAQ Global Market's minimum bid price requirement. If we are unable to resolve a potential future deficiency, our Ordinary Shares could be delisted from the NASDAQ Global Market, in which case investors may face material adverse consequences, including, but not limited to, the lack of a trading market for our Ordinary Shares, reduced liquidity and decreased analyst coverage of our shares. We, in turn, would face much greater difficulty in obtaining additional financing to fund our operations and other strategic plans.

***We may be subject to any number of legal proceedings.***

On December 16, 2014, a class action lawsuit was filed against us and certain of our current and former officers and directors in the U.S. District Court for the Southern District of New York. The complaint, brought by a putative class of investors, alleges, among other things, that our officers and directors made false or misleading statements relating to the results of our Phase 3 study for our MDX drug candidate. On May 20, 2015, we moved to dismiss the complaint. On March 30, 2016, the Court accepted the motion to dismiss all charges against the Company.

On February 17, 2017, a class action lawsuit was filed against us and certain of our current officers (one of whom also is a director) in the U.S. District Court for the Southern District of New York. The case was filed on behalf of a putative class of investors who purchased or acquired our securities between August 13, 2015 and January 17, 2017. The complaint asserted violations of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 thereunder. The complaint alleged, among other things, that we and the individual defendants made false or misleading statements relating to the results of our second Phase 3 clinical trial for our MDX drug candidate.

Such legal proceedings, regardless of their outcome, could be costly, divert management's attention, or damage our reputation and demand for our products. Litigation, particularly in the United States, is inherently unpredictable and unexpectedly high awards of damages can result if we receive an adverse verdict. In many cases, particularly in the United States, the practice of the plaintiffs' bar is to claim damages (compensatory, punitive and statutory) in extremely high amounts. Accordingly, it is difficult to quantify the potential exposure to claims in many proceedings of the type mentioned above. Unfavorable resolution of current and similar future proceedings could have a material adverse effect on our financial condition and results of operations. We may become subject to monetary and/or non-monetary sanctions and/or may be required to make significant provisions in our accounts related to legal proceedings, which could have a material adverse effect on our financial condition and results of operations.

***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 we were to be characterized as a passive foreign investment company, or PFIC, for U.S. tax purposes, U.S. holders of our Ordinary Shares could have adverse U.S. income tax consequences.***

If we were to be characterized as a PFIC under the U.S. Internal Revenue Code of 1986, as amended, or the Code, in any taxable year during which a U.S. taxpayer owns Ordinary Shares, such U.S. holder could be liable for additional taxes and interest charges upon certain distributions by us and any gain recognized on a sale, exchange or other disposition, including a pledge, of the Ordinary Shares, whether or not we continue to be a PFIC. 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 believe that we may be deemed a PFIC. 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. Were we to be classified as a PFIC, a U.S. investor may be able to mitigate some of the adverse U.S. federal income tax consequences with respect to owning the Ordinary Shares for our taxable year ended December 31, 2016, provided that such U.S. investor is eligible to make, and successfully makes, a "mark-to-market" election. U.S. investors could also mitigate some of the adverse U.S. federal income tax consequences of us being classified as a PFIC by making a "qualified electing fund" election, provided that we provide the information necessary for a U.S. investor to make such an election. We intend to make available to U.S. investors upon request the information necessary for U.S. holders to make qualified electing fund elections. 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. For more information see Item 10.E. Taxation "U.S. Federal Income Tax Consequences."

***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 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. In recent months and following the results of MEASURE, several analysts dropped coverage of our company or downgraded their price targets. We do not have any control over these analysts and we cannot provide any assurance that remaining analysts will cover us or provide favorable coverage. If any of the analysts who may cover us adversely change their recommendation regarding our 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. Moreover, the Israeli Companies Law 5759 – 1999, or the Israeli Companies Law, imposes certain restrictions on our ability to declare and pay dividends. See Item 10.B. Articles of Association “Dividend and Liquidation Rights” for additional information.

***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 the Sarbanes-Oxley Act, listing requirements 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 the NASDAQ Stock Market may also impose various additional requirements on public companies. As a result, we incur additional legal, accounting and other expenses that we did not incur as a nonpublic company. These expenses are at least several hundred thousand dollars annually.

***The JOBS Act 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;
- our ability not to comply with new accounting principles that do not apply to public companies until such accounting principles become applicable to private companies; and
- 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.

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 the completion of our initial public offering in 2013, (b) in which we have total annual gross revenue of at least \$1.07 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 30<sup>th</sup>, and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

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.

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

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

In addition, as a foreign private issuer, we are exempt from the rules and regulations under the Exchange Act related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders are exempt from the reporting and short-swing profit recovery provisions contained in Section 16 of the Exchange Act. In addition, we are not required under the Exchange Act to file annual, quarterly and current reports and financial statements with the SEC as frequently or as promptly as domestic U.S. issuers whose securities are registered under the Exchange Act. Also, although a recent amendment to the Israeli Companies Law will require us to disclose the annual compensation of our five most highly compensated senior officers on an individual basis (rather than on an aggregate basis, as was permitted under the Israeli Companies Law for Israeli public companies listed overseas, such as in the U.S., prior to such amendment), this disclosure will not be as extensive as that required of a U.S. domestic issuer. For example, it currently appears as if the disclosure required under Israeli law would be limited to compensation paid in the immediately preceding year without any requirement to disclose option exercises and vested stock options, pension benefits or potential payments upon termination or change of control. These exemptions and leniencies will reduce the frequency and scope of information and protections to which you are entitled as an investor.

#### **Risks Related to Israeli Law and Our Operations in Israel**

***Provisions of Israeli law may make it easy for our shareholders to demand that we convene a shareholders meeting, and/or allow shareholders to convene a shareholder meeting without the consent of our management, which may disrupt our management's ability to run our company.***

Section 63(b) of the Israeli Companies Law may allow any one or more of our shareholders holding at least 5% of our voting rights to demand that we convene an extraordinary shareholders meeting. Also, in the event that we deny to convene an extraordinary shareholders meeting pursuant to such a request, Section 64 of the Israeli Companies Law provides that such shareholders may independently convene an extraordinary shareholders meeting and require us to cover the costs. If our shareholders decide to exercise these rights in a way inconsistent with our management's strategic plans, our management's ability to run our company may be disrupted, and this process may entail significant costs to us.

***Our business and the market price of our stock could be negatively affected as a result of a proxy fight.***

On April 12, 2017, Brosh Capital L.P., Exodus Capital L.P., and certain of their affiliates, or the Brosh Group, who together purport to beneficially own approximately 16.8% of our Ordinary Shares, called an extraordinary general meeting of shareholders in order to, among other things, remove all current members of the Board of Directors and to elect five new directors nominated by the Brosh Group. This extraordinary general meeting is scheduled to take place on May 23, 2017. The Company intends to pursue legal action to confirm its view that the extraordinary general meeting is being called unlawfully by the Brosh Group. The Board of Directors has recommended that shareholders vote against the removal of the current directors and against the election of the nominees of the Brosh Group, and the Company is soliciting proxies from shareholders on this basis. Our business, operating results or financial condition could be harmed by this proxy contest because, among other things:

- Responding to the proxy contest is costly and time-consuming, is a significant distraction for our Board of Directors, management and employees, and diverts the attention of our Board of Directors and senior management from the pursuit of our business strategy, which could adversely affect our results of operations and financial condition;

- Perceived uncertainties as to our future direction, our ability to execute on our strategy, or changes to the composition of our Board of Directors or senior management team may lead to the perception of a change in the direction of our business, instability or lack of continuity which may be exploited by our competitors, and may result in the loss of potential business opportunities and make it more difficult to attract and retain qualified personnel and business partners; and

- The expenses for legal and advisory fees and administrative and associated costs incurred in connection with responding to the proxy contest and the related litigation may be substantial.

In addition, the market price of our common stock could be subject to significant fluctuation or otherwise be adversely affected by the uncertainties described above or the outcome of the proxy contest.

***Provisions of Israeli law and our amended and restated 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 our outstanding shares. Furthermore, the shareholders, including those who indicated their acceptance of the tender offer, may, at any time within six months following the completion of the tender offer, petition an Israeli court to alter the consideration for the acquisition, unless the acquirer stipulated in its tender offer that a shareholder that accepts the offer may not seek such appraisal rights.

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 Taxation Considerations" for additional information.

Our amended and restated 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.

***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, the Hamas militant group and the Hezbollah. 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. Since October 2000, there have been increasing occurrences of terrorist violence. In 2006, a conflict between Israel and the Hezbollah in Lebanon resulted in thousands of rockets being fired from Lebanon into Israel. In 2008, Israel engaged in an armed conflict with Hamas in the Gaza Strip, which involved missile strikes against Israel and negatively affected business conditions in Israel. In 2012 and 2014, Israel experienced a similar armed conflict, resulting in hundreds of rockets being fired from the Gaza Strip. Ongoing and revived hostilities or other Israeli political or economic factors, such as, an interruption of operations at the Tel Aviv airport, could prevent or delay shipments of our components or products. If continued or resumed, these hostilities may negatively affect business conditions in Israel in general and our business in particular. In the event that hostilities disrupt the ongoing operation of our facilities or the airports and seaports on which we depend to import and export our supplies and any product candidates, our operations may be materially adversely affected.

In addition, since 2010 political uprisings and conflicts in various countries in the Middle East, including Egypt and Syria, are affecting the political stability of those countries. It is not clear how this instability will develop and how it will affect the political and security situation in the Middle East. This instability has raised concerns regarding security in the region and the potential for armed conflict. Any potential future conflict could also include missile strikes against parts of Israel, including our offices and facilities. Such instability may lead to deterioration in the political and trade relationships that exist between the State of Israel and certain other countries. 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. Several countries, principally in the Middle East, still restrict doing business with Israel and Israeli companies, and additional countries may impose restrictions on doing business with Israel and Israeli companies if hostilities in Israel or political instability in the region continues or increases. Similarly, Israeli companies are limited in conducting business with entities from countries that are considered to be in a state of war with Israel. 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 or for any resulting disruption in our operations. 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 and the government may cease providing such coverage or the coverage might not suffice to cover potential damages. 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.

***Exchange rate fluctuations between the U.S. dollar and the New Israeli Shekel currencies may increase our expenses.***

The vast majority of our expenses are in U.S. dollars and New Israeli Shekels, or NIS. Our functional currency is the U.S. dollar and substantially all of our financial resources are denominated by 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. For instance, in 2016, approximately 20% of our expenses were denominated in NIS. Changes of 5% and 10% in the U.S. dollar - NIS exchange rate would have increased/decreased our operating expenses by 0.97% and 1.86%, respectively. The exchange rate as of December 31, 2016 was \$1.00 = NIS 3.845. 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.

***In the past, we received Israeli government grants for certain of our research and development activities. The terms of those grants may require us, in addition to payment of royalties, to satisfy specified conditions in order to manufacture products and transfer technologies outside of Israel. We may be required to pay penalties in addition to repayment of the grants.***

Our research and development efforts, during the period between May 1, 2009 and April 30, 2010, were financed in part through royalty-bearing grants, in an amount of \$106,494 that we received from the Israel Innovation Authority, or the IIA, (formerly known as the Office of the Chief Scientist) of the Israeli Ministry of Economy and Industry. With respect to such grants we are obligated to pay royalties at a rate of 3% to 5% on sales proceeds from MDX, according to the IIA's approval, the company is required to pay royalties from any income generated in connection with delayed release metadoxine tablets up to the total amount of grants received, linked to the U.S. dollar and bearing interest at an annual rate of LIBOR applicable to dollar deposits.

A recent amendment, or Amendment No. 7, to the Law for the Encouragement of Research, Development and Technological Innovation in the Industry, 1984-5744, or the R&D Law, mandated the formation of the IIA to replace the Chief Scientist. Pursuant to Amendment No. 7, the IIA may establish new guidelines and promulgate new regulations under the R&D Law. These changes in the structure of the IIA and the R&D Law may affect our existing or future IIA programs and related obligations. At this stage, we cannot predict what changes, if any, the new authority may make.

The R&D Law and the regulations promulgated thereunder provide that when a company develops know-how, technology or products using IIA grants, the terms of these grants and the R&D Law restrict the transfer of such know-how, and the transfer of manufacturing or manufacturing rights of such products, technologies or know-how outside of Israel, without the prior approval of the IIA. Therefore, if aspects of our technologies are deemed to have been developed with IIA funding according to the R&D Law, the discretionary approval of the IIA may be required for any transfer to third parties outside of Israel of know-how or manufacturing or manufacturing rights related to those aspects of such technologies, and may result in payment of increased royalties (both increased royalty rates and increased royalties ceilings) and/or payment of additional amounts to the IIA. We may not receive those approvals. Furthermore, according to the R&D Law, the IIA may impose certain conditions on any arrangement under which it permits us to transfer technology or development out of Israel (including for the purpose of manufacturing).



The R&D Law and the regulations promulgated thereunder provide that the transfer of IIA-supported technology or know-how outside of Israel may involve the payment of additional amounts depending upon the value of the transferred technology or know-how, the amount of IIA support, the time of completion of the IIA-supported research project and other factors up to a maximum of six times the amount of grants received. These restrictions and requirements for payment may impair our ability to sell our technology assets outside of Israel or to outsource or transfer development or manufacturing activities with respect to any product or technology outside of Israel. Furthermore, the consideration available to our shareholders in a transaction involving the transfer outside of Israel of technology or know-how developed with IIA funding (such as a merger or similar transaction) may be reduced by any amounts that we are required to pay to the IIA.

Our obligations and limitations pursuant to the R&D Law are not limited in time and may not be terminated by us at will. As of the date hereof, we have not been required to pay any royalties with respect to the IIA grants. As of the date hereof, production of bulk drug substance and drug products required for our clinical trials does not involve manufacture of IIA supported products, technologies or know-how, and/or transfer of IIA supported technologies or know-how, and therefore no IIA's approval has been sought after or required in connection with such production by our third-party manufacturers.

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

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

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

The rights and responsibilities of the holders of our Ordinary Shares are governed by our amended and restated 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 the Company and other shareholders, and to refrain from abusing its power in the Company. See Item 7. "Major Shareholders and Related Party Transactions" 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.

***We are subject to anti-takeover provisions that could delay or prevent our acquisition by another entity.***

Provisions of Israeli corporate and tax law and of our amended and restated articles of association may have the effect of delaying, preventing or making more difficult any merger or acquisition of us. In addition, any merger or acquisition of us will require the prior consent of the IIA, if intellectual property is removed from Israel, as well as the Investment Center of the Israeli Ministry of Industry, Trade and Employment, or the Investment Center. Israeli law regulates mergers, votes required to approve a merger, acquisition of shares through tender offers and transactions involving significant shareholders. Any of these provisions may make it more difficult to acquire us. Accordingly, our acquisition by another entity could be delayed or prevented even if it would be beneficial to our shareholders.

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

Our male 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). In this connection, we note that our Chief Financial Officer and Chief Operating Officer, Dr. Tomer Berkovitz, is 37 years old. In the event of a military conflict, they and other of our key personnel or consultants 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.

## ITEM 4. INFORMATION ON THE COMPANY

### 4.A. History and development

We are an Israeli corporation based in Tel Aviv and were incorporated in 2008. Our principal executive offices are located at Azrieli Triangle Building, 132 Derech Menachem Begin, 39<sup>th</sup> Floor, Tel Aviv 6701101 Israel, and our telephone number is +972 72 220 4661. Our website address is [www.alcobra-pharma.com](http://www.alcobra-pharma.com). The information contained on, or that can be accessed through, our website is not part of this form. 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 of 1933, or the Securities Act, as modified by 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” such as not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002. We could remain an “emerging growth company” for up to five years from our initial public offering in 2013, or until the earliest of (a) the last day of the first fiscal year in which our annual gross revenue exceeds \$1.07 billion, (b) the date that we become a “large accelerated filer” as defined in Rule 12b-2 under the U.S. Securities Exchange Act of 1934, as amended, or the Exchange Act, which would occur if the market value of our Ordinary Shares that is held by non-affiliates exceeds \$700 million as of the last business day of our most recently completed second fiscal quarter, or (c) the date on which we have issued more than \$1 billion in nonconvertible debt during the preceding three-year period. Our wholly owned U.S. subsidiary, Alcobra, Inc., has been appointed our agent in the United States and is located at 101 West Elm Street, Suite 350, Conshohocken, PA, 19428.

We did not have any significant capital expenditures in 2014, 2015 and 2016. We have financed our capital expenditures with cash generated from proceeds from sales of our equity securities. We do not anticipate any significant capital expenditures in fiscal year 2017.

### 4.B. Business overview

#### Who We Are

We are an emerging pharmaceutical company primarily focused on the development and commercialization of proprietary pharmaceutical products. Our product candidates include: (i) ADAIR, a proprietary, abuse-deterrent oral formulation of immediate-release (short-acting) dextroamphetamine for the treatment of ADHD and Narcolepsy; and (ii) MDX, a proprietary oral drug, for the treatment of ADHD and other cognitive disorders, including Fragile X. We are currently exploring strategic alternatives, which may include acquisition of new assets and/or partnering or monetization of our existing products.

#### ADAIR for the Treatment of ADHD

Stimulant abuse is unique and challenging since the abuse and addiction risks of stimulants are not restricted to those who are prescribed the medications. Published data report that stimulants are almost twice as likely to be diverted (i.e., given away or sold) than other scheduled medications, such as opioid, sleep or anxiety medications. It has been reported that between 25-60% of teenagers and college students with ADHD have been approached at some point to give away or sell their prescription stimulants and over 60% of college students with ADHD admit to having diverted their ADHD prescription medication.

Immediate-Release, or IR, stimulants are more prone to abuse than Extended-Release stimulants and are the fastest growing market in the ADHD market in recent years. According to IMS, between 2010 and 2016, the total US prescription count for ADHD medications grew by 44%, from almost 49 million to over 70 million prescriptions, and half of that growth went to IR stimulants. In 2016, 26 million prescriptions were filled in the United States for IR stimulants.

In terms of routes of abuse, published studies report that 40% or more of people who misuse or abuse prescription stimulants, do so by snorting or injecting these products. These methods of abuse drive a more rapid increase in dopamine levels that drive the subjective, or re-enforcing effects of these drugs. Consequently, these abuse routes are thought to bring the abuser one step closer to addiction and dependence.

Abuse of prescription central nervous system, or CNS stimulants is a large and growing public health challenge, yet the ADHD market is devoid of any abuse-deterrent products. This unmet need prompted us to design ADAIR as an oral formulation of an IR short-acting dextro-amphetamine, and included the development and in vitro testing of multiple formulations, followed by the selection of the optimal, proprietary formulation of ADAIR that is intended to introduce certain barriers limiting this product’s abuse by snorting or injecting.

We held a pre-IND meeting with the FDA in January 2017 to present our drug candidate and discuss the development path and requirements to support an NDA filing for ADAIR. The meeting results confirmed a roadmap for a potentially rapid 505(b)(2) development path towards a planned NDA submission for ADAIR in the second half of 2018.

We intend to be the first to introduce a proprietary abuse-deterrent IR dextro-amphetamine drug to the market, and intend to leverage our agility, flexibility and know-how to utilize such a position for the benefit of patients, physicians and our community.

### **MDX for the Treatment of ADHD**

In contrast to the most common available treatments, which involve the use of stimulants, MDX is not a stimulant and employs a different mechanism of action that is neither dopaminergic (related to dopamine) nor noradrenergic (related to norepinephrine). To date, we have conducted several clinical studies in MDX for ADHD, including two Phase 3 studies described below.

In October 2014, we reported the results of a 300 subject double-blind placebo-controlled Phase 3 study in adult ADHD. The study's primary efficacy endpoint did not reach statistical significance. A non-significant favorable trend was observed on the primary efficacy measure, the change from baseline to endpoint in the investigator version of the 18 item Conners Adult ADHD Rating Scale (CAARS-Inv). Other secondary measures showed strong or statistically significant trends. Similar to previous studies, MDX showed a favorable safety profile.

In the second quarter of 2015, we launched the MEASURE study (MDX Evaluation in Adults — Study of Response and Efficacy). The MEASURE study was our second Phase 3 study of MDX in adults with ADHD. The study included design and operational elements to potentially mitigate placebo response and reduce treatment response variability. In September 2016, the FDA placed a full clinical hold on our IND applications for MDX in ADHD and Fragile X. The FDA indicated that the clinical hold was due to adverse neurophysiological findings in long-term pre-clinical studies. Following the clinical hold and our meeting with the FDA, we decided to analyze the data of Full Analysis Set (n=283) from the study. In January 2017, we reported that the MEASURE study did not reach the primary efficacy measure, the change from baseline to endpoint in the CAARS-Inv.

### **MDX for the Treatment of Fragile X**

We are also studying MDX for the treatment of Fragile X, a rare neurogenetic disorder related to autism marked by severe intellectual disability. In June 2015, we reported that our Phase 2 exploratory clinical study of MDX in adolescent and adult patients with Fragile X did not achieve statistical significance on the primary measure, the change from baseline to endpoint in the inattentive subscale of the ADHD Rating Scale-IV, yet demonstrated statistically significant improvements in certain clinically meaningful behavioral and cognitive endpoints, including the Vineland II Daily Living Skills Assessment. The FDA has granted fast track designation and Orphan Drug status to MDX for the treatment of Fragile X.

In October 2015, we met with the FDA to discuss the results of our Phase 2 study in Fragile X and the requirements for NDA submission of MDX in this therapeutic indication. The FDA concurred that results from a single short-term, adequate and well-controlled efficacy study in adolescents and adult patients with Fragile X may be sufficient to support a claim of efficacy for approval of MDX in this indication (in line with the FDA's Guidance for Industry — Providing Evidence of Effectiveness for Human Drug and Biological Products, May 1998). We plan to submit a separate application for pediatric patients (ages 4-11) following FDA approval via a supplemental NDA. The FDA confirmed that the Vineland II Daily Living Skills Assessment could serve as the primary assessment in the adolescents and adults Fragile X pivotal study. In September 2016, the FDA placed a full clinical hold on our IND applications for MDX in ADHD and Fragile X. We may explore business development opportunities for Fragile X outside the United States.

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, MDX, ADAIR or any other product candidate. As of December 31, 2016, we had an accumulated deficit of \$95.6 million.

### **Our Strategic Plan**

Our objective is to develop and commercialize proprietary pharmaceutical products. To this effect, we intend to develop and seek marketing approvals from the FDA and other worldwide regulatory bodies for ADAIR, MDX and other potential product candidates. We may seek partnership or monetization opportunities for MDX and/or ADAIR. In addition, we explore strategic alternatives, including transformative M&A opportunities, to enhance our pipeline. To achieve these objectives, we plan to:

- seek the necessary regulatory approvals to complete the clinical development of ADAIR for the treatment of ADHD and, if successful, file for marketing approval in the United States and other territories;
- seek the necessary regulatory approvals to complete the clinical development of MDX independently or in conjunction with other pharmaceutical companies for the treatment of ADHD and/or Fragile X in adults and children, and, if successful, file for marketing approval in the United States, Europe, and/or other territories;
- seek monetization opportunities for MDX;
- prepare to commercialize ADAIR by establishing independent distribution capabilities or in conjunction with other pharmaceutical companies in the U.S. and other key markets; and
- continue our business development activities and seek partnering, licensing, M&A opportunities or other transactions to further develop our pipeline and drug-development capabilities and take advantage of our financial resources for the benefit of increasing shareholder value.

## **About Stimulant Abuse**

Stimulants, including over-the-counter and prescription medicines and illicitly manufactured and distributed drugs, are among the most widely abused substances. The most severe public health and societal problems related to stimulants result from abuse of illicitly manufactured stimulants including cocaine, methamphetamine, and various synthetic stimulants.

The class of drugs collectively referred to as “stimulants” includes amphetamine-based medicines placed in Schedule II of the CSA, methylphenidate and prescription cocaine. Schedule II is reserved for drugs that carry the highest risk of abuse and dependence yet which have been approved for medicinal use. The most widely used first line medications for ADHD are the amphetamine and methylphenidate-containing stimulant products. The methylphenidate-containing products are all single active entity products, whereas the amphetamine products included amphetamine as well as mixed amphetamine salts.

Prescription stimulants, while being an established, effective and recommended pharmacologic treatment for ADHD, are also widely misused and abused; however, users of this category of product do not demonstrate singular patterns of use, or associated risks and outcomes. Nonmedical use of prescription stimulants includes both abuse, e.g., to “get high” and produce “euphoria”, as well as misuse, e.g., to enhance the ability to meet occupational demands, alertness while driving, and improve academic performance by enhancing alertness and counteracting fatigue and sleepiness. Abuse can produce severe adverse consequences, and on rare occasions also death, and contributes to diversion of medicines from prescribed users, as well as illicit marketing. Furthermore, nonmedical use of prescription stimulants, even for the intent of occasional enhancement of alertness and performance, can also lead to more harmful patterns of use of stimulants.

Prescription products are often diverted for use by nasal insufflation, smoking and injecting. An abuse-deterrent formulation may do little to discourage oral ingestion to enhance occupational or academic performance, i.e., misuse, but, depending on the properties of the formulation, could reduce the risks of adverse effects by anyone who would attempt to abuse it by nasal insufflation, smoking or injecting, and reduce the contribution of prescription stimulants to problems associated with stimulant abuse. Some studies suggest a relatively higher rate of abuse of IR formulations relative to extended release, or ER, formulations, although all of these medications carry the risk of abuse.

### **Potential Harms, Side Effects, and Other Public Health Consequences of Stimulant Abuse**

Abuse of amphetamines and other stimulants is associated with a number of negative health consequences. These individual and public health concerns have been extensively studied and well characterized in the medical literature.

#### *Acute Stimulant Intoxication*

Acute stimulant intoxication may result in a number of cardiovascular-related adverse events, including chest pain, myocardial infarction, palpitations, arrhythmias, thromboembolism, tachycardia, sinus bradycardia, ventricular premature depolarization, ventricular tachycardia degeneration resulting in the need for defibrillation, asystole, peripheral vasculopathy and/or sudden death from respiratory or cardiac arrest, as well as other adverse events such as strokes, seizures, pneumothorax, headaches and tinnitus. Stimulant intoxication is also associated with several psychiatric symptoms, including rambling speech, transient ideas, paranoid ideation, auditory hallucinations, tactile hallucinations and psychosis.

High dosages of amphetamines and other stimulants can lead to aggressive or violent behavior (which may lead to self-harm or harm to others), intense temporary anxiety resembling panic disorder or generalized anxiety disorder or mania, as well as paranoid ideation and psychotic episodes that resemble schizophrenia. Taking extremely high doses of stimulants may also result in dangerously high body temperatures, irregular heartbeat, cardiovascular problems and seizures.

#### *Consequences of Chronic Stimulant Misuse/Abuse*

Although it remains unclear whether the misuse of controlled medications precedes other substance use behaviors, stimulant misuse is correlated with a higher risk for substance use, with some evidence suggesting greater severity relative to controls.

Long-term stimulant abuse disorder can lead to chaotic behavior, social isolation, aggressive behavior and sexual dysfunction. Individuals exposed to amphetamine-type stimulants have been reported to develop stimulant use disorder in as rapidly as one week.

Furthermore, individuals may increase their use of stimulant products after abuse of amphetamines due to being conditioned to the positive reinforcing effects of euphoria, increased energy and enhanced social and vocational interactions. Users subsequently find that higher doses produce stronger psychoactive effects, and that non-approved routes of administration produce even greater effects. Tolerance to euphoria develops, followed by even more frequent use of larger amounts of stimulants.

Tolerance will develop with repeated use, and withdrawal symptoms (hypersomnia, increased appetite, dysphoria) may occur and enhance cravings. Stimulant withdrawal can lead to depression, suicidal ideation, irritability, anhedonia, emotional lability and disturbances in attention and concentration. There may be temporary depressive symptoms that may meet the criteria for major depressive episode. Stimulant use can also lead to conditioned responses to drug-related stimuli, which may lead to relapse in someone with a previous stimulant use disorder.

Extended abuse of stimulants can lead to psychological symptoms, such as hostility or paranoid psychosis. In addition to health status, the consequences of such substance use impact the individuals using drugs, their families and society at large, with severe repercussions possible at both the individual and public health level resulting from the chronic abuse and/or misuse of stimulants, such as teenage pregnancy, domestic violence, motor vehicle accidents, crime, poor work performance and impaired personal relationships.

#### **Regulatory Support for Abuse-Deterrent Technologies**

The general pharmacologic rationale for abuse-deterrent stimulants is similar to the rationale of abuse-deterrent opioids used to treat and manage pain as described in the FDA 2015 Guidance on Abuse-Deterrent Opioid. The FDA clearly articulated the rationale for the development of abuse-deterrent technologies, as well as cited its limitations, in its 2015 Guidance, pp. 1-2:

*Prescription opioid products are an important component of modern pain management. However, abuse and misuse of these products have created a serious and growing public health problem. One potentially important step towards the goal of creating safer opioid analgesics has been the development of opioids that are formulated to deter abuse. FDA considers the development of these products a high public health priority. Because opioid products are often manipulated for purposes of abuse by different routes of administration or to defeat extended-release (ER) properties, most abuse-deterrent technologies developed to date are intended to make manipulation more difficult or to make abuse of the manipulated product less attractive or less rewarding. It should be noted that **these technologies have not yet proven successful at deterring the most common form of abuse—swallowing a number of intact capsules or tablets to achieve a feeling of euphoria.** Moreover, the fact that a product has abuse-deterrent properties does not mean that there is no risk of abuse. It means, rather, that **the risk of abuse is lower than it would be without such properties.** Because opioid products must in the end be able to deliver the opioid to the patient, there may always be some abuse of these products.*

Regulatory communications regarding the application of abuse-deterrent technologies for approved stimulants continue to emerge. In 2014, Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research, stated that the FDA encourages the development of abuse-deterrent formulations for controlled substances, while also noting that the science surrounding abuse-deterrent technology is relatively new. In public meetings, FDA officials have made comments related to interest in the application of abuse-deterrent technologies for stimulants, as well as other drugs of abuse. In practice, it has been evident that the FDA engages with sponsors of abuse-deterrent formulations on a product-by-product basis, sometimes requiring an abuse-deterrent assessment as part of the development to inform approval and labeling processes by the FDA.

## **Relationship between Route of Administration, Speed of Onset and Abuse Potential**

Abuse-deterrent stimulants would be expected to contribute to comprehensive drug control and public health improvement by potentially reducing at least the most dangerous routes of abuse of prescription stimulants. Such formulations would potentially reduce the attractiveness of prescription stimulants as targets for diversion by those who prefer to tamper and otherwise use these stimulants by riskier routes of administration. However, because a large number of patients derive significant benefit from appropriate use of these prescription stimulants, any addition of an abuse-deterrent technology must preserve therapeutic access and utility of the medication.

Speed of onset/route of administration has been accepted as being important in evaluating an abuse-deterrent formulation, even though there have been few laboratory studies confirming its relationship with abuse potential. The relationship between route of administration, the rate of onset of subjective effects, and the abuse potential of drugs is generally accepted due to a history of anecdotal reports and clinical experience with drug abusers, though there is little epidemiological data to confirm this relationship.

In general, the oral route is associated with lower abuse liability because of slower absorption rates and slower onset of effects compared to other routes of administration. Inhalation, insufflation and injection of drugs are associated with far more rapid absorption and faster onset of effects when compared to oral ingestion. In general, oral use of stimulants results in the slowest rate of absorption, while insufflation is relatively faster; smoking and intravenous, or IV, use of stimulants evoke even more rapid absorption, and more intense and rapid physiological and subjective responses.

Amphetamine, like cocaine, forms molecules that are highly soluble in lipids, and is subsequently rapidly transported to the brain through the blood-brain barrier. Routes of administration that deliver the drug directly into the bloodstream (insufflation, smoking, IV), bypassing the digestive system, would be expected to cause faster onset of psychoactive effects. Therefore, reducing the risk of abuse via insufflation, smoking, and injection is a potential public health goal, because the speed of the absorption of stimulants is an important determinant of a product's abuse potential as is the case for opioids, and is also related to the overall potential risks of the drug product.

Many people who use amphetamines and other stimulants for the purposes of getting high prefer routes of administration that provide rapid onset of effects. Recreational users often administer psychostimulants at doses several-fold higher than those approved for therapeutic use. In order to achieve its maximum pharmacologic effect, the largest quantity of drug must be delivered into the CNS in the shortest possible time. For instance, a published study found that the reinforcing properties of methylphenidate occur when the drug elicits a large and fast dopamine increase but has only therapeutic properties when there is a slow, steady-state increase in dopamine caused by the drug. This leads drug abusers to progress from relatively safe methods of self-administration, such as oral ingestion of marketed doses of stimulants, to increasingly higher dosages and more dangerous routes of administration, e.g., smoking, insufflating and injecting.

Insufflation and oral administration of d-amphetamine in the range of 2.5-15 milligrams, or mg, produces a number of similar psychoactive effects to those caused from the use of cocaine (alertness, energetic vitality, confident assertiveness and a decrease in appetite and fatigue). Absorption through insufflation, however, is faster with more intense effects relative to oral administration.

In addition, the misuse and abuse of stimulants via alternate routes (i.e., other than oral) are associated with a number of other negative outcomes that may have greater impact on the individual and public health than those associated with oral abuse. Beyond the effects noted above in common with oral administration, abuse via insufflation can lead to sinusitis, irritation, bleeding of the nasal mucosa, and a perforated nasal septum. Smoking can lead to increased risk for respiratory problems such as coughing, bronchitis and pneumonitis.

Abuse via injection may lead to puncture marks and 'tracks'. Frequent injection may lead to increased risk of infection, including endocarditis and its complications such as stroke and transient ischemic attack, Hepatitis B, human immunodeficiency virus, and other blood-borne diseases. Injection has been found to be a significant predictor of the severity of psychological morbidity associated with amphetamine abuse, and avoidance of injection has been recommended as a step that users can take to reduce the negative psychological impact of amphetamine use.

## **Prevalence of Prescription Stimulant Misuse/Abuse**

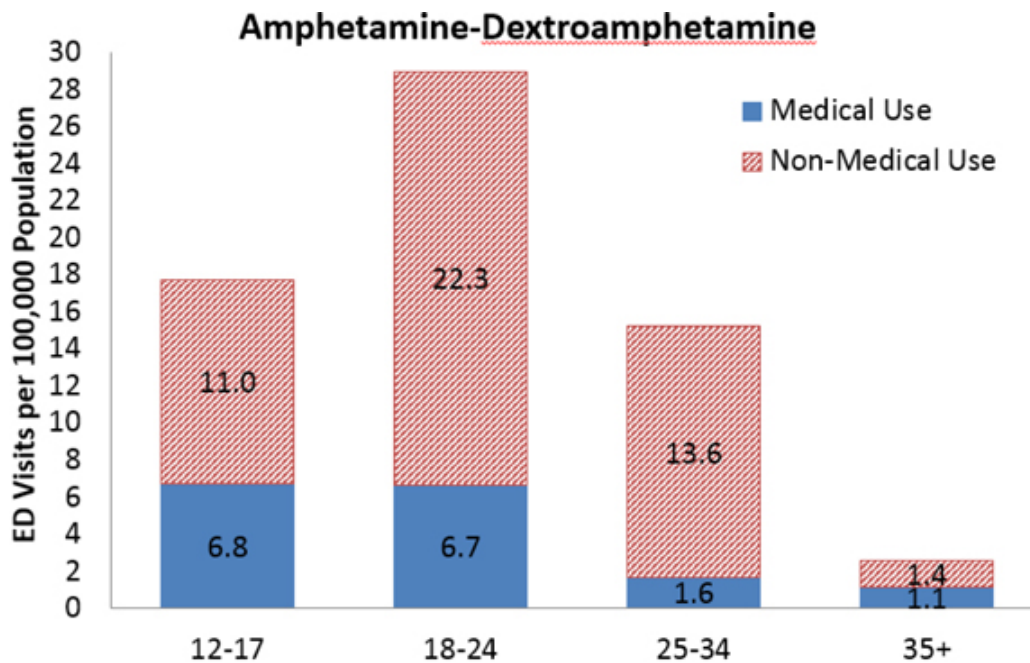
The National Survey on Drug Use and Health, or NSDUH, is an annual household-based survey of the U.S. population aged 12 years and older, which is used to estimate national prevalence statistics. It includes questions regarding nonmedical use of stimulants and queries lifetime use of some specific drugs. It does not ask about the use of specific drugs for the past year or past month, but rather asks about "stimulants" as a category separate from cocaine and methamphetamine. The data from the NSDUH are the most frequently cited for estimating the prevalence of drug misuse and abuse at a national level.

According to the 2015 NSDUH report, over 5 million individuals ages 12 years or older in the United States misused prescription stimulants in the previous year. This figure represents approximately 2% of the U.S. population in that age group. Rates of misuse of prescription stimulants increased from age 12 and peaked at age 21 where an estimated 10% of the population reported misuse of prescription stimulants, before declining in older adults. Among those who misused prescription stimulants, over 90% misused prescription amphetamines, e.g., Adderall, dextroamphetamine.

In addition to NSDUH, there are other surveillance efforts in the United States that can be used to monitor drug abuse, including abuse of stimulants. These efforts include the Drug Abuse Warning Network Emergency Department, or DAWN-ED.

DAWN-ED collected data from hospital emergency department visits that involve nonmedical use of prescription and over-the-counter medications as well as dietary supplements. Nonmedical use is defined in the DAWN system as: (1) taking a higher than prescribed or recommended dose of a pharmaceutical (contrary to directions or labeling); (2) taking a pharmaceutical product prescribed for another individual; (3) malicious poisoning of one individual by another; or (4) substance abuse involving pharmaceuticals. A location-stratified sample of 233 hospitals contributed data for the 2011 annual report (the last year from which data are available); sample weights were applied to estimate national figures taking into account hospital size and ownership, metropolitan area and underlying population. DAWN-ED data cannot be used to estimate prevalence, however, since the system relies on spontaneous visits to these facilities. The 2011 DAWN-ED data (2011) for stimulants and other drugs shows that whereas analgesics including opioids were by far the most frequently reported CNS drug involved in emergency department visits reported by DAWN-ED. More than 40,000 emergency department visits involving nonmedical use of stimulants were reported by the DAWN system, confirming that non-medical use of stimulants is also a serious problem. The DAWN-ED data show that the vast majority of visits related to use of amphetamine-dextroamphetamine were due to nonmedical use (Figure 1). Data from 2004-2011 show that the estimated number of emergency department visits related to nonmedical use of amphetamine-dextroamphetamine formulations rose dramatically over this period, while rates of nonmedical use of other stimulants have remained relatively low and stable (Figure 2).

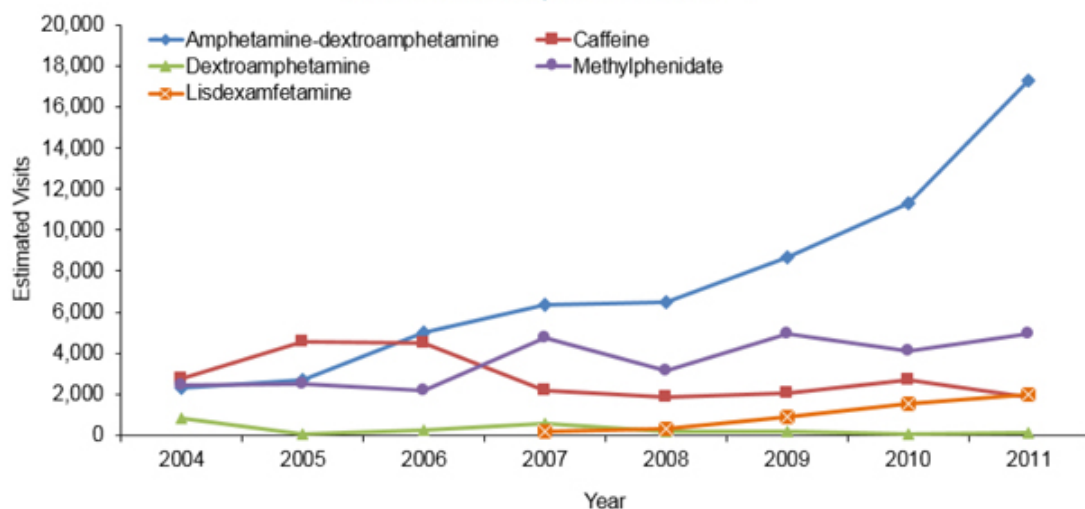
Figure 1: DAWN: Rates of ED Visits by Type of Use and Age (years), 2011



Source: Drug Abuse Warning Network – Emergency Department

Figure 2: DAWN: Estimated ED Visits Related to Nonmedical Use of CNS Stimulants, 2004-2011.

## Estimated ED Visits Related to Nonmedical Use of CNS Stimulants, 2004-2011



**Notes:**

- 1) DAWN reported a total of 1,244,872 estimated visits related to nonmedical use of pharmaceuticals in 2011. CNS stimulants accounted for 40,648 (3.3%) of these reports. Drug mentions are not mutually exclusive.
- 2) For the years 2004-2011, DAWN did not release dextroamphetamine estimates due to reliability issues. Similarly, for the years 2007 & 2008, DAWN did not release lisdexamfetamine estimates. The estimates reported in this figure for those drugs and those specific years were calculated from DAWN public-use datasets.

Source: Drug Abuse Warning Network – Emergency Department

Monitoring the Future, or MTF, is a national annual survey that has been conducted every year since 1975 by the University of Michigan on behalf of the U.S. National Institutes of Health. The survey of 8th, 10th, 12th graders is used to measure prevalence and attitudes concerning drug abuse. This survey also collects data on a sample of college students and young adults. The survey includes questions regarding past month, past year and lifetime prevalence of use of various drugs, including stimulants. The MTF report reported in 2015 that the prevalence of non-medical use of prescription amphetamines such as Adderall had grown to 7.5% of all 12<sup>th</sup> graders. In comparison, the prevalence figures for non-medical use by young adults and college students were 7.7% and 10.7%, respectively.

### Epidemiologic Data on Routes of Administration

Review of published literature on nonmedical amphetamine use seems to identify two distinct patterns of misuse/abuse, correlating with different routes of administration and populations. In surveys of undergraduate and graduate student populations, misuse of amphetamines is commonly reported for the purposes of cognitive enhancement (improving work/academic performance, studying for exams) and generally involves oral misuse. Oral use is the most common route of administration among this population. Alternatively, publications reporting on amphetamine abuse in populations of drug users, toxic exposures and experienced drug abusers generally include descriptions of routes that deliver the drug in the most rapid and efficient way possible, such as IV injection.

Although it remains unclear whether the misuse of controlled medications precedes other substance use behaviors, stimulant misusers manifest not only a higher risk for substance use disorder but also a more severe form of it when compared to controls.

While the publicly available sources of epidemiological data do not contain the necessary information to validate this theory of distinct populations of misusers and abusers, the published studies examined in this document seem to support it. Studies of nonmedical use of stimulants conducted in educational settings (colleges, universities), where misuse was most likely associated with sporadic cognitive enhancement, showed that the population surveyed reported misuse primarily through the oral route and also through insufflation (snorting). There were also reports of smoking and injection among members of this population. In contrast, among experienced amphetamine abusers, it has been reported that rates of injection were much higher and in some cases dominated the routes of administration for use.



## Therapeutic Needs and Potential Benefits

### Role of IR Stimulants in Treatment of ADHD

Currently, we are not aware of any approved stimulants in the United States with abuse deterrent labeling, as exists for abuse deterrent opioid painkillers. Clinicians and patients benefit from having a range of treatment options for ADHD, as patients' needs vary. IR stimulants are useful for treatment of ADHD in pediatric and adult patients.

Clinical evidence of the efficacy of both IR and ER stimulants suggests that effective treatment of ADHD depends on delivery of appropriate dosing throughout the day. Patients may use a combination of short and long-acting formulations in order to achieve maximal effect. Short-acting stimulants can be used in some patients with ADHD to avoid sleep disturbances.

### Prescribing Data

Prescribing data provides additional evidence of the therapeutic need for IR amphetamine (AMP) products. From 2010 to 2016, prescriptions for ADHD stimulants increased 44%, from close to 49 million to over 70 million prescriptions. During that period, prescriptions for IR stimulants increased nearly 75% (14.7 million to 25.6 million) (source: IMS Health, National Prescription Audit™ [NPA™]). IR stimulants are the most commonly prescribed medication for adults with ADHD and constitute 50% of ADHD prescriptions for adults (vs. 46% ER stimulants and 4% non-stimulant medicines). Of those prescriptions for IR stimulants, the majority were for IR AMP (84% vs. 16% IR methylphenidate [MPH]).

### ADAIR Product Description

We are developing ADAIR to create barriers to the intranasal, or IN, and IV abuse of IR amphetamine. ADAIR was selected as the lead candidate abuse-deterrent dextroamphetamine sulfate formulation following an extensive evaluation of multiple prototypes tested by dissolution and lab abuse-deterrence assessments, as compared to the evaluation of 10 mg IR dextroamphetamine sulfate reference tablets. ADAIR is an oral, semi-solid, liquid-filled, hard gelatin capsule of an abuse-deterrent IR formulation of dextroamphetamine sulfate, currently manufactured as 10 mg capsules. Additional dosage forms (5–30 mg) are planned.

A set of abuse-deterrence studies, largely based on the FDA guidelines from April 2015 "Abuse-Deterrent Opioids — Evaluation and Labeling; Guidance for Industry," and March 2016 "General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products," have been conducted in collaboration with Capsugel. The physically manipulated preparation of ADAIR (grinding, crushing or cutting the capsule following thermal pre-treatment) could not appreciably pass through a 500 micrometer, or  $\mu\text{m}$ , filter, a particle size deemed unsuitable for insufflation. In contrast, 42-47% of the physically manipulated IR dextroamphetamine reference tablet passed through the 500  $\mu\text{m}$  filter, suggesting that it could be insufflated. In comparison with the IR dextroamphetamine reference tablet, ADAIR demonstrated reduced syringeability across a range of volumes of water (2, 5 and 10 milliliters), needle gauges (26, 23, 20 and 18 gauge), in ambient or hot water, and when passed through a cigarette filter. ADAIR mixed in water yielded a viscous, cloudy material, which was usually impossible, and at other times difficult, to syringe. Texture analysis demonstrated that the force required to push the plunger with a manipulated ADAIR filled syringe is far greater than that with manipulated IR dextroamphetamine reference tablet. These studies demonstrate that, as compared to the IR dextroamphetamine reference tablet, ADAIR could display deterrence properties for abuse via IN and IV routes of administration.

### Clinical Development Plan

We intend to develop ADAIR for registration through the 505(b)(2) approval pathway, based on a single pivotal bioequivalence study comparing ADAIR and IR dextroamphetamine 10 mg tablet, and to request additional labeling based on studies which demonstrate the IN and IV abuse-deterrence characteristics of the product. The FDA's 505(b)(2) pathway permits the filing of an NDA that contains full safety and efficacy reports, but where at least some of the information required for approval comes from studies not conducted by or for the applicant. Such information could include the FDA's findings of safety and efficacy in the approval of a similar drug, and for which the applicant has not obtained a right of reference and/or published literature. This approach could expedite the development program for our product candidate by potentially decreasing the amount of clinical data that we would need to generate in order to obtain FDA approval.

The pivotal bioequivalence study will evaluate dextroamphetamine concentrations upon oral administration of ADAIR at a dose of 10 mg (intact capsule) compared to dextroamphetamine concentrations with oral administration of the reference comparator, IR dextroamphetamine sulfate 10 mg tablet. Bioequivalence will be established using statistical analyses as specified by FDA guidance.

A food effect study will evaluate dextroamphetamine concentrations upon oral administration of ADAIR at a dose of 10 mg (intact capsule) given after an overnight fast compared to the dextroamphetamine concentrations with oral administration of ADAIR at a dose of 10 mg (intact capsule) given after consumption of a standard high fat meal. Bioavailability will be established using statistical analyses as specified by FDA guidance.

We will consider conducting an IN human abuse potential study following the evaluation of the feasibility of administering the ADAIR formulation in the nose. A human abuse potential study is conducted in experienced drug users. The drug-liking response to IN ADAIR will be compared with the drug-liking response to IN dextroamphetamine. In addition, the drug-liking response to IN ADAIR will be compared with the drug-liking response to placebo. To demonstrate IN abuse-deterrence, ADAIR should show reduced drug-liking compared to dextroamphetamine, and drug-liking similar to placebo.

We may also consider conducting a Phase 3 study in adults with ADHD (the FDA approved label for dextroamphetamine sulfate tablets already includes adults for the narcolepsy indication, but does not include adults for the ADHD indication). The extension of the label to adults is highly relevant given that most substance abuse of stimulants is observed in younger adults.

## About ADHD

### The ADHD Market

According to IMS Health, the United States market capitalization for ADHD treatment is estimated to be approximately \$10 billion annually, which accounted for approximately 90% of the global ADHD market in 2016. The difference in market sizes between the United States and other countries is driven by different rates of diagnosis and treatment, different pricing, and the number of available brand name medications (non-U.S. markets are dominated by generic drugs). Global prevalence rates of the disease are estimated to be approximately 8-10% of school-aged children and approximately 4-5% of the adult population. Adult diagnosis and treatment, which has grown at approximately 10% annually over the last few years, is forecasted to grow in the near future due to increased disease awareness and less sociological stigmatization towards the condition. In the United States, the rate of treatment with prescription medications is approximately 70% in children and 45% in adults. In 2016, over 70 million prescriptions were filled in the United States for approved ADHD medications whereas less than 44 million prescriptions were filled in 2009. The U.S. market is projected to continue to grow in mid-single digits, driven by an increased prescription rate for adult ADHD. The growth of IR Amphetamines has averaged over 12% annually over the past five years and is projected to continue to grow faster than the overall ADHD market in the foreseeable future.

The international ADHD market is projected to grow at a faster rate than the U.S. market in part because of higher disease recognition and acceptance is expected to increase in both Japan and Europe. The estimated growth rate for the non-U.S. markets is also higher due to the recent launches of major ADHD drugs that have already been marketed in the U.S., such as Vyvanse and Intuniv.

### Development of ADHD Symptoms

Once perceived to only affect children, ADHD is now known to persist into adolescence and adulthood in a sizeable number of cases. The following table illustrates how the nature of ADHD symptoms changes with age:

<b>Children</b>	<b>Adolescents</b>	<b>Adults</b>
<b>Hyperactive</b>	<b>Easily distracted</b>	<b>Shifts activities</b>
<b>Aggressive</b>	<b>Inattentive</b>	<b>Easily bored</b>
<b>Low frustration tolerance</b>		<b>Impatient</b>
<b>Impulsive</b>		<b>Restless</b>

Approximately 50% of adults who suffered from ADHD as children continue to have symptoms of the disorder as adults, with over 90% experiencing attention deficit symptoms and about 35% of them experiencing hyperactivity-impulsivity symptoms. As the majority of sufferers of ADHD age, their symptoms tend toward impatience, restlessness, boredom and low concentration levels from the more aggressive hyperactivity and impulsive behavior evident in children.

Although the definitive causes of ADHD are still unclear, current research suggests that ADHD is caused by an interaction between environmental factors and genetic predispositions. Biologic factors that reportedly increase the risk of having ADHD include maternal smoking, drug or alcohol abuse during pregnancy, brain injury and exposure to toxins.

### Impact of Untreated and Undertreated ADHD

ADHD is believed to be one of the most under-diagnosed and under-treated mental health conditions facing children and adults. ADHD increases health risks, adverse social externalities and economic costs as illustrated in the following table. Despite the disorder being highly treatable, most adults with ADHD remain undiagnosed and untreated.

The following table illustrates the effects on society when ADHD remains untreated:

**Healthcare System**  
 ñ 50% in bicycle accidents  
 ñ 33% in ER visits  
 2-4x more car accidents

**Patient**  
 ñ criminal activity  
 ñ incarceration

**Family**  
 3-5x more divorce/separation  
 2-4x more sibling fights

**School and Occupation**  
 46% expelled  
 35% drop out  
 Lower occupational status

**Society**  
 Substance use disorders:  
 2x risk and earlier onset  
 Less likely to quit in adulthood

**Employer**  
 Increased parental absenteeism and  
 lower productivity

## Diagnosis of ADHD

The diagnosis of ADHD is obtained by a psychiatric assessment which is intended to eliminate other potential causes. A formal diagnosis is completed by a qualified physician and is based on a number of set criteria. The Diagnostic and Statistical Manual of Mental Disorders, fourth edition, or DSM-V, diagnostic criteria are most widely used to diagnose ADHD.

- *DSM-V criteria.* The American Psychiatric Association provides a set of standardized criteria for classifying mental disorders known as the Diagnostic and Statistical Manual of Mental Disorders, or DSM. These criteria are based on the premise that attention deficit are distinct and differentiated conditions that are abnormalities resulting from biological origins that can be reliably and objectively measured. The diagnostic criteria include:
  - inattention – the patient makes careless mistakes in activities and is easily distracted;
  - hyperactivity – the patient fidgets, squirms, talks excessively or displays restless behavior;
  - impulsiveness – the patient interrupts others and cannot wait for a turn;
  - there must be clear evidence of significant impairment in social, school, or work functioning;
  - signs of impairment present before 12 years of age and present in two or more settings (school/work and home); and
  - signs are not better accounted for by another mental disorder.

The DSM-V criteria are becoming more prevalent as the diagnostic measure for ADHD in Europe and Japan. If the DSM-V criteria are used, rather than an alternative measure in declining use, a diagnosis of ADHD is three to four times more likely. Consequently, the size of the market in Europe and Japan is set to grow with improved diagnosis rates driven by adoption of the DSM-V criteria.

## Key Products – ADHD

The table below lists the four, most sold (to the best of our knowledge) drugs to treat ADHD in 2014 on a worldwide basis are shown in the following table, together with the drug brand name, owner, and historic or expected peak sales. Of the drugs listed, Vyvanse, Concerta and Adderall XR are stimulants and Strattera is a non-stimulant drug.

<b>Brand (launch)</b>	<b>Generic Name</b>	<b>Owner</b>	<b>Global Sales in 2016 U.S. Dollars in Millions</b>	<b>Peak Global Sales U.S. Dollars in Millions</b>
Vyvanse (2007)	Lisdexamfetamine	Shire	2,014	> 2,500 (est. 2019)
Concerta (2000)	OROS Methylphenidate	J&J	863	1,326 (2009)
Strattera (2002)	Atomoxetine	Eli Lilly	855	855 (est. 2016)
Adderall XR (2001)	Mixed Amphetamine Salts	Shire	364	1,102 (2008)

### *Limitations of Current Treatment Options for ADHD*

Because of the significant side effects and abuse potential associated with current stimulant treatment options for ADHD which are classified in the same controlled substance category as narcotics, there is a significant need to develop safe and effective treatment alternatives or formulations which are less prone to tampering and abuse.

Historically, the first line of treatment for ADHD was through stimulants, such as methylphenidate and amphetamine. These are classified as Schedule II controlled substances that can cause dependence and abuse. The danger of prescription drug abuse is one of the main concerns of physicians who treat ADHD. ADAIR was specifically designed to reduce the risk of tampering and abusing stimulants by snorting or injecting them.

### **About Fragile X**

#### **Description of Fragile X**

Fragile X is a genetic disorder that is characterized by a high number (>200) of repeated DNA base sequences, or CGG Repeats, in the X chromosome. Fragile X is diagnosed by a blood test that measures the amount of CGG Repeats and, according to the Orphan Drug Act, is a rare disease. These repeated sequences are associated with a change in the amount of Fragile X Mental retardation protein, or FMRP, produced by the cell. A greater reduction in FMRP is associated with more severe physical symptoms and intellectual disability. Through the regulation of protein levels in nerve cells in the brain, FMRP is thought to be involved with brain pathways that undergo change to facilitate learning and memory.

Fragile X is the most common single gene cause of intellectual disability and autism and an unmet medical need exists with no approved drugs for the treatment of Fragile X. Fragile X is named for the broken microscopic appearance of the X chromosome, one of the sex-linked chromosomes that is observed in people with the syndrome. Fragile X affects all ethnic groups worldwide, with the full mutation expansions in FMR1 ( $\geq 200$  CGG Repeats) occurring at an estimated frequency of 1:3600 males and 1:4000 to 6000 females.

#### **Fragile X Symptoms**

Not every individual with the Fragile X mutation will show signs or symptoms of Fragile X, and disabilities will range from mild to severe. In males, Fragile X is associated with moderate to severe intellectual disability. Most females with Fragile X will have a learning disability and about 25% of them will have an intellectual disability. Since females with Fragile X have one normal X chromosome and one chromosome with Fragile X, and either of the two X chromosomes is active in a given cell, females tend to have milder symptoms than males. Both males and females with Fragile X may show delay in acquiring language skills early in their life.

Individuals with Fragile X often have a number of behavioral symptoms, including inattention, hyperactivity, impulsivity, autistic symptoms, shyness, aggression, social anxiety, hand flapping, hand biting, and high sensitivity to being touched. Autism spectrum disorder, or ASD, is seen in approximately 30% of males and 20% of females with Fragile X, and an additional 30% of Fragile X individuals display autistic symptoms without having the ASD diagnosis. ADHD is commonly diagnosed in Fragile X, and has been reported to occur in approximately 60-75% of males with Fragile X.

#### **Limitations of Treatment Options for Fragile X**

The FDA has not approved any drugs specifically for the treatment of Fragile X or its symptoms. Individuals with Fragile X are treated based upon their symptoms. If the individual has ADHD or ADHD symptoms, the individual might be treated with ADHD medications, such as stimulants, atomoxetine and alpha-2 agonists (guanfacine or clonidine). If there are symptoms of aggression or irritability, the individual might be treated with antipsychotic medications. Anxiety symptoms might be treated with anti-anxiety drugs such as selective serotonin reuptake inhibitors. If there are seizures, the individual might be treated with anti-convulsant drugs.

#### **MDX Overview and Mechanism of Action**

MDX is a proprietary, combined rapid onset ER formulation of the chemical pyridoxine pyroglutamate, which is more commonly known as metadoxine. MDX consists of a single bi-layer oral tablet, which includes both a rapid onset release metadoxine formulation and a slow release metadoxine formulation together providing the desired dual release profile. The new extended-release formulation prolongs the human plasma levels of metadoxine for up to 12 hours, which results in enhanced efficacy benefits.

Metadoxine has been available since the 1980s in IR forms for the acute treatment of alcohol intoxication and the chronic treatment of alcoholic liver disease. Metadoxine was approved for these indications in Italy, Portugal, Hungary, Russia, India, China, Mexico and Thailand. A literature survey covering over 20 years of post-marketing surveillance identifies only a few cases of minor adverse events. To our knowledge, no drug-related serious adverse events have ever been reported. We have multiple claims in our issued patents and pending patent applications that may prevent the use of metadoxine by others to treat ADHD, Fragile X and other cognitive disorders.

Our working hypothesis regarding MDX mechanism of action is that metadoxine mediates a potential therapeutic benefit in neuronal impairment by facilitating synaptic plasticity underlying learning and memory. In support of this hypothesis, we observed a dose-dependent reduction of the overall synaptic excitability, enhanced GABAergic inhibitory synaptic transmission and specific pHMRI profile of reduced brain activity, indicating that metadoxine may rescue neuronal hyperexcitability and neuronal circuit dysfunctions and may be beneficial in several neurodevelopmental disorders, such as FXS in whom there is excitatory/inhibitory synaptic transmission imbalance.

### **Commercialization**

Mr. David Baker, our Chief Commercial Officer, leads our pre-commercialization activities. However, we currently do not have any internal sales or distribution infrastructure. In the event that we receive regulatory approval for ADAIR, MDX or any other product candidate we may develop, we intend, where appropriate, to pursue commercialization relationships with pharmaceutical companies and other strategic partners providing for distribution through their sales and marketing organizations, or build an internal commercial infrastructure.

### **Third-Party Reimbursement**

Sales of pharmaceutical products depend in significant part on the availability of coverage and adequate reimbursement by third-party payors, such as state and federal governments, including Medicare and Medicaid, managed care providers, and private insurance plans. Decisions regarding the extent of coverage and amount of reimbursement to be provided for ADAIR and/or MDX will be made on a plan by plan basis.

Within the Medicare program, as self-administered drugs, ADAIR and/or MDX would be reimbursed under the expanded prescription drug benefit known as Medicare Part D. This program is a voluntary Medicare benefit administered by private plans that operate under contracts with the federal government. These Part D plans negotiate discounts with drug manufacturers, which may be passed on to each of the plan's enrollees. Historically, Part D beneficiaries have been exposed to significant out-of-pocket costs after they surpass an annual coverage limit and until they reach a catastrophic coverage threshold. However, changes made by recent legislation will reduce this patient coverage gap, known as the donut hole, by reducing patient responsibility in that coverage range. Because the vast majority of patients treated with ADHD medications are under 65 years old, Medicare has a relatively small impact on ADHD medications and this would also be expected for ADAIR and/or MDX.

An ongoing trend has been for third-party payors, including the U.S. government, to apply downward pressure on the reimbursement of pharmaceutical products. Also, the trend towards managed health care in the United States and the concurrent growth of organizations such as health maintenance organizations tend to result in lower reimbursement for pharmaceutical products. We expect that these trends will continue as these payors implement various proposals or regulatory policies, including various provisions of the recent health reform legislation that affect reimbursement of these products. There are currently, and we expect that there will continue to be, a number of federal and state proposals to implement controls on reimbursement and pricing, directly and indirectly.

There is an emerging trend in state legislation requiring the addition of abuse-deterrent formulations of opioid painkillers to be added to managed care formularies. Because there are no stimulants currently approved with similar abuse-deterrent labeling, such legislation has not had an impact on stimulants; however, this could favorably impact the reimbursement of a product like ADAIR in the future.

### **Research and Development**

We sponsor and conduct clinical research activities with investigators and institutions to measure key clinical outcomes that are necessary in order for us to be able to file an NDA with the FDA and equivalent filings with other regulatory authorities. For the years ended December 31, 2016, 2015 and 2014, we incurred \$18,391,000, \$13,461,000, and \$25,105,000, respectively, of research and development expenses.

In June 2015, we entered into the Services Agreement with Encap, pursuant to which Encap provides formulation development and clinical manufacturing services of ADAIR to us. The term of the Services Agreement is for the longer of two years or the completion or termination of the services provided pursuant to the Services Agreement. For the years 2015 and 2016, we incurred expenses of \$127,000 and \$306,000, respectively, in connection with the Services Agreement.

## Grants from the IIA

Our research and development efforts, during the period between May 1, 2009 and April 30, 2010, were financed in part through royalty-bearing grants, in an amount of \$106,494 that we received from the OCS (today the IIA). With respect to such grants we are committed to pay certain royalties. Regardless of any royalty payment, we are further required to comply with the requirements of the Research Law with respect to those past grants. When a company develops know-how, technology or products using IIA grants, the terms of these grants and the Research Law restrict the transfer of such know-how, and the transfer of manufacturing or manufacturing rights of such products, technologies or know-how outside of Israel, without the prior approval of the IIA. We do not believe that these requirements will materially restrict us in any way.

## Manufacturing

We currently have no manufacturing facilities and no experience with commercial-scale manufacturing. We currently rely on third-party manufacturers to produce bulk drug substance and drug products required for our clinical trials, respectively. We have entered into a customary clinical trial material manufacturing agreement. Supply under the agreement is done by purchase orders, there are no minimum purchase requirements or unusual financial arrangements and the agreement is terminable at will by either party. We plan to continue to rely upon contract manufacturers and, potentially, collaboration partners to manufacture commercial quantities of our drug product candidates if and when we receive approval for marketing by the applicable regulatory authorities.

We have not identified secondary raw material supplier (for drug substance) nor manufacturer for drug substance and drug product. We do not have a long-term commercial supply arrangement in place with any of our contract manufacturers. If we need to identify additional suppliers and manufacturers, we would not be able to do so without significant delay and likely significant additional cost.

Our third-party manufacturers, their facilities and all lots of drug substance and drug products used in our clinical trials are required to be in compliance with current Good Manufacturing Practices, or cGMP. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. The manufacturing facilities for our products must meet, and continue to meet, cGMP requirements and FDA satisfaction before any product is approved and we can manufacture commercial products. Contract manufacturers often encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel.

In February 2016, and pursuant to the provision of the Services Agreement as abovementioned, we entered into a term sheet with Capsugel, an affiliate of Encap, in connection with commercial manufacturing of the Product containing the active pharmaceutical ingredient forming ADAIR. Subject to certain exceptions, the term sheet is not binding, until a supply agreement, or the Supply Agreement, is executed by the parties. No Supply Agreement has been entered into between the parties as of the date hereof. Per the term sheet, among others, the following covenants of the parties are binding: (i) subject to certain terms and conditions and the entry into the Supply Agreement, Capsugel shall manufacture the Product for us and we shall purchase the Product from Capsugel for a period of at least five years; (ii) Capsugel is restricted from selling, developing or otherwise commercializing for any third party, for a period of nine years, abuse deterrent formulation for immediate release amphetamine or methylphenidate containing products; (iii) certain pricing covenants; and (iv) certain one-time milestone payments to be paid by us upon receipt of certain FDA approvals or other similar regulatory approvals and, subject to certain exceptions, certain royalties payments to be paid by us. The parties agreed that the term of the Supply Agreement will be for a period of seven years with a right to terminate the Supply Agreement for a material breach by the other party not cured within 90 days.

## Competition

We face competition from established pharmaceutical companies that currently market a wide range of drugs to treat ADHD and symptoms of Fragile X. All of these competitors have far greater marketing and research capabilities than we do. We also face potential competition from academic institutions, government agencies and private and public research institutions, among others, which may in the future develop products to treat ADHD and Fragile X. All of these companies and institutions may have products in development that are superior to ADAIR. Our commercial opportunity would be reduced significantly if our competitors develop and commercialize products that are safer, more effective and convenient, have fewer side effects and/or are less expensive than the expected price of ADAIR. Public announcements regarding the development of competing drugs could adversely affect the price of our stock and the commercial potential of ADAIR.

In addition, the following compounds are under development in clinical trials for ADHD: dasotraline (Sunovion) (Phase 3), eltoprazine (Amarantus) (Phase 2), centanafadine (Neurovance) (Phase 2), and AR08 (Arbor) (Phase 2). These compounds are all non-stimulants, however, none of them have a similar mechanism of action as MDX. In addition, a number of formulations of amphetamine and methylphenidate stimulants are under development, such as SHP 465 (Shire) and HLD-200 (Highland Therapeutics), although these are not considered to be direct competitors to MDX.

The following compounds are under development in clinical trials for Fragile X: NNZ-2566 (Neuren) (Phase 2) and ganoxalone (Marinus) (Phase 2), ZYN-002 (Zynerba) (Phase 2).

While we are aware of no abuse-deterrent stimulants approved by the FDA or other regulatory agencies, there are several under development: KemPharm (methylphenidate extended release), Durect (methylphenidate extended release), Collegium (methylphenidate extended release), Ensysce (dextroamphetamine), Egalet (compound undisclosed) and Grunenthal (amphetamine, methylphenidate).

These lists of competitive compounds under development may not be exhaustive.

## Intellectual Property

We seek patent protection in the United States and internationally for MDX, ADAIR, and any other products that we may develop. Our policy is to pursue, maintain and defend patent rights developed internally and to protect the technology, inventions and improvements that are commercially important to the development of our business.

We currently have four issued U.S. patents, covering the composition of the sustained release form of MDX, the use of metadoxine for ADHD, and new molecular derivatives of metadoxine. We also have patent applications directed to Abuse-Deterrent Amphetamine Immediate-Release (ADAIR) We also have eight issued patents in Australia, Canada, Japan, India, Israel, Mexico, Russia and Europe that cover the composition of the sustained release form of MDX. The European patent includes the following territories: Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czech Republic, Germany, Denmark, Estonia, Spain, Finland, France, United Kingdom, Greece, Croatia, Hungary, Ireland, Iceland, Italy, Lithuania, Latvia, Luxembourg, Monaco, Malta, Netherlands, Norway, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia and Turkey. Additionally, we have eight issued patents in Australia, China, Eurasia, Hong Kong, Israel Japan, Mexico and New Zealand that cover the use of metadoxine for ADHD. The Eurasian patent includes the following territory: Russian Federation. We cannot be sure that any additional 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. There is also a significant risk that any issued patents will have substantially narrower claims than those that are currently sought. Even with respect to any patents that may be issued to us, we cannot be sure that any such patents will be commercially useful in protecting our technology. Any patents issued with respect to our current patent applications directed to composition of the sustained release form of MDX, the use of metadoxine for ADHD, and new molecular derivatives of metadoxine would expire from 2028 to 2030. Any patents that issue with respect to ADAIR will expire 2036 and 2037. We also rely on trade secrets to protect our product candidates. Our commercial success also depends in part on our non-infringement of the patents or proprietary rights of third parties. For a more comprehensive discussion of the risks related to our intellectual property, please see Item 3.D. Risk Factors “Risks Related to Our Intellectual Property.”

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. This risk is exacerbated for us because metadoxine is manufactured and used in a number of foreign countries in other applications and is widely available. The manufacture of metadoxine and its use in other indications will not infringe our intellectual property rights, and will make it more difficult to monitor and enforce any patent rights that may be issued to us.

Our success depends in part on our ability to:

- preserve trade secrets;
- prevent third parties from infringing upon our proprietary rights; and
- operate our business without infringing the patents and proprietary rights of third parties, both in the United States and internationally.

We also protect our proprietary technology and processes, in part, by confidentiality and invention assignment agreements with our employees, consultants, scientific advisors and other contractors. These agreements 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. To the extent that our employees, consultants, scientific advisors or other contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

## 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.

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and related regulations. Drugs are also subject to other federal, state and local statutes and regulations. Failure to comply with the applicable U.S. 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 IRB of a clinical hold on trials, the FDA's refusal to approve pending applications or supplements, 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 any candidate drug product 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 U.S. or abroad.

## Marketing Approval

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

- nonclinical laboratory and animal tests;
- submission of an IND application which must become effective before clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use or uses;
- pre-approval inspection of manufacturing facilities and clinical trial sites; and
- FDA approval of an NDA which must occur before a drug can be marketed or sold.

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

We will need to successfully complete additional pre-clinical and clinical trials in order to be in a position to submit a new drug application to the FDA. Future trials may not begin or be completed on schedule, if at all. 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 vendors 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 subjects to participate in a study; and
- supply of the drug.

We must reach an agreement with the FDA on the proposed protocols for our future clinical trials in the U.S. A separate submission to the FDA 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.



## **ADAIR**

On February 7, 2017, we reported reaching a regulatory milestone in the development of ADAIR (Abuse-Deterrent, Amphetamine Immediate-Release), a proprietary, abuse-deterrent oral formulation of immediate-release (short-acting) dextroamphetamine that is currently under development for the treatment of ADHD. ADAIR is being specifically designed to limit abuse by snorting or injecting. On January 26, 2017, Alcobra held a pre-IND meeting with the U.S. Food and Drug Administration (FDA) to discuss the details of the proposed rule 505(b)(2)-based development program. The FDA provided guidance on the necessary steps towards an NDA, which is expected to be submitted before the end of 2018.

Our plan is to conduct nonclinical and clinical trials for ADAIR and if those trials are successful, seek marketing approval from the FDA. To achieve this objective, the following development plan was proposed by Alcobra and reviewed by the FDA:

- Nonclinical studies assessing the ADAIR formulation safety profile
- Filing an IND (Investigational New Drug) application
- Conducting a Pivotal Bio-Equivalence study in healthy volunteers comparing ADAIR and its reference listed drug
- Conducting further laboratory studies and a Human Abuse Potential (HAP) study (if feasible) to evaluate ADAIR's abuse deterrent characteristics in order to establish labeling language regarding abuse deterrence against snorting and injection

An NDA (New Drug Application) could be filed to the FDA only after achieving success in each of the above milestones.

As with similar abuse deterrent products, the ADAIR development program requires special regulatory management and controls, this may raise further risks to the program, e.g.:

- Good communication and collaboration with multiple departments within the FDA, e.g., Division of Psychiatry Products, Office of Pharmaceutical Quality, Control Substance Staff, Office of Surveillance and Epidemiology, and also outside the Agency with the Drug Enforcement Administration (DEA) as being classified 'Schedule II' drug product.
- Following NDA submission, the FDA may call for an expert Advisory Committee (as seen with recent NDA applications for Abuse-Deterrent Opioids products). Such committees, which are partially open to the public, are called to discuss the overall risk-benefit profile of the product, and whether the applicant has demonstrated abuse-deterrent properties for their product that would support labeling.

## **MDX**

On January 9, 2017, we reported receipt of official minutes from meeting with the Division of Psychiatry Products of the FDA held in early December 2016. This face-to-face meeting was held to discuss the ongoing Clinical Hold for MDX and paths to resume human clinical trials with MDX. The official minutes reflected the FDA's agreement to review the data collected thus far in our Phase 3 MEASURE Study and consider it in a future NDA submission of MDX for treatment of ADHD. The FDA and we agreed that such an analysis could provide important information with regard to the effectiveness of MDX, as well as information on its safety and tolerability, allowing a more informed discussion of future development activities, as needed.

On January 17, 2017, we reported top-line results from the MEASURE clinical study - the second Phase 3 clinical trial for MDX for the treatment of ADHD in adult patients. In this trial, MDX did not meet the primary endpoint of demonstrating a statistically significant difference from placebo in the change from baseline of the investigator rating of the Conners' Adult ADHD Rating Scales (CAARS).

We are exploring various strategic alternatives for MDX, e.g. for the treatment of Fragile X Syndrome in Europe where the Immediate-release MDX formulation is currently marketed, while minimizing any additional investment of our existing resources on this drug candidate.

### **Orphan Drug Designation**

We received Orphan Drug Designation for metadoxine, the active ingredient in MDX for the treatment of Fragile X in the United States and in Europe.

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan Drug Designation is intended to assist and encourage companies to develop safe and effective therapies for the treatment of rare diseases and disorders. In addition to providing a seven year term of market exclusivity upon final FDA approval, orphan drug designation also positions a company to be able to leverage a wide range of financial and regulatory benefits, including government grants for conducting clinical trials, waiver of expensive FDA user fees for the potential submission of a New Drug Application, and certain tax credits. Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug or biological product as defined by the FDA or if our drug or biological candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status in the European Union has similar but not identical benefits in the European Union.

### **Fast Track Designation**

We obtained a fast track designation for MDX for Fragile X. Fast track designation is intended to facilitate development and expedite review of drugs to treat serious and life-threatening conditions so that an approved product can reach the market expeditiously. This designation may involve frequent interactions with the FDA. If the product meets the regulatory requirements it may also be eligible for priority review or rolling review of the NDA.

Some products granted fast track designation will not continue to meet the criteria for fast track designation. A drug product in a fast track development program may not continue to meet the criteria if the drug: (i) no longer demonstrates a potential to address unmet medical need, or (ii) is not being studied in a manner that shows the drug product can treat a serious condition and meets an unmet medical need. The drug product may no longer demonstrate a potential to address unmet medical need, for example, if a new product was approved under a traditional approval that addressed the same need or if emerging clinical data failed to show that the product in a fast track development program had the anticipated advantage over available therapy. When fast track designation is no longer supported by emerging data or the designated drug development program is no longer being pursued, the FDA may choose to send a letter notifying the sponsor that the program is no longer designated as a fast track drug development program.

### **FDA Post-Approval Requirements**

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including requirements for record-keeping and reporting of adverse experiences with the drug. Drug manufacturers are required to register their facilities with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMPs, which impose certain quality processes, manufacturing controls and documentation requirements upon us and our third-party manufacturers in order to ensure that the product is safe, has the identity and strength, and meets the quality and purity characteristics that it purports to have. Certain states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. We cannot be certain that we or our present or future suppliers will be able to comply with the cGMP and other FDA regulatory requirements. If our present or future suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, fail to approve any NDA or other application, require us to recall a drug from distribution, shut down manufacturing operations or withdraw approval of the NDA for that drug. Noncompliance with cGMP or other requirements can result in issuance of warning letters, civil and criminal penalties, seizures and injunctive action.

### **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 the safety and efficacy of a drug that are consistent with FDA approval, and 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 the 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. The FDA may decide that an NDA will be approved only following completion of additional pediatric studies.

## **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 the Health Insurance Portability and Accountability Act, or 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 Section 6002 of the PPACA, commonly referred to as the “Physical Payments Sunshine Act” requires 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**

As mentioned, in March 2010, the 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.

This legislation is expected to impact the scope of healthcare insurance, the insurance refunds from the insurance companies and possibly also on the costs of medical products.

## **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.

#### 4.C. Organizational structure

Our sole wholly-owned subsidiary is Alcobra, Inc., a Delaware corporation.

#### 4.D. Property, plants and equipment

Our headquarters is currently located in Tel Aviv, Israel and consists of approximately 7,170 square feet of leased office space under a lease for five years, starting May 25, 2015. Since August 2015, we have subleased 969 square feet of our Tel Aviv office space, so our current office space in Tel Aviv is 6,201 square feet (including common areas). We may seek to sublease additional space as we adjust our resources following the reduction in force as discussed in item 6.D. We have also leased an additional office in Petah Tikva, Israel of approximately 1,400 square feet for our clinical study. The Petach Tikva lease ends in August 2017 and we are currently seeking to sublease the office earlier. Our wholly owned subsidiary, Alcobra Inc. leases an office for our U.S. employees in the greater Philadelphia area, with approximately 3,500 square feet.

#### ITEM 4A. UNRESOLVED STAFF COMMENTS

None.

#### ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

##### Overview

We are an emerging biopharmaceutical company primarily focused on the development and commercialization of our proprietary drug candidates, including ADAIR and MDX. 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, MDX, ADAIR or any other product candidate. We are currently exploring strategic alternatives, which may include acquisition of new assets and/or partnering or monetization of our existing products. As of December 31, 2016, we had an accumulated deficit of \$95.6 million.

##### Operating Expenses

Our current operating expenses consist of three components – research and development expenses, pre-commercialization expenses and general and administrative expenses.

##### Research and Development Expenses

Our research and development expenses consist primarily of expenses related to 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 research and development expenses.

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

<i>(in thousands of U.S. dollars)</i>	December 31,		
	2016	2015	2014
Cost to third party clinical consultants and expenses related to conducting clinical trials	\$ 14,050	\$ 9,733	\$ 21,239
Salaries and related personnel expenses	2,831	2,179	1,521
Share-based compensation	707	768	1,773
Travel expenses	282	240	190
Other expenses	521	541	382
Total	<u>\$ 18,391</u>	<u>\$ 13,461</u>	<u>25,105</u>

##### Pre-commercialization Expenses

Pre-commercialization expenses consist primarily salary and related expenses, share-based compensation expense and professional services fees in connection with business development and market research for our products.

The following table discloses the breakdown of pre-commercialization expenses:

<i>(in thousands of U.S. dollars)</i>	<b>December 31,</b>		
	<b>2016</b>	<b>2015</b>	<b>2014</b>
Share-based compensation	\$ 390	\$ 308	\$ 616
Professional services	339	310	1,067
Salaries and related personnel expenses	617	538	355
Travel expenses	34	48	69
Other expenses	39	41	27
Total	<u>\$ 1,419</u>	<u>\$ 1,245</u>	<u>\$ 2,134</u>

#### **General and Administrative Expenses**

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

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

<i>(in thousands of U.S. dollars)</i>	<b>December 31,</b>		
	<b>2016</b>	<b>2015</b>	<b>2014</b>
Share-based compensation	\$ 1,403	\$ 1,289	\$ 1,700
Professional services	1,875	1,813	2,172
Salaries and related personnel expenses	1,565	1,418	1,498
Travel expenses	210	160	224
Other expenses	304	312	245
Total	<u>\$ 5,357</u>	<u>\$ 4,992</u>	<u>\$ 5,839</u>

#### **Results of Operations**

	<b>December 31,</b>		
	<b>2016</b>	<b>2015</b>	<b>2014</b>
	<i>(in thousands of U.S. dollars)</i>		
Research and development expenses	\$ 18,391	\$ 13,461	\$ 25,105
Pre-commercialization expenses	1,419	1,245	2,134
General and administrative expenses	5,357	4,992	5,839
Operating loss	\$ 25,167	\$ 19,698	\$ 33,078
Financial income, net	(637)	(300)	(227)
Tax expenses (benefits)	73	51	(17)
Net loss	<u>\$ 24,603</u>	<u>\$ 19,449</u>	<u>\$ 32,834</u>
Unrealized loss on available-for-sale marketable securities	6	-	-
Total comprehensive loss	<u>\$ 24,609</u>	<u>\$ 19,449</u>	<u>\$ 32,834</u>

#### **Comparison of the Year ended December 31, 2016 to the Year Ended December 31, 2015 to the Year Ended December 31, 2014**

##### **Research and development expenses**

Our research and development expenses for the year ended December 31, 2016, amounted to \$18,391,000, representing an increase of \$4,930,000, or 37%, compared to \$13,461,000 for the year ended December 31, 2015. The difference resulted primarily from an increase in third-party clinical expenses related to conducting our second Phase 3 study in adult ADHD in 2016 (MEASURE).

Our research and development expenses for the year ended December 31, 2015, amounted to \$13,461,000, representing a decrease of \$11,644,000, or 46%, compared to \$25,105,000 for the year ended December 31, 2014. The difference is primarily due to a decrease in third-party clinical expenses related to the completion of our first Phase 3 study in adult ADHD in October 2014.

#### ***Pre-commercialization expenses***

Our pre-commercialization expenses for the year ended December 31, 2016, amounted to \$1,419,000, representing an increase of \$174,000, or 14%, compared to \$1,245,000 for the year ended December 31, 2015. The difference resulted primarily from an increase in share-based compensation and salaries and related personnel expenses.

Our pre-commercialization expenses for the year ended December 31, 2015, amounted to \$1,245,000, representing a decrease of \$889,000, or 42%, compared to \$2,134,000 for the year ended December 31, 2014. The difference is primarily due to a decrease in share-based compensation and professional services expenses in the amount of \$757,000.

#### ***General and administrative expenses***

Our general and administrative expenses totaled \$5,357,000 for the year ended December 31, 2016, an increase of \$365,000 or 7%, compared to \$4,992,000 for the year ended December 31, 2015. The difference resulted primarily from an increase of \$114,000 in share-based compensation expenses and an increase of \$147,000 in salaries and related personnel expenses.

Our general and administrative expenses totaled \$4,992,000 for the year ended December 31, 2015, a decrease of \$847,000 or 14.5%, compared to \$5,839,000 for the year ended December 31, 2014. The difference resulted primarily from a decrease of \$411,000 in share-based compensation expenses and a decrease of \$359,000 in professional services expenses.

#### ***Operating loss***

As a result of the foregoing, our operating loss for the year ended December 31, 2016, was \$25,167,000, an increase of \$5,469,000, or 28%, compared to an operating loss of \$19,698,000 for the year ended December 31, 2015.

Operating loss for the year ended December 31, 2015, was \$19,698,000, a decrease of \$13,380,000, or 40%, compared to an operating loss of \$33,078,000 for the year ended December 31, 2014.

#### ***Financial income***

We recognized financial income of \$637,000 for the year ended December 31, 2016, representing an increase of \$337,000, or 112%, compared to financial income of \$300,000 for the year ended December 31, 2015. The increase resulted primarily from interest income on bank deposits during 2016.

We recognized financial income of \$300,000 for the year ended December 31, 2015, representing an increase of \$73,000, or 32%, compared to financial income of \$227,000 for the year ended December 31, 2014. The increase resulted primarily from interest income on bank deposits during 2015.

#### ***Tax Expenses***

Our tax expenses consist of tax liabilities of our wholly owned subsidiary, Alcobra Inc., resulting from services Alcobra Inc. provides to us in accordance with an arms' length services agreement.

We recognized \$73,000 of tax expenses for the year ended December 31, 2016, as compared to tax expenses of \$51,000 for the year ended December 31, 2015, an increase of \$22,000, or 43%.

We recognized \$51,000 of tax expenses for the year ended December 31, 2015, as compared to tax benefits of \$17,000 for the year ended December 31, 2014, an increase of \$68,000.

#### ***Unrealized loss on available-for-sale marketable securities***

We have started to invest in marketable securities in 2016. As a result, we recognized \$6,000 unrealized loss on available-for-sale marketable securities for the year ended December 31, 2016.

## **Total Comprehensive Loss**

As a result of the foregoing, our total comprehensive loss for the year ended December 31, 2016 was \$24,609,000, an increase of \$5,160,000, or 27%, compared to \$19,449,000 for the year ended December 31, 2015.

Our loss for the year ended December 31, 2015 was \$19,449,000, as compared to \$32,834,000 for the year ended December 31, 2014, a decrease of \$13,335,000, or 41%.

## **Critical Accounting Policy and Estimates**

We describe our significant accounting policies more fully in Note 2 to our consolidated financial statements for the year ended December 31, 2016. 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 consolidated 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.

## **Share-Based Compensation and Fair Value of Ordinary Shares**

We account for share-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 option-pricing model, or Black-Scholes, as a fair value method for our options awards. Black-Scholes 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* - The expected volatility is calculated based upon actual historical stock price movements over the most recent periods ending on the grant date. Since our shares started trading in NASDAQ in May 2013, quoted prices of our share are available for three and a half years only. Due to insufficient historical data, in cases where the expected term is longer than the available historical data on the grant date, the expected volatility determination was based on a weighted average of our and 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 Capital Market and NASDAQ Global Market quotes.

## Impairment of Marketable Securities

Our marketable securities are classified as available-for-sale securities. We assess our available-for-sale marketable securities on a regular basis for other-than-temporary impairment. Pursuant to the accounting guidance in ASC 320 “Investments- Debt and Equity Securities”, if we have a security with a fair value less than its amortized cost and we intend to sell the security or it is more likely than not we will be required to sell the security before it recovers, an other-than temporary impairment has occurred and we must record the entire amount of the impairment in earnings. If we do not intend to sell the security or it is not more likely than not we will be required to sell the security before it recovers in value, we must estimate the net present value of cash flows expected to be collected. If the amortized cost exceeds the net present value of cash flows, such excess is considered a credit loss and an other-than-temporary impairment has occurred. The credit loss component is recognized in earnings and the residual portion of the other-than-temporary impairment is recorded in other comprehensive income. The determination of credit losses requires significant judgment and actual results may be materially different than our estimate. We consider the likely reason for the decline in value, the period of time the fair value was below amortized cost, changes in and performance of the underlying collateral, the ability of the issuer to meet payment obligations, changes in ratings and market trends and conditions.

We measure our money market funds and marketable securities at fair value. Money market funds and marketable securities are classified within Level 1 or Level 2. This is because these assets are valued using quoted market prices or alternative pricing sources and models utilizing market observable inputs.

## Emerging Growth Company

Subject to certain conditions set forth in the JOBS Act, as an “emerging growth company”, we elected to rely on other exemptions, including without limitation, (i) providing an auditor’s attestation report on our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the PCAOB regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements (auditor discussion and analysis). These exemptions will apply for a period of five years following the completion of our initial public offering or until we are no longer an “emerging growth company,” whichever is earlier.

## Liquidity and Capital Resources

### Overview

Since our inception through December 31, 2016, we have funded our operations principally with \$129.6 million from the sale of Ordinary Shares, preferred shares and convertible notes. As of December 31, 2016, we had \$2.3 million in cash and cash equivalents, \$14.9 million invested in marketable securities and an additional amount of \$33 million in short-term bank deposits.

	Years Ended December 31,		
	2016	2015	2014
	(in thousands of U.S. dollars)		
Operating activities	\$ (19,241)	\$ (18,148)	\$ (28,326)
Investing activities	4,881	(33,842)	(8,407)
Financing activities	6	66,472	-
Net increase (decrease) in cash and cash equivalents	\$ (14,354)	\$ 14,482	\$ (19,919)

### Operating Activities

Net cash used in operating activities of \$19.2 million during the year ended December 31, 2016 was primarily used for payment of \$13.2 million for clinical trials and other third-party related expenses and for professional services, \$0.5 million for travel expenses, \$0.5 million for rent expenses and \$4.9 million in salary payments, offset by \$0.5 million of interest income. The remaining amount of \$0.6 million was for miscellaneous expenses.

Net cash used in operating activities of \$18.1 million during the year ended December 31, 2015 was primarily used for payment of \$13.5 million for clinical trials and other third party related expenses and for professional services, \$0.4 million for travel expenses, \$0.5 million for rent expenses and an aggregate of \$3.1 million in salary payments. The remaining amount of \$0.6 million was for other miscellaneous expenses.



Net cash used in operating activities of \$28.3 million during the year ended December 31, 2014 was primarily used for payment of \$24.2 million for clinical trials and other third party related expenses and for professional services, \$0.5 million for travel expenses and an aggregate of \$3.3 million in salary payments. The remaining amount of \$0.3 million was for other miscellaneous expenses.

### **Investing Activities**

Net cash provided by investing activities of \$4.9 million during the year ended December 31, 2016 reflected the withdrawal of short-term deposits into cash in the amount of \$20 million, proceeds from maturity and redemption of marketable securities in the amount of \$1.6 million and \$0.7 million, respectively, offset by the investment in marketable securities in the amount of \$17.3 million and the purchase of property and equipment of \$0.1 million.

Net cash used in investing activities of \$33.8 million during 2015 reflected the investment of cash into short-term deposits and long-term deposits in the amount of \$14.5 million and \$19 million, respectively, the purchase of property and equipment of \$0.2 million and the investment in a restricted bank deposit of \$0.1 million.

Net cash provided by investing activities of \$8.4 million during 2014 reflected the withdrawal of short-term deposits into cash in the amount of \$8.5 million and the purchase of property and equipment of \$0.1 million.

### **Financing Activities**

There were no financing activities in the year ended December 31, 2016 except of immaterial exercise of options by an employee in a total amount of \$6,000.

Net cash provided by financing activities of \$66.5 million in the year ended December 31, 2015, consisted of net proceeds from two follow on public offerings. On January 14, 2015, we completed a public offering of 7,475,000 Ordinary Shares. The offering price was \$4.00 per share, and the net proceeds to us from the sale of the shares were approximately \$27.9 million. On November 18, 2015, we completed a public offering of 6,379,198 Ordinary Shares. The offering price was \$6.50 per share, and the net proceeds to us from the sale of the shares were approximately \$38.6 million.

There were no financing activities in the year ended December 31, 2014.

### **Current Outlook**

We have financed our operations to date primarily through proceeds from sales of our Ordinary Shares and other equity securities. 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 two years. We believe that we will need to raise additional funds before we have positive cash flow from operations.

As of December 31, 2016, our cash, cash equivalents, short-term deposits and marketable securities totaled \$50.2 million. Our current investment policy has the following objectives: (i) preserve principal (capital); (ii) maintain liquidity in accordance with cash flow requirements; and (iii) maximize the rate of return within the stated guidelines in the policy. To achieve these goals, we invest available cash in bank deposits with banks that have a credit rating of at least Baa1/BBB+ and in tradable securities with high credit quality and trading liquidity, including U.S. Treasury bonds, money market funds, and corporate debt instruments that carry a rating of A2/A or better.

Our cash management is monitored by the Audit Committee.

In light of the disappointing results of MEASURE and our focus on ADAIR and other potential strategic opportunities, we are currently in the process of adjusting our resources to the new corporate strategy. We are in a process of reduction in force and will continue to evaluate the needed resources on an ongoing basis. We expect the resource adjustment to result in a significant reduction in fixed costs, including salaries, professional services, and travel.

We believe that our existing cash resources will be sufficient to fund our projected cash requirements approximately through 2018 including the cost of our ADAIR program through NDA submission. Nevertheless, we will require significant additional financing in the future to fund our operations, clinical development plan, and to commercialize ADAIR after we obtain regulatory approval, and/or in connection with other strategic transactions. Our future capital requirements will depend on many factors, including:

- potential costs associated with transformational business developments or M&A transactions;

- the progress and costs of our pre-clinical studies, clinical trials and other research and development activities;
- the scope, prioritization and number of our clinical trials and other research and development programs;
- any cost that we may incur under in- and out-licensing arrangements relating to our drug candidate that we may enter into in the future;
- the costs and timing of obtaining regulatory approval for our drug candidate;
- 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 candidate;
- 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 candidate;
- the magnitude of our general and administrative expenses; and
- payments to the IIA.

Until we can generate significant recurring revenues, we expect to satisfy our future cash needs through our existing cash, cash equivalents, investment in marketable securities and short-term deposits, the net proceeds from the current offering, debt or equity financings, asset sales, or by out-licensing applications of our drug candidate. 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.

#### 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, 2016:

	Total	Less than 1 year	1-3 years	4-5 years	More than 5 years
	<b>(in thousands of U.S. dollars)</b>				
Operating leases:					
Facility	\$ 744	\$ 457	\$ 287	-	-
Motor Vehicles	13	13	-	-	-
Total	\$ 757	\$ 470	\$ 287	-	-

### ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

#### 6.A. Directors and senior management

##### Executive Officers and Directors

The following table sets forth information regarding our executive officers, key employees and directors as of April 27, 2017:

<b>Name</b>	<b>Age</b>	<b>Position</b>
Howard B. Rosen (1)	59	Chairman of the Board of Directors
Daniel E. Geffken (1) (3)	60	Director
Dr. Aharon Schwartz (1)	74	Director
Ofer Segev (1) (2) (3)	57	Director
Dr. Joao Siffert (1)	52	Director
Orli Tori (1) (2)	53	Director
Arieh Ben Yosef (1) (2) (3)	64	Director
Dr. Yaron Daniely	41	Chief Executive Officer, President and Director
Dr. Tomer Berkovitz	37	Chief Financial Officer, Chief Operating Officer
David Baker	54	Chief Commercial Officer
Dr. Jonathan Rubin	55	Chief Medical Officer
David Siner	43	Senior Director Chemistry, Manufacturing and Control
Dr. Johanna Schumann	36	SVP Preclinical Development
Irena Katsman	37	VP Finance
Elad Ben David	40	Director Regulatory Affairs

(1) Indicates independent director under NASDAQ rules.

(2) Member of our Audit Committee.

(3) Member of our Compensation Committee.

*Howard B. Rosen* has served on our Board since the closing of our initial public offering in May 2013 and as our Chairman since February 2014. Since 2008, Mr. Rosen has served as a consultant to several companies in the biotechnology industry. He has also served as a lecturer at Stanford University in Chemical Engineering since 2008 and in Management since 2011. Mr. Rosen has served as a director at AcelRx Pharmaceuticals (Nasdaq: ACRX), Inc., a company developing products for pain relief, since 2008, as its interim Chief Executive Officer from April 2015 to March 2016 and from April 2016 to March 2017, as its Chief Executive Officer. Mr. Rosen served as interim President and Chief Executive Officer of Pearl Therapeutics, Inc., a company focused on developing combination therapies for the treatment of highly prevalent chronic respiratory diseases, from June 2010 to March 2011. From 2004 to 2008, Mr. Rosen was Vice President of Commercial Strategy at Gilead Sciences, Inc., a biopharmaceutical company. From 2003 until 2004, Mr. Rosen was President of ALZA Corporation, a pharmaceutical and medical systems company that merged with Johnson & Johnson, a global healthcare company, in 2001. Prior to that, from 1994 until 2003, Mr. Rosen held various positions at ALZA Corporation. Mr. Rosen is also a member of the board of directors a number of private biotechnology companies as follows: Entrega, Inc. and Kala Pharmaceuticals, Inc. Previously, Mr. Rosen served on the board of directors of a number of public companies, as follows: Pharsight Corporation, a company focused on providing software products and consulting services to biopharmaceutical companies that was acquired by Tripos International in 2008 and CoTherix, Inc., a biopharmaceutical company that was acquired by Actelion Pharmaceuticals Ltd. in 2007. Mr. Rosen holds a B.S. in Chemical Engineering from Stanford University, an M.S. in Chemical Engineering from the Massachusetts Institute of Technology and an M.B.A. from the Stanford Graduate School of Business.

*Daniel E. Geffken* has served on our Board since our initial public offering in May 2013. Since October 2011, he has been Managing Director of Danforth Advisors, LLC, a management consulting firm that provides financial and strategic support to emerging life science companies. Mr. Geffken has also been the chief financial officer or chief operating officer of eight companies, four of which were U.S. public reporting companies and six of which were life science companies. He has a B.S. in Economics from The Wharton School, University of Pennsylvania, and a M.B.A. from Harvard Business School.

*Dr. Aharon Schwartz* joined our Board as Chairman in January 2013, serving as our chairman until February 2014. He retired from Teva Pharmaceutical Industries Ltd. where he served in a number of positions from 1975 through 2011, the most recent being Vice President, Head of Teva Innovative Ventures from 2008. He is also the chairman of the board of directors of BioLineRx Ltd., BioCancell Therapeutics Inc., CureTech Ltd. and director of several other biotechnology companies. Dr. Schwartz received his Ph.D. in Organic Chemistry from the Weizmann Institute, his M.Sc. in organic chemistry from the Technion Institute of Technology and a B.Sc. in Chemistry and Physics from the Hebrew University of Jerusalem. He has received a second Ph.D. in the History and Philosophy of Science from the Hebrew University of Jerusalem.

*Ofer Segev* has served as a director since August 2016. Mr. Segev has been Chief Financial Officer and Chief Operating Officer at AlgoSec, Inc., a network security policy management solutions provider, since February 2017. Mr. Segev has over 25 years of management experience in the high-tech and services sectors. Previously, he served as the Vice President of Finance and Chief Financial Officer of AudioCodes Limited, a communications company traded on the Nasdaq Global Select Market, from November 2014 through April 2015. Prior to that, Mr. Segev served as the Chief Executive Officer and as a director of Ness Technologies Srl from 2012 to 2013 and as its Chief Financial Officer from 2007 to 2012. Mr. Segev also serves as a director of Varonis System Inc. Mr. Segev holds a B.A. in economics and accounting from Bar-Ilan University in Israel, and has studied at the Kellogg School of Management at Northwestern University.

*Dr. Joao Siffert* joined our Board in July 2015. Since August 2011, Dr. Siffert has led the Research and Development Organization at Avanir Pharmaceuticals, Inc., a specialty pharmaceutical company focused on development and commercialization of neurology products. Dr. Siffert is currently the Executive Vice President, R&D and Chief Medical Officer, responsible for R&D, regulatory, quality, CMC and commercial supply, as well as medical affairs and pharmacovigilance. Prior to joining Avanir, Dr. Siffert served as Vice President and Chief Medical Officer at Ceregene, Inc., a biotechnology company focused on the development of neurotrophic gene therapies for Alzheimer's and Parkinson's diseases, from September 2007 to August 2011. Prior to his work at Ceregene, Dr. Siffert served as the Chief Medical Officer at Avera Pharmaceuticals, a specialty pharmaceutical company, from May 2005 to September 2007. Prior to joining Avera, Dr. Siffert held positions with Pfizer (from February 2002 to May 2005) first as a medical director for Relpax and subsequently as the worldwide medical team leader of Lyrica and Neurontin, focusing in areas of pain and epilepsy. Prior to Pfizer, Dr. Siffert held academic positions at Beth Israel Medical Center, NY where he served as director of the Adult Neuro-Oncology program, and Albert Einstein College of Medicine, where he was an assistant professor of neurology. Dr. Siffert completed residencies in pediatrics at New York University School of Medicine and in neurology at Harvard Medical School. Dr. Siffert was certified by the American Board of Neurology and Psychiatry in 1996. He holds an M.D. from the University of Sao Paulo School of Medicine, Brazil as well as an M.B.A. from Columbia University Graduate School of Business.

*Orli Tori* joined our Board in August 2016. Ms. Tori is an experienced executive with over 20 years of practice in leading teams towards their goals and beyond. Since 2012 and until recently, Ms. Tori served as Chief Executive Officer of BIRAD Ltd., managing Bar Ilan University's IP and commercialization efforts as well as all research collaborations with Industry. During her tenure, the company built a diverse portfolio of companies based on University IP. Before joining BIRAD, Ms. Tori spent 20 years in the pharmaceutical industry, fulfilling different positions including, General Manager of Neopharm Israel Ltd. from 2007 through 2012, (\$200 Million revenues), and SVP Corporate BD of the Neopharm Group, and was responsible for the group overall corporate development activities, including structuring, negotiating and closing transactions. Ms. Tori serves as a board member at Collplant Ltd. (CLPT) and is former chairperson of the Israeli Technology Transfer Organization. Ms. Tori obtained her M.Sc. in Microbiology (cum laude) and B.Sc. in Life Sciences at Tel Aviv University in Tel Aviv, Israel, and graduated the Executive Program for senior business managers at the Tel Aviv University School of Business.

*Arieh Ben Yosef* joined our Board in May 2014. Mr. Ben Yosef is currently the Chief Executive Officer at Herd MOONitor Ltd. Mr. Ben Yosef has served as a director of Insuline Medical Ltd. (TASE: INSL) since October 2010, which is focused on improving the performance of current insulin treatment methods. From August 2000 to July 2014, Mr. Ben Yosef served as a director of Microwave Networks Inc., a provider of microwave communications products and services. From 2006 to 2012, Mr. Ben Yosef was employed by Teledata Networks Ltd., a global provider of access network products and solutions for Telecom Service Providers, in the positions of Chief Financial Officer, Executive Vice President for Finance & Operations and later on as the General Manager of the company. From 2000 to 2004, Mr. Ben Yosef served as the President of Elisra Inc. and from 1998 to 2000 as the CFO of Tadiran Electronic Industries Inc. Mr. Ben Yosef holds a M.B.A. from the Hebrew University of Jerusalem.

*Dr. Yaron Daniely* became our President and Chief Executive Officer and a Director in March 2010. Immediately prior to joining us and since 2007, Dr. Daniely was the President and Chief Executive Officer of NanoCyte, Inc., a company that develops transdermal delivery technologies based in Caesarea, Israel. Before NanoCyte and from 2004, Dr. Daniely was the General Manager of Gamida Cell—Teva Joint Venture Ltd., a joint venture company that acquired an exclusive license to develop and commercialize a Phase 3-stage cell therapy product for treatment of Leukemia and Lymphoma based in Jerusalem, Israel. From 2003-2007, Dr. Daniely also served as the Vice President of Business Development of Gamida Cell Ltd., and engaged in several licensing and financial transactions for the Company. In addition, he was a director of Bioblast Ltd., a private company incorporated in Israel. Dr. Daniely holds a B.Sc. degree in Biological Sciences from Florida International University, and holds a Ph.D. from the Sackler Institute of Graduate Biomedical Sciences at the New York University School of Medicine. Following his doctoral program, Dr. Daniely served as an NIH Visiting Fellow in its Cell Biology section and a Postdoctoral Fellow in the Department of Molecular Cell Biology at The Weizmann Institute for Science in Israel. Subsequently, he received an Executive M.B.A. from the Technion, Israel Institute of Technology.

*Dr. Tomer Berkovitz* joined us in May 2014 as our Chief Financial Officer and in January 2016 was appointed to the additional position of Chief Operating Officer. Immediately prior to joining Alcobra, and from 2008, he was an Executive Director in J.P. Morgan's Investment Banking Division in New York, where he played a leading role in numerous capital market and mergers and acquisitions transactions. In this capacity, he advised senior management and boards of directors of J.P. Morgan's key U.S. clients, including several S&P 500 healthcare firms. Prior to joining J.P. Morgan, Dr. Berkovitz worked in Citigroup's Investment Bank in New York. From 2000 to 2003, he served as an economist in the Financial Advisory Unit to the Chief of Staff of the Israel Defense Forces. Dr. Berkovitz holds a Ph.D. in Finance and Economics from Columbia Business School and has published a number of corporate finance articles in leading academic and practitioner journals. He also holds an M.Sc. in Finance and Accounting and a B.A. in Economics and Management, both from Tel-Aviv University.

*David Baker* joined us in January 2014 as our Chief Commercial Officer. Prior to joining us, Mr. Baker worked at Shire Pharmaceuticals for 10 years, most recently as Vice President of Commercial Strategy and New Business in the Neuroscience Business Unit. In that role, he led the commercial assessment of neuroscience licensing opportunities, managed commercial efforts on pipeline CNS products, and led the long term strategic planning process. Previously, he served as Global General Manager for Vyvanse® where he led the launch of Vyvanse, led the launch of the adult indication for Vyvanse, and led global expansion efforts including successful establishment of a partnership in Japan and launches in Canada and Brazil. Prior to that, Mr. Baker served as Vice President of Marketing for all of Shire's ADHD products. He has been directly involved with the commercialization of five approved ADHD medications. From 1990 - 2004, Mr. Baker worked at Merck where he held positions of increasing responsibility in marketing, sales, market research and business development. In addition to his knowledge and experience with CNS medications, Mr. Baker's therapeutic expertise includes osteoporosis, migraine and hyperlipidemia. Mr. Baker graduated Magna Cum Laude with a bachelor's degree in Economics and Computer Science from Duke University. He earned a M.B.A. in Marketing from Duke's Fuqua School of Business.

*Dr. Jonathan Rubin* serves as our Chief Medical Officer. He joined us in August 2013 after working at Shire Pharmaceuticals for more than six years, from 2007 through 2013, serving as a Medical Director in Global Medical Affairs supporting multiple products within the ADHD portfolio. As a Medical Director in Global Medical Affairs at Shire Pharmaceuticals, Dr. Rubin developed and implemented Global Medical Affairs strategic plans, planned and supervised medical launch activities in the United States and assisted with the design, execution and interpretation of Phase 2, 3 and Phase 4 studies. Dr. Rubin also served as the Director of Scientific Licensing Assessment at Shire Pharmaceuticals in 2011 where he identified and evaluated new opportunities for business development. Dr. Rubin began his pharmaceutical industry career as a medical consultant for Noven Pharmaceuticals in 2002. Until 2007 Dr. Rubin cared for children and adolescents with ADHD for 15 years at his General and Developmental-Behavioral Pediatric practice in Margate and Coconut Creek, Florida. He graduated with a B.S. from Yale University and an M.D. from the University of Connecticut, completed a pediatric residency at Albert Einstein/Montefiore, completed an Ambulatory Pediatric Fellowship at Boston Children's Hospital and received an M.B.A. from Columbia Business School.

*David Siner*, serves as our Senior Director CMC, joined Alcobra in August 2014. He previously served with Neurim Pharmaceuticals Ltd an Israeli drug development company from 2007 to through 2014 serving as Director of CMC. In this role, he managed the global CMC operations and drug development, including CMC regulatory affairs in direct contact with worldwide agencies in Europe, Asia, Oceania, South America, Israel and South Africa in accordance with GMP, GDP and GLP and ICH guidelines. He also managed the chain of supply and Quality Assurance tasks with several global pharmaceutical companies. Prior to his role at Neurim Ltd., David served as analytical chemist at Charles River Laboratories Montreal Canada from 2004 to 2007. David holds a B.A in Chemistry from the Technion Institute of Technology in Haifa Israel and a M.Sc. from the Faculty of Medicine at the Tel-Aviv University Israel in Developmental Biology.

*Dr. Johanna Schumann* serves as our Senior Vice President for Preclinical Development. She joined us in August 2013 after working at BioLineRx, an Israeli drug development company, from 2010 through 2013, serving as Preclinical Development Manager. In this role, she designed, managed and executed preclinical activities, including toxicology, pharmacokinetics and pharmacodynamics studies, in accordance with the relevant regulatory authorities' guidelines, for multiple preclinical phase drug development projects and medical indications. Dr. Schumann holds a B.Sc. in Life Sciences from the Hebrew University of Jerusalem, and an M.Sc. and Ph.D. in Pharmacology from the School of Pharmacy, The Hebrew University of Jerusalem.

*Irena Katsman*, our Vice President for Finance, joined Alcobra in April 2015. Immediately prior to joining Alcobra and since 2008, Ms. Katsman served as Finance Manager of Omrix Biopharmaceuticals, a Johnson & Johnson company. Ms. Katsman began her career as a certified public accountant at PricewaterhouseCoopers. Ms. Katsman is a certified public accountant and holds a B.A. in Economics and Accounting from the Hebrew University of Jerusalem and an M.B.A. from Tel Aviv University.

*Elad Ben David*, serves as our Director of Regulatory Affairs. He joined Alcobra in June 2015 after working as a Regulatory Affairs Manager at Isorad Ltd., an Israeli radiopharmaceutical company from 2013 through 2015, in this role he managed all regulatory affairs operations and strategies. Prior to his role at Isorad Ltd, Elad served as a Regulatory Affairs Specialist at Lumenis (2012-2013), a medical device company and a global leader in the field of energy-based technologies (laser, IPL and RF) for the surgical, ophthalmology and aesthetic markets. In this role, he provided regulatory strategy and support to R&D and business teams, reviewing and filing regulatory submissions to international regulatory authorities. Prior to his role at Lumenis, Elad served as a Regulatory Affairs Project Manager at Dexel Pharma (2007-2012), an Israeli pharmaceutical company, in this role he managed the interaction with international regulatory authorities, regulatory compliance of products from development stage, marketing authorizations and post approval regulatory operations. Elad holds an M.B.A. in international management and marketing from Ruppin Academic Center, M.Sc. in Life Sciences form Tel Aviv University, and a B.Sc. in Life Sciences form Tel Aviv University.

## 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, 2016. All amounts reported in the table reflect the cost to us, in U.S. Dollars, as recognized in our financial statements for the year ended December 31, 2016. Amounts paid in NIS are translated into U.S. dollars at the rate of NIS 3.84 = 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, 2016.

Name and Position	<u>Base Salary</u>	<u>Benefit Cost (1)</u>	<u>Share-Based Payment (2)</u>	<u>Bonus (3)</u>	<u>Total</u>
Dr. Yaron Daniely Chief Executive Officer, President and Director	\$ 384,000	\$ 113,000	\$ 907,000	\$ 85,000	\$ 1,489,000
Dr. Tomer Berkovitz Chief Financial Officer, Chief Operating Officer	300,000	106,000	385,000	93,000	884,000
David Baker Chief Commercial Officer	317,000	57,000	372,000	88,000	834,000
Dr. Jonathan Rubin Chief Medical Officer	310,000	55,000	142,000	73,000	580,000
Hanna Ron Senior Vice President CMC	116,000	49,000	73,000	22,000	260,000

- (1) Include the social benefits paid by us on behalf of the employees, including convalescence pay, contributions made by the company to an insurance policy or a pension fund, work disability insurance, life insurance, medical insurance, severance, educational fund and payments for social security. It also includes leased vehicle cost for some of the employees.
- (2) Represents the equity-based compensation expenses recorded in our consolidated financial statements for the year ended December 31, 2016 based on the options' grant date fair value in accordance with accounting guidance for equity-based compensation.
- (3) Does not include bonus payments for 2015 to Dr. Yaron Daniely and Dr. Tomer Berkovitz in the amount of \$150,000 and \$100,000 respectively, which were approved by our shareholders and paid in 2016.

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, 2016 was approximately \$3.3 million. This amount includes salaries, consulting fees, directors' fees, car expenses and vacation, pension, severance, retirement or similar benefits or expenses, employer's taxes and bonuses expenses in an amount of \$0.6 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, share-based compensation in the amount of \$2.2 million was recorded in 2016.

## **Employment Agreements with Executive Officers**

We have entered into written employment agreements with all of our executive officers. Each of these agreements contains provisions regarding non-competition, confidentiality of information and ownership of inventions. The non-competition provision applies for a period that is generally 12 months following termination of employment. The employment agreements also include severance for certain key employees subject to our compensation policy. The enforceability of covenants not to compete in Israel and the United States is subject to limitations. In addition, we are required to provide notice prior to terminating the employment of our executive officers, other than in the case of a termination for cause.

## **Directors' Service Contracts**

Other than with respect to our directors that are also executive officers, we do not have written agreements with any director providing for benefits upon the termination of his employment with our company.

We are also required to maintain an office holder compensation policy that sets 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.

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."

Our shareholders approved a Compensation Policy in February 2014, which was subsequently amended in July 2015 and in July 2016 that meets the above requirements.

## **6.C. Board practices**

### ***Board of Directors***

Under the Israeli Companies Law, our Board of Directors is vested with the power to set corporate policy and oversee our business. 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 amended and restated articles of association, our Board of Directors must consist of at least five and not more than eleven directors. Our Board of Directors consists of eight directors. We have only one class of directors.

Our directors are each elected at the annual general meeting of our shareholders and serve until the next annual general meeting. Such election is subject to the selection, or recommendation for the Board of Director's selection, by a majority of independent directors. Directors may 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 amended and restated articles of association.

In addition, our amended and restated articles of association allow our Board of Directors to appoint directors, to fill vacancies on our Board of Directors, for a term of office equal to the remaining period of the term of office of the directors whose offices have been vacated, or appoint new additions to Board of Directors up to the maximum number of directors.

Under the Israeli Companies Law, nominations for directors may be made by any shareholder holding at least one percent (1%) of our outstanding voting power. However, any such shareholder may make such a nomination only if a written notice of such shareholder's intent to make such nomination has been given to our Board of Directors. Any such notice must include certain information which is 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 the financial statements of the Company 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. Mr. Ben Yosef has such accounting and financial expertise.

#### ***External Directors***

Under the Israeli Companies Law, except as provided below, companies incorporated under the laws of the State of Israel that are publicly traded, including Israeli companies with shares listed on the NASDAQ, are required to appoint at least two external directors, who meet the qualifications requirements set forth in the Israeli Companies Law.

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.

Pursuant to newly enacted regulations under the Israeli Companies Law, the Board of Directors of a company such as the Company is not required to have external directors if: (i) the company does not have a controlling shareholder (as such term is defined in the Israeli Companies Law); (ii) a majority of the directors serving on the Board of Directors are "independent," as defined under NASDAQ Listing Rule 5605(a)(2); and (iii) the company follows NASDAQ Rule 5605(e)(1), which requires that the nomination of directors be made, or recommended to the Board of Directors, by a Nominating Committee of the Board of Directors consisting solely of independent directors, or by a majority of independent directors. We meet all these requirements. On June 7, 2016, our Board of Directors resolved to adopt the corporate governance exemption set forth above, and accordingly we no longer have external directors as members of our Board of Directors.

#### ***Leadership Structure of the Board***

In accordance with the Israeli Companies Law and our amended and restated 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 Mr. Howard Rosen to serve as 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.

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

Under the Israeli Companies Law, our Audit Committee is responsible for:

- determining whether there are deficiencies in the business management practices of our Company, and making recommendations to the Board of Directors to improve such practices;
- determining whether to approve certain related party transactions (including transactions in which an office holder has a personal interest and whether such transaction is extraordinary or material under the Companies Law) (see Item 16G. - “Corporate Governance - Approval of Related Party Transactions under Israeli law”);
- examining our internal controls and internal auditor’s performance, including whether the internal auditor has sufficient resources and tools to dispose of its responsibilities;
- examining the scope of our auditor’s work and compensation and submitting a recommendation with respect thereto to our Board of Directors or shareholders, depending on which of them is considering the appointment of our auditor;
- establishing procedures for the handling of employees’ complaints as to the management of our business and the protection to be provided to such employees;
- determining whether certain acts of an office holder not in accordance with his or her fiduciary duty owed to the Company are extraordinary or material and to approve such acts and certain related party transactions (including transactions in which an office holder has a personal interest) and whether such transaction is extraordinary or material under the Companies Law (see Item 16G. - “Corporate Governance - Approval of Related Party Transactions under Israeli Law”);
- deciding whether to approve and to establish the approval process (including by tender or other competitive proceedings) for certain transactions with a controlling shareholder or in which a controlling shareholder has a personal interest; and
- determining the process of approving of transactions that are not negligible, including determining the types of transactions that will be subject to the approval of the Audit Committee.

#### ***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 the requirements for such committee under the Israeli Companies Law, as described below. The Audit Committee Charter is posted on our website.

### *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 Ms. Tori, Mr. Segev and Mr. Ben Yosef. Our Board of Directors has determined that Mr. Ben Yosef is an audit committee financial expert as defined by the SEC rules and has the requisite financial sophistication 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 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.

### **Compensation Committee**

Under the Israeli Companies Law, the Board of Directors of a public company must appoint a Compensation Committee.

Under the Listing Rules of NASDAQ, we are required to maintain a Compensation Committee consisting entirely of independent directors (or the determination of such compensation solely by the independent members of our Board of Directors).

Our Compensation Committee consists of Mr. Geffken, who serves as the chairperson of the committee, Mr. Ben Yosef and Mr. Segev, all of whom are independent under the listing standards of the Listing Rules of NASDAQ.

Under the Israeli Companies Law, our Compensation Committee is responsible for (i) proposing a an office holder compensation policy to the Board of Directors, (ii) proposing necessary revisions to the compensation policy and examining 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 office holder compensation policy, whether to exempt an engagement with an unaffiliated nominee for the position of Chief Executive Officer from requiring shareholders’ approval. Under the regulations promulgated under the Israeli Companies Law, certain exemptions and reliefs with respect to the Compensation Committee are granted to companies whose securities are traded outside of Israel.

The Companies Law provides that our compensation policy must serve as the basis for the decisions concerning the financial terms of employment or engagement of executives and directors, including exculpation, insurance, indemnification or any monetary payment or obligation of payment in respect of employment or engagement. The compensation policy must be approved (or reapproved) not longer than every three years, and relate to certain factors, including advancement of the company’s objective, 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 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 or 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 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 a director or executive 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.

Our compensation policy, consistent with the foregoing Companies Law requirements, was adopted by our shareholders on February 17, 2014 and since then it was amended several times.

#### *Compensation Committee - Charter*

Our Board of Directors has adopted a Compensation Committee Charter setting forth the responsibilities of the Compensation Committee consistent with the Listing Rules of NASDAQ and the requirements under the Companies Law, as described above. The Compensation Committee Charter requires that our Compensation Committee be comprised of at least three members. The Compensation Committee Charter is posted on our website.

#### *Nominating Committee*

Our Board of Directors does not have an independent Nominating Committee. As indicated above, the election of members of our Board of Directors is subject to the selection, or recommendation for the Board of Director's selection, by a majority of our independent directors.

#### *Internal auditor*

Under the Israeli Companies Law, the board of directors of an Israeli public company must appoint an internal auditor recommended by the audit committee 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, CPA, a partner at 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**

Our management consists of our Chief Executive Officer, Chief Financial Officer, Chief Medical Officer, Chief Commercial Officer, Senior Director CMC (chemistry manufacturing and controls), VP for Finance, SVP for Preclinical Development and Director of Regulatory Affairs. We further have service agreements with U.S.-based regulatory consultants as well as additional U.S.-based clinical consultants who are members of our clinical advisory board. We believe that we maintain good relations with all of them. We are currently undergoing a reduction in force and at the end of the process we expect to have 12 employees.

Over the past three years, the number of our employees by function was as follows:

<i>Function</i>	<b>December 31,</b>		
	<b>2016</b>	<b>2015</b>	<b>2014</b>
Research, development and quality assurance	11	12	8
Pre-Commercialization	2	2	1
Administration, finance and operation	6	5	4
Total	<u>19</u>	<u>19</u>	<u>13</u>

Over the past three years, the number of our employees by geographic area was as follows:

<b>Geographic area</b>	<b>December 31,</b>		
	<b>2016</b>	<b>2015</b>	<b>2014</b>
Israel	14	15	10
United States	5	4	3
<b>Total</b>	<b>19</b>	<b>19</b>	<b>13</b>

#### **6.E. Share ownership**

As of April 27, 2017, each of our executive officers and directors, other than Dr. Daniely, beneficially owned less than 1% of our issued and outstanding Ordinary Shares. Dr. Daniely beneficially owned 2.6% of our Ordinary Shares.

The following table summarizes information about the options to purchase our Ordinary Shares owned by Dr. Daniely that were outstanding as of April 27, 2017:

<b>NUMBER OUTSTANDING</b>	<b>EXERCISE PRICE</b>	<b>EXPIRATION DATE</b>
340,460	\$ 0.33	November 15, 2020
89,553	\$ 8.00	January 2, 2023
37,500	\$ 23.85	February 17, 2020
400,000	\$ 5.63	March 30, 2020
192,487	\$ 4.55	July 18, 2021

On March 13, 2017, an additional 319,365 options were granted to Dr. Daniely with an exercise price of \$1.19 per share and which expire on March 12, 2022. Such grant of options is subject to the approval of our shareholders.

#### **2010 Incentive Option Plan**

We maintain one equity incentive plan - our 2010 Incentive Option Plan, or our 2010 Plan. As of April 27, 2017, a total of 4,487,334 shares were reserved for issuance under our 2010 Plan, of which options to purchase 4,152,727 Ordinary Shares were issued and outstanding thereunder (out of which 482,365 options are subject to the approval of our shareholders). Of such outstanding options, options to purchase 1,487,033 Ordinary Shares were vested as of April 27, 2017, with a weighted average exercise price of \$5.89 per share.

Our 2010 Plan, which was adopted by our Board of Directors in February, 2010, and approved by our shareholders in July 2015, provides for the grant of options to our and our affiliates' respective directors, employees, office holders, service providers and consultants. On December 16, 2014, our Board of Directors adopted an appendix to the 2010 Plan for U.S. residents, which was later approved by our shareholders. The initial reserved pool under our 2010 plan has been increased by our Board of Directors a number of times, and most recently on March 13, 2017.

The 2010 Plan is administered by our Board of Directors or by a committee thereof, which shall determine, subject to Israeli and U.S. law, the grantees of awards and various terms of the grant. The 2010 Plan provides for granting options in compliance with Section 102 of the Israeli Income Tax Ordinance, 1961, or the Ordinance, and under the U.S. Revenue Code of 1986, as amended.

Options granted under the 2010 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 2010 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 2010 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, or pursuant to a vesting schedule that is determined according to pre-specified performance milestones in accordance with company's objectives. Options that are not exercised within the pre-specified option term (generally five or ten years from the grant date) expire, unless otherwise determined by the Board 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: (i) pursuant to resolutions of our Board of Directors, 2,711,570 options will become fully vested; (ii) other outstanding options 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 seven 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 April 25, 2017, or a different date, if so provided in the table below or footnotes thereof.

According to our transfer agent, as of April 25, 2017, there were three record holders of our Ordinary Shares, one of which (Cede & Co., the nominee of the Depository Trust Company) is a U.S. holder holding 99% of our Ordinary Shares. The number of record holders in the United States is not representative of the number of beneficial holders nor is it representative of where such beneficial holders are resident since many of these Ordinary Shares are held by brokers or other nominees. None of our shareholders have 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 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 Alcobra Ltd., Azrieli Triangle Building, 132 Derech Menachem Begin, 39th Floor, Tel Aviv 6701101 Israel.

Name	Ordinary Shares Beneficially Owned	
	Number	Percentage
Exodus Capital L.P., Exodus Management Israel Ltd. and its subsidiaries (1)	4,619,599	16.8%
Franklin Resources, Inc., Charles B. Johnson, Rupert H. Johnson, Jr., Franklin Advisers, Inc. (2)	4,477,500	16.2%
RA Capital Management, LLC, RA Capital Healthcare Fund, L.P. and Peter Kolchinsky (3)	2,392,583	8.7%
Udi Gilboa (4)	2,360,816	8.6%
Baker Bros. Advisors LP, Baker Bros. Advisors (GP) LLC, Felix J. Baker, Julian C. Baker (5)	2,336,359	8.5%
Venrock Healthcare Capital Partners, L.P., VHCP Co-Investment Holdings, LLC, Venrock Healthcare Capital Partners II, L.P., VHCP Co-Investment Holdings II, LLC, VHCP Management, LLC, VHCP Management II, LLC, Bong Koh and Anders Hove (6)	2,196,373	8.0%
Broadfin Capital, LLC, Broadfin Healthcare Master Fund, Ltd. and Kevin Kotler (7)	2,057,106	7.5%
David M. Slager, Regals Fund LP and Regals Capital Management LP (8)	1,720,725	6.2%

- (1) Based solely on an Amendment 6 to Schedule 13D filed with the SEC April 12, 2017, and which reflects holdings as of April 6, 2017.
- (2) Based solely on an Amendment 1 to Schedule 13G filed with the SEC November 9, 2016, and which reflects holdings as of October 31, 2016.
- (3) Based solely on a Schedule 13G filed with the SEC October 21, 2016, and which reflects holdings as of October 13, 2016.
- (4) Based solely on an Amendment 2 to Schedule 13G filed with the SEC on February 16, 2016, and which reflects holdings as of December 31, 2015.
- (5) Based solely on a Schedule 13G filed with the SEC on February 16, 2016, and which reflects holdings as of December 31, 2015.
- (6) Based solely on an Amendment 2 to Schedule 13G filed with the SEC on February 14, 2017, and which reflects holdings as of December 31, 2016.
- (7) Based solely on an Amendment 2 to Schedule 13G filed with the SEC on February 13, 2017, and which reflects holdings as of December 31, 2016.
- (8) Based solely on an Amendment 2 to Schedule 13G filed with the SEC on February 14, 2017, and which reflects holdings as of December 31, 2016.

## **7.B. Related party transactions**

### ***Employment Agreements***

We have entered into written employment agreements with each of our executive officers. These agreements provide for notice periods of varying duration for termination of the agreement by us or by the relevant executive officer, during which time the executive officer will continue to receive base salary and benefits. We have also entered into customary non-competition, confidentiality of information and ownership of inventions arrangements with our executive officers. However, the enforceability of the noncompetition provisions may be limited under applicable law.

### ***Options***

Since our inception we have granted options to purchase our Ordinary Shares to our officers and certain of our directors. Such option agreements may contain acceleration provisions upon certain merger, acquisition, or change of control transactions. We describe our option plans under Item 6.E. "Share Ownership" above. If the relationship between us and an executive officer or a director is terminated, except for cause (as defined in the various option plan agreements), options that are vested will generally remain exercisable for ninety days after such termination.

### ***Indemnification Agreements and Insurance Coverage***

Our amended and restated 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' & Officers' insurance for each of our officers and directors.

## **7.C. Interests of experts and counsel**

Not applicable.

## **ITEM 8. FINANCIAL INFORMATION**

### **8.A. Consolidated statements and other financial information**

See Item 18. Financial Statements.

## Legal Proceedings

On December 16, 2014, a class action lawsuit was filed against us and certain of our current and former officers and directors in the U.S. District Court for the Southern District of New York. The complaint, brought by a putative class of investors, alleges, among other things, that our officers and directors made false or misleading statements relating to the results of our Phase 3 study for our MDX drug candidate. On May 20, 2015, we moved to dismiss the complaint. On March 30, 2016, the Court accepted the motion to dismiss all charges against the Company.

On February 17, 2017, a class action lawsuit was filed against us and certain of our current officers (one of whom also is a director) in the U.S. District Court for the Southern District of New York. The case was filed on behalf of a putative class of investors who purchased or acquired our publicly-traded securities between August 13, 2015 and January 17, 2017. The complaint asserted violations of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 thereunder. The complaint alleged, among other things, that we and the individual defendants made false or misleading statements relating to the results of our second Phase 3 clinical trial for our MDX drug candidate.

Such legal proceedings, regardless of their outcome, could be costly, divert management attention, or damage our reputation and demand for our products. Litigation, particularly in the United States, is inherently unpredictable and unexpectedly high awards of damages can result if we receive an adverse verdict. In many cases, particularly in the United States, the practice of the plaintiffs' bar is to claim damages (compensatory, punitive and statutory) in extremely high amounts. Accordingly, it is difficult to quantify the potential exposure to claims in many proceedings of the type mentioned above. Unfavorable resolution of current and similar future proceedings could have a material adverse effect on our financial condition and results of operations. See Item 3.D. Risk Factors "We may be subject to any number of legal proceedings, which may be expensive and could divert management attention."

## 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 "Dividend and Liquidation Rights" for additional information.

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

## 8.B. Significant changes

Except as disclosed elsewhere in this annual report, there have been no other significant changes from December 31, 2016, 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 Capital Market under the symbol "ADHD" since May 22, 2013. Starting from March 28, 2014, our Ordinary Shares have been listed on the NASDAQ Global Market. Prior to that date, there was no public trading market for our Ordinary Shares. Our initial public offering was priced at \$8.00 per share on May 21, 2013. The following table sets forth for the periods indicated the high and low sales prices per ordinary share as reported on the NASDAQ Capital Market and the NASDAQ Global Market:

<b>Annual Information:</b>		<b>Low</b>	<b>High</b>
2013	\$	6.50	26.96
2014		3.12	25.44
2015		3.68	9.50
2016		1.77	6.50
<b>Quarterly Information</b>			
First Quarter 2015	\$	3.68	8.30
Second Quarter 2015		5.38	8.84
Third Quarter 2015		5.61	9.50
Fourth Quarter 2015		5.28	8.78
First Quarter 2016		3.15	6.50
Second Quarter 2016		3.61	5.75
Third Quarter 2016		1.95	5.36
Fourth Quarter 2016		1.77	2.90
<b>Monthly Information:</b>			
October 2016	\$	1.90	2.90
November 2016		1.77	2.23
December 2016		1.80	2.53
January 2017		0.83	2.58
February 2017		1.08	1.46
March 2017		1.08	1.38
April 2017 (through April 25, 2017)		1.01	1.25

**9.B. Plan of distribution**

Not applicable.

**9.C. Market for Ordinary Shares**

Our Ordinary Shares are listed on the NASDAQ Global Market.

**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 51-409899-5. Section 1.2 of our amended and restated 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 the 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:

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

If it is determined that an office holder has a personal interest in a transaction, 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 amended and restated 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 the Israeli Companies Law, generally a director who has a personal interest in an extraordinary transaction which is brought for discussion before our Board of Directors or its committees 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 generally be invalid.

Our amended and restated 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, audit committee, our board of directors and the shareholders.

### ***Borrowing Powers***

Pursuant to the Israeli Companies Law and our amended and restated articles of association, our Board of Directors may exercise all powers and take all actions that are not required under law or under our amended and restated articles of association to be exercised or taken by our shareholders or other corporate bodies, including the power to borrow money for company purposes.

### ***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 amended and restated 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 amended and restated 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 amended and restated 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 our amended and restated 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 amended and restated 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 amended and restated 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 amended and restated articles of association and the laws of the State of Israel do not restrict in any way the ownership or voting of 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 is required by the Israeli Companies Law to make a tender offer to all of the company's shareholders for the purchase of all of the issued and outstanding shares of the company.

A person wishing to acquire shares of an Israeli public company and who would as a result hold over 90% of the issued and outstanding share capital of a certain class of shares is required to make a tender offer to all of the shareholders who hold shares of the same class for the purchase of all of the issued and outstanding shares of the same class.

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

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

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

### **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. For example, any merger or acquisition of us will require the prior consent of the Chief Scientist, as well as the Investment Center. See Item 3.D. Risk factors "We are subject to anti-takeover provisions that could delay or prevent our acquisition by another entity."

#### ***Requirement of Disclosure of Shareholder Ownership***

There are no provisions of our amended and restated 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 amended and restated 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**

None.

#### **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 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 amended and restated articles of association nor the laws of the State of Israel restrict in any way the ownership or voting of ordinary shares by non-residents 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 should 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 Taxation 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**

As of January 1, 2016, Israeli resident companies, such as us, are generally subject to corporate tax at the rate of 25%. As of January 1, 2017, the corporate tax rate is reduced to 24% and as of January 1, 2018 should be further reduced to 23%. Between January 1, 2014 and December 31, 2015, the corporate tax rate was 26.5%.

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) its business is managed and controlled from 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, 2016, an additional income tax at a rate of 2% will be imposed on high earners whose annual taxable income or gain exceeds NIS 803,520. As of January 1, 2017, an additional income tax at a rate of 3% will be imposed on high earners whose annual taxable income or gain exceeds NIS 640,000.

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 in a general meeting of shareholders, 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 whether by virtue of shares, rights to shares or other rights, or in any other manner, including by means of voting or trusteeship agreements.

The term “Israeli Resident” for Individuals is generally defined under Israeli Income Tax Ordinance [New Version], 1961 (the “Israeli Tax Ordinance”) as an individual whose center of life is in Israel. According to the Israeli Tax Ordinance, 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) the place of the individual’s permanent home; (b) the place of residence of the individual and his family; (c) the place of the individual’s regular or permanent place of business 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.

#### **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, 2016, an additional tax at a rate of 2% will be imposed on high earners whose annual income or gains exceed NIS 803,520. As of January 1, 2017, an additional income tax at a rate of 3% will be imposed on high earners whose annual taxable income or gain exceeds NIS 640,000.

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 (currently, up to 50% for individuals and as of January 1, 2016, 25% for Israeli resident corporations .. As of January 1, 2017, the corporate tax rate is reduced to 24% and as of January 1, 2018 should be further reduced to 23%).

#### **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 Shares at the rate of 25% (or 30% for individuals, if such individual 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 tax certificate is obtained from the Israeli Tax Authority authorizing withholding-exempt remittances or a reduced rate of tax pursuant to an applicable tax treaty.

A non-Israeli resident who receives dividends from which tax was withheld is generally exempt from the duty to file tax returns in Israel in respect of such income.

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 outstanding shares of the voting stock 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 not more than 25% of the gross income of the paying corporation for such prior taxable year (if any) consists certain interest or dividends, 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’ shareholders 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**

Currently, Israeli law 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. The Company 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 passive foreign investment company, or 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 Taxation 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 believe that we may be deemed a PFIC. 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, or 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 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 was drafted to: (i) preserve principal (capital); (ii) maintain liquidity in accordance with cash flow requirements; and (iii) maximize the rate of return within the stated guidelines in the policy. Accordingly, a 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 investment policy is monitored by the Company’s Audit Committee.

Our market risk exposure is primarily a result of foreign currency 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 foreign 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 2016, approximately 20% of our expenses were denominated in NIS. Changes of 5% and 10% in the \$/NIS exchange rate would have increased/decreased the operation expenses by 0.97% and 1.86%, respectively. However, these historical figures may not be indicative of future exposure, as we expect that the percentage of our NIS denominated expenses will decrease in the future, therefore further 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.

### **Interest Rate Risk**

We are also exposed to limited market risk related to fluctuations in interest rates and market prices. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. The primary objective of our investment activities is to preserve our capital to fund our operations.

As of December 31, 2016, our cash, cash equivalents, short-term deposits and marketable securities totaled \$50.2 million. Our current investment policy has the following objectives: (i) preserve principal (capital); (ii) maintain liquidity in accordance with cash flow requirements; and (iii) maximize the rate of return within the stated guidelines in the policy. To achieve these goals, we invest available cash in bank deposits with banks that have a credit rating of at least Baa1/BBB+ and in tradable securities with high credit quality and trading liquidity, including U.S. Treasury bonds, money market funds, and corporate debt instruments that carry a rating of A2/A or better. A portion of our investments may be subject to interest rate risk and could fall in value if market interest rates increase. Our interest rate exposure is mitigated by the short-term duration of our investments. We do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate risk exposure. We have not been exposed nor do we anticipate being exposed to material risks due to changes in interest rates.

**ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES**

The Company does 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, 2016, 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**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based principally on the framework and criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission as of the end of the period covered by this report. Based on that evaluation, our management has concluded that our internal control over financial reporting was effective as of December 31, 2016 at providing reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

**(c) Attestation Report of the Registered Public Accounting Firm**

This annual report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting due to an exemption for emerging growth companies provided in the JOBS Act.

**(d) Changes in Internal Control over Financial Reporting**

During the year ended December 31, 2016, 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 Mr. Ben Yosef, a member of our audit committee, is an audit committee financial expert, as defined under the rules under the Exchange Act, and is 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.alcobra-pharma.com](http://www.alcobra-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, 2016 and 2015.

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, 2016 and 2015:

	Year Ended	
	December 31,	
	2016	2015
Audit fees <sup>(1)</sup>	\$ 87	\$ 87
Audit-related fees <sup>(2)</sup>	-	90
Tax fees <sup>(3)</sup>	25	35
All other fees	-	-
Total	<u>\$ 112</u>	<u>\$ 212</u>

(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 in connection with two public offerings in 2015.

(3) Includes professional fees related to tax returns, transfer pricing and consulting on state and sales tax in the United States and Israeli tax.

**Pre-Approval of Auditors' Compensation**

Our audit committee has 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.

**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, requires 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 the NASDAQ Stock Market. 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 the NASDAQ Stock Market 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 the NASDAQ Stock Market, we have elected to follow the provisions of the Israeli Companies Law, rather than the Listing Rules of the NASDAQ Stock Market, with respect to the following requirements:

- *Distribution of periodic reports to shareholders; proxy solicitation.* As opposed to the Listing Rules of the NASDAQ Stock Market, 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.
- *Compensation of officers.* Israeli law and our amended and restated 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 the NASDAQ Stock Market with respect to the Chief Executive Officer and all other executive officers. Instead, compensation of executive officers is determined and approved by our Compensation Committee and our Board of Directors, and in certain circumstances by our shareholders, either in consistency with our office holder compensation policy or, in special circumstances in deviation therefrom, 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 our Company (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 of disinterested shareholders, or (ii) the total shares held by non-controlling and disinterested shareholders voted against the arrangement does not exceed two percent (2%) of the voting rights in our Company.

Additionally, approval of the compensation of a director, including a director who is also an executive officer, 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 for an external director, as set forth in the Companies Law, 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.

A director or executive officer may not be present when the board of directors of a company discusses or votes upon the terms of his or her compensation, unless the chairman of the board of directors determines that he or she should be present to present the transaction that is subject to approval.

- *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 consolidated financial statements, and the related notes thereto, and the Reports of Independent Public Accountants are filed as a part of this annual report.

<a href="#">Report of Independent Registered Public Accounting Firm</a>	F-2
<a href="#">Consolidated Balance Sheets</a>	F-3
<a href="#">Consolidated Statements of Comprehensive Loss</a>	F-4
<a href="#">Consolidated Statements of Changes in Shareholders' Equity</a>	F-5
<a href="#">Consolidated Statements of Cash Flow</a>	F-6
<a href="#">Notes to Consolidated Financial Statements</a>	F-7 - F-24

**ITEM 19. EXHIBITS****EXHIBIT INDEX**

<b>EXHIBIT NUMBER</b>	<b>DESCRIPTION OF DOCUMENT</b>
1.1	Amended and Restated Articles of Association of the Company, filed as Exhibit 3.2 to Form F-1/A filed on March 19, 2013 (File No. 333-186003) and incorporated herein by reference
4.1	Form of Representative's Warrant Agreement, filed as Exhibit 4.2 to Form F-1/A filed on April 25, 2013 (File No. 333-186003) and incorporated herein by reference
4.2	Consulting Agreement between the Company and Adler Consulting LLC, dated November 2010, filed as Exhibit 10.1 to Form F-1/A filed on January 14, 2013 (File No. 333-186003) and incorporated herein by reference
4.3	Alcobra Ltd. 2010 Incentive Option Plan, as amended
4.4	Form of Indemnification Agreement, filed as Exhibit 10.4 to Form F-1/A filed on February 19, 2013 (File No. 333-186003) and incorporated herein by reference
4.5 <sup>oo</sup>	Letter of Approval from the Office of Chief Scientist, filed as Exhibit 10.8 to Form F-1/A filed on February 19, 2013 (File No. 333-186003) and incorporated herein by reference
4.6	Employment agreement between the Company and Yaron Daniely, dated March 4, 2010, filed as Exhibit 10.9 to Form F-1/A filed on April 25, 2013 (File No. 333-186003) and incorporated herein by reference
4.7	Employment agreement between the Company and Jonathan Rubin, dated July 25, 2013, filed as Exhibit 10.13 to Form F-1/A filed on October 22, 2013 (File No. 333-191714) and incorporated herein by reference
4.8	Alcobra Ltd. Amended and Restated Compensation Policy for Company Office Holders, as adopted on July 19, 2016, filed as Exhibit 99.2 to Form 6-K filed on June 8, 2016 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
15.1	Consent of Kost, Forer, Gabbay & Kasierer, a member of Ernst & Young Global

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The following materials from our Annual Report on Form 20-F for the year ended December 31, 2016 formatted in XBRL (eXtensible Business Reporting Language): (i) the Consolidated Balance Sheets, (ii) the Consolidated Statements of Comprehensive Loss, (iii) the Consolidated Statements of Changes in Shareholders' Equity, (iv) the Consolidated Statements of Cash Flows and (v) the Notes to Consolidated Financial Statements, tagged as blocks of text and in detail

∞ English translation of original Hebrew document.

#### SIGNATURES

Alcobra 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.

ALCOBRA LTD.

By: /s/ Dr. Yaron Daniely  
Dr. Yaron Daniely  
Chief Executive Officer and President

Date: April 28, 2017

ALCOBRA LTD. AND ITS SUBSIDIARY  
CONSOLIDATED FINANCIAL STATEMENTS  
AS OF DECEMBER 31, 2016  
U.S. DOLLARS IN THOUSANDS

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ey.com

**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

**To the Board of Directors and Shareholders of**

**ALCOBRA LTD.**

We have audited the accompanying consolidated balance sheets of Alcobra Ltd. and its subsidiary (the "Company") as of December 31, 2016 and 2015, and the related consolidated statements of comprehensive loss, shareholders' equity and cash flows for each of the three years in the period ended December 31, 2016. 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 also 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 management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the consolidated financial position of Alcobra Ltd. and its subsidiary at December 31, 2016 and 2015, and the consolidated results of their operations and their cash flows for each of the three years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

Tel-Aviv, Israel  
April 27, 2017

/s/ KOST FORER GABBAY & KASIERER  
A Member of EY Global

**CONSOLIDATED BALANCE SHEETS**

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

	December 31,	
	2016	2015
<b>ASSETS</b>		
<b>CURRENT ASSETS:</b>		
Cash and cash equivalents	\$ 2,304	\$ 16,658
Short-term bank deposits	33,000	34,022
Marketable securities	14,938	-
Prepaid expenses and other receivables	1,057	1,666
<b>Total current assets</b>	<b>51,299</b>	<b>52,346</b>
<b>LONG-TERM ASSETS:</b>		
Long-term bank deposits	-	19,000
Other long-term assets	29	110
Property and equipment, net	240	227
<b>Total long-term assets</b>	<b>269</b>	<b>19,337</b>
<b>TOTAL ASSETS</b>	<b>\$ 51,568</b>	<b>\$ 71,683</b>
<b>LIABILITIES AND SHAREHOLDERS' EQUITY</b>		
<b>CURRENT LIABILITIES:</b>		
Trade payables	\$ 528	\$ 57
Accrued expenses and other liabilities	3,812	2,295
<b>Total current liabilities</b>	<b>4,340</b>	<b>2,352</b>
<b>SHAREHOLDERS' EQUITY</b>		
Ordinary shares of NIS 0.01 par value - 50,000,000 shares authorized at December 31, 2016 and 2015; 27,867,119 and 27,865,244 issued shares at December 31, 2016 and 2015, respectively; 27,562,795 and 27,560,920 shares outstanding at December 31, 2016 and 2015, respectively	74	74
Treasury shares - 304,324 ordinary shares at December 31, 2016 and 2015	*)	*)
Additional paid-in capital	142,780	140,274
Accumulated other comprehensive loss	(6)	-
Accumulated deficit	(95,620)	(71,017)
<b>Total shareholders' equity</b>	<b>47,228</b>	<b>69,331</b>
<b>TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY</b>	<b>\$ 51,568</b>	<b>\$ 71,683</b>

\*) Represents an amount less than \$ 1.

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

**CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS**

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

	December 31,		
	2016	2015	2014
Research and development expenses	\$ 18,391	\$ 13,461	\$ 25,105
Pre-commercialization expenses	1,419	1,245	2,134
General and administrative expenses	5,357	4,992	5,839
Operating loss	25,167	19,698	33,078
Financial income, net	(637)	(300)	(227)
Net loss before taxes	24,530	19,398	32,851
Taxes on income	73	51	(17)
Net loss	<u>\$ 24,603</u>	<u>\$ 19,449</u>	<u>\$ 32,834</u>
Unrealized loss on available-for-sale marketable securities	6	-	-
Total comprehensive loss	<u>\$ 24,609</u>	<u>\$ 19,449</u>	<u>\$ 32,834</u>
Basic and diluted net loss per share	<u>\$ (0.89)</u>	<u>\$ (0.90)</u>	<u>\$ (2.40)</u>
Weighted average number of Ordinary shares used in computing basic and diluted net loss per share	<u>27,562,657</u>	<u>21,638,207</u>	<u>13,674,818</u>

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

## STATEMENTS OF CHANGES IN SHAREHOLDERS' EQUITY

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

	Ordinary Shares		Treasury shares		Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total shareholders' equity
	Number	Amount	Number	Amount				
Balance as of January 1, 2014	13,636,709	\$ 39	304,324	\$ *)	\$ 67,383	\$ -	\$ (18,734)	\$ 48,688
Issuance of shares upon exercise of options	1,174	*)	-	-	-	-	-	*)
Issuance of shares upon cashless exercise of warrants	64,839	*)	-	-	-	-	-	*)
Share-based compensation	-	-	-	-	4,089	-	-	4,089
Net loss	-	-	-	-	-	-	(32,834)	(32,834)
Balance as of December 31, 2014	13,702,722	39	304,324	*)	71,472	-	(51,568)	19,943
Issuance of shares upon exercise of options	4,000	*)	-	-	13	-	-	13
Issuance of shares upon public offering (\$4.00 per share), net of \$ 203 issuance expenses	7,475,000	19	-	-	27,884	-	-	27,903
Issuance of shares upon public offering (\$6.50 per share), net of \$ 421 issuance expenses	6,379,198	16	-	-	38,540	-	-	38,556
Share-based compensation	-	-	-	-	2,365	-	-	2,365
Net loss	-	-	-	-	-	-	(19,449)	(19,449)
Balance as of December 31, 2015	27,560,920	74	304,324	*)	140,274	-	(71,017)	69,331
Issuance of shares upon exercise of options	1,875	*)	-	-	6	-	-	6
Unrealized loss on available-for-sale marketable securities	-	-	-	-	-	(6)	-	(6)
Share-based compensation	-	-	-	-	2,500	-	-	2,500
Net loss	-	-	-	-	-	-	(24,603)	(24,603)
Balance as of December 31, 2016	<u>27,562,795</u>	<u>\$ 74</u>	<u>304,324</u>	<u>\$ *)</u>	<u>\$ 142,780</u>	<u>\$ (6)</u>	<u>\$ (95,620)</u>	<u>\$ 47,228</u>

\*) Represents an amount less than \$ 1.

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

## CONSOLIDATED STATEMENTS OF CASH FLOWS

U.S. dollars in thousands

	Year ended December 31,		
	2016	2015	2014
<b>Cash flows from operating activities</b>			
Net loss	\$ (24,603)	\$ (19,449)	\$ (32,834)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	61	51	31
Amortization of premium on marketable securities	123	-	-
Share-based compensation	2,500	2,365	4,089
Decrease (increase) in prepaid expenses and other receivables	667	(1,077)	(313)
Decrease (increase) in other long-term assets	23	(15)	(38)
Increase (decrease) in trade payables	471	(248)	258
Increase in accrued expenses and other liabilities	1,517	225	481
Net cash used in operating activities	<u>(19,241)</u>	<u>(18,148)</u>	<u>(28,326)</u>
<b>Cash flows from investing activities</b>			
Purchase of property and equipment, net	(74)	(181)	(79)
Investment in marketable securities	(17,372)	-	-
Proceeds from (investment in) short-term bank deposit	20,022	(14,500)	8,486
Proceeds from maturity of marketable securities	1,604	-	-
Proceeds from redemption of marketable securities	701	-	-
Investment in long-term bank deposit	-	(19,000)	-
Investment in restricted bank deposit	-	(161)	-
Net cash provided by (used in) investing activities	<u>4,881</u>	<u>(33,842)</u>	<u>8,407</u>
<b>Cash flows from financing activities</b>			
Issuance of share capital upon public offering	-	66,459	-
Exercise of options	6	13	-
Net cash provided by financing activities	<u>6</u>	<u>66,472</u>	<u>-</u>
Increase (decrease) in cash and cash equivalents	(14,354)	14,482	(19,919)
Cash and cash equivalents at the beginning of the year	<u>16,658</u>	<u>2,176</u>	<u>22,095</u>
Cash and cash equivalents at the end of the year	<u>\$ 2,304</u>	<u>\$ 16,658</u>	<u>\$ 2,176</u>

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



**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS****U.S. dollars in thousands, except share data**

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**NOTE 1:- GENERAL**

- a. Alcobra Ltd. was incorporated in Israel and commenced its operation on February 7, 2008. During July 2013, a wholly-owned subsidiary was incorporated in the State of Delaware named Alcobra Inc. (the "Subsidiary").
- b. Alcobra Ltd. and the Subsidiary (collectively "the Company") are an emerging biopharmaceutical company primarily focused on the development and commercialization of proprietary pharmaceutical products. The Company's product candidates include: (i) Abuse-Deterrent Amphetamine Immediate-Release ("ADAIR"), a proprietary, abuse-deterrent oral formulation of immediate-release (short-acting) dextroamphetamine for the treatment of Attention Deficit Hyperactivity Disorder ("ADHD") and Narcolepsy; and (ii) Metadoxine Extended Release ("MDX"), a proprietary oral drug, for the treatment of ADHD and other cognitive disorders, including Fragile X. In January 2017, the Company announced that the Phase III in adult ADHD study failed to show a positive statistical outcome on the primary efficacy endpoint. Following these clinical results, the Company may not generate any future revenues from MDX or its underlying intellectual property. The Company do not plan to invest additional significant capital in the development of MDX. Instead, it exploring strategic alternatives for partnering or monetizing MDX for ADHD and other indications in various territories, but may not be able to complete such transactions due to limited demand or other reasons. The Company strategy is to complete the development of, obtain regulatory approval for, and successfully commercialize, ADAIR and/or any other product candidate the Company may develop in the future in a timely manner.
- c. The Company has not generated revenue from the sale of any product, and does not expect to generate significant revenue unless and until the Company obtains marketing approval of, and commercialize, MDX, ADAIR, or any other product candidate. During the year ended December 31, 2016, the Company has incurred a loss of \$ 24,603 and had a negative cash flow from operating activities of \$ 19,241. The accumulated deficit as of December 31, 2016 is \$ 95,620. The Company is required and plans to continue to finance its operations through equity or similar financing rounds. The Company's management believes that its current financial resources will be sufficient to continue the development of the Company's products at least for twelve months from the date of this report.

**NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES**

The consolidated 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.

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS****U.S. dollars in thousands, except share data**

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**NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)**

## b. Financial statements in U.S. dollars:

The Company finances its operations 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 and reporting 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 standard codification ("ASC") 830, "Foreign Currency Matters", of the Financial Accounting Standards Board ("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.

## c. Principles of consolidation:

The consolidated financial statements include the accounts of Alcobra Ltd. and its Subsidiary. Intercompany transactions and balances have been eliminated upon consolidation.

## d. Cash equivalents:

Cash equivalents are short-term unrestricted highly liquid investments that are readily convertible to cash with original maturities of three months or less at acquisition.

## e. Bank deposits:

Bank deposits with maturities of more than three months but less than one year are included in short-term bank deposits. Such short-term deposits are stated at cost which approximates market values.

Bank deposits with maturities of more than one year are included in long-term bank deposits. The Company's long-term deposits do not have contractual maturities that exceed 2 years. Such long-term deposits are stated at cost which approximates market values.

As of December 31, 2016, the Company's bank deposits are in U.S. dollars and bear interest at a weighted average annual interest rate of 1.72%.

## f. Investment in marketable securities:

The Company accounts for investments in marketable securities in accordance with ASC No. 320, "Investments- Debt and Equity Securities". Management determines the appropriate classification of its investments at the time of purchase and reevaluates such determinations at each balance sheet date.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

## NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

The Company classified all of its debt and equity securities as available-for-sale securities. Available-for-sale securities are carried at fair value, with the unrealized gains and losses reported in accumulated other comprehensive income (loss) in shareholders' equity. Realized gains and losses on sales of investments are included in financial income, net and are derived using the specific identification method for determining the cost of securities.

The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization together with interest and dividends on securities are included in financial income, net.

The Company has classified all marketable securities as short-term, even though the stated maturity date may be one year or more beyond the current balance sheet date, because it is probable that the Company may sell these securities prior to maturity.

The Company recognizes an impairment charge when a decline in the fair value of its investments in debt securities below the amortized cost basis of such securities is judged to be other-than-temporary impairment ("OTTI"). Factors considered in making such a determination include the duration and severity of the impairment, the reason for the decline in value, the potential recovery period and if the entity has the intent to sell the debt security, or if it is more likely than not that it will be required to sell the debt security before recovery of its amortized cost basis. However, if an entity does not expect to sell a debt security, it will still need to evaluate expected cash flows to be received and determine if a credit loss exists. In the event of a credit loss, only the amount of impairment associated with the credit loss is recognized in earnings. Amounts relating to factors other than credit losses are recorded in OCI. The Company did not recognize OTTI on its marketable securities during the year ended December 31, 2016.

## g. 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 electronic equipment	15-33
Office furniture and equipment	6
Clinical and medical equipment	15
Leasehold improvement	The shorter of term of the lease or the useful life of the asset

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 2016, 2015 and 2014, no impairment losses have been identified.

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS****U.S. dollars in thousands, except share data**

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**NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)**

## h. Other long-term assets:

Other long-term assets mainly include long-term deposits for office lease and motor vehicles under operating leases, presented at their cost.

## i. Research and development expenses:

Research and development expenses are expensed as incurred. Those expenses include payments to third party clinical consultants, expenses related to conducting clinical and pre-clinical trials, salaries and related personnel expenses, travel expenses and share based compensation expenses to research and development employees. During 2016, 2015 and 2014, no grants were received from governmental entities to fund the Company's research and development expenses.

## j. Severance pay:

The Company's liability for its Israeli employees regarding severance pay is pursuant to Section 14 of the Israeli severance pay law ("Section 14"). All the Israeli employees are included under this section, and entitled only to monthly deposits, at a rate of 8.33% of their monthly salary, made in the employee's name with insurance companies. Payments in accordance with Section 14 release the Company from any future severance payments in respect of those employees. The fund is made available to the employee at the time the employer-employee relationship is terminated, regardless of cause of termination. The severance pay liabilities and deposits under Section 14 are not reflected in the balance sheet as the severance pay risks have been irrevocably transferred to the severance funds.

Severance pay expense for the years ended December 31, 2016, 2015 and 2014, amounted to \$ 159, \$ 130 and \$ 102, respectively.

## k. Employee benefit plan:

Since 2014, the Company's U.S. operations maintain a retirement plan (the "U.S. Plan") that qualifies as a deferred salary arrangement under Section 401(k) of the Internal Revenue Code. Participants in the U.S. Plan may elect to defer a portion of their pre-tax earnings, up to the Internal Revenue Service annual contribution limit. The Company matches 100% of each participant's contributions up to 3%. Contributions to the U.S. Plan are recorded during the year contributed as an expense in the consolidated statement of operations.

Total employer 401(k) contributions under the U.S. Plan for the years ended December 31, 2016, 2015 and 2014 were \$ 26, \$ 21 and \$ 21, respectively.

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS****U.S. dollars in thousands, except share data**

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**NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)**

## l. 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, 2016 and 2015 the Company has not recorded a liability for uncertain tax positions.

## m. Concentrations of credit risk:

Financial instruments that potentially subject the Company to concentrations of credit risk consist principally of cash and cash equivalents, bank deposits and marketable securities.

The majority of the Company's cash and cash equivalents and bank deposits are deposited in major banks in Israel. Generally, these deposits may be withdrawn upon demand and therefore bear minimal risk. Marketable securities are held mainly by Alcobra Ltd., and are invested in securities denominated in the U.S. dollar.

The Company's marketable securities consist of investments in foreign bank that have a credit rating of at least Baa1/BBB+ and corporate debentures that carry a rating of at least A2/A. The Company's investment policy, approved by the Board of Directors, limits the amount that the Company may invest in any one type of investment or issuer, thereby reducing credit risk concentrations.

The Company has no off-balance-sheet concentration of credit risk such as foreign exchange contracts, option contracts or other foreign hedging arrangements.

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS****U.S. dollars in thousands, except share data**

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**NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)**

## n. Fair value of financial instruments:

The Company measures its investment in money market funds classified as cash equivalents and marketable securities at fair value. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or a liability. A three-tier fair value hierarchy is established as a basis for considering such assumptions and for inputs used in the valuation methodologies in measuring fair value:

Level 1 - Valuations based on quoted prices in active markets for identical assets that the Company has the ability to access. Since valuations are based on quoted prices that are readily and regularly available in an active market, valuation of these products does not entail a significant degree of judgment.

Level 2 - Valuations based on one or more quoted prices in markets that are not active or for which all significant inputs are observable, either directly or indirectly.

Level 3 - Valuations based on inputs that are unobservable and significant to the overall fair value measurement.

The fair value hierarchy also requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value.

## o. Basic and diluted net loss per share:

Basic net loss per share is computed based on the weighted average number of ordinary shares outstanding during each year. Diluted net 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."

The total weighted average number of shares related to the outstanding options and warrants excluded from the calculations of diluted net loss per share, since they would have an anti-dilutive effect, was 2,563,498, 1,755,766 and 1,053,055 for the years ended December 31, 2016, 2015 and 2014, respectively.

## p. Accounting for share-based compensation:

The Company accounts for share-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 comprehensive loss based on the accelerated method.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

## NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

The Company selected the Black-Scholes-Merton ("Black-Scholes") option-pricing model as the fair value method for of its share-options awards. The Black-Scholes 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* - The expected volatility is calculated based upon actual historical stock price movements over the most recent periods ending on the grant date. Since the Company's shares started trading in NASDAQ in May 2013, quoted prices of the Company's share are available for three and a half years only. Due to insufficient historical data for the Company, in cases where the expected term is longer than the available historical data on the grant date, the expected volatility determination was based on a weighted average of the Company and 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 United States Securities Exchange Commission's 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.

The Company used the Black-Scholes option-pricing model to determine the fair value of grants made in 2016, 2015 and 2014. The following assumptions were applied in determining the compensation cost:

	Year ended December 31,		
	2016	2015	2014
Risk-free interest rate	0.8-1.1%	0.9-2.1%	0.7-2.8%
Expected option term (years)	2.6-4.5	2.3-7	3-10
Expected price volatility	82-92%	78-87%	65-89%
Dividend yield	-	-	-

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS****U.S. dollars in thousands, except share data**

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**NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)**

## q. Comprehensive income:

The Company accounts for comprehensive income in accordance with ASC 220, "Comprehensive Income". Comprehensive income generally represents all changes in shareholders' equity during the period except those resulting from investments by, or distributions to, shareholders. The Company determined that its items of other comprehensive income relate to unrealized gains and losses on available-for-sale marketable securities.

Other comprehensive loss for the year ended December 31, 2016, resulted only from unrealized loss on available-for-sale marketable securities and amounted to \$ 6.

## r. Recently adopted accounting standards:

In August 2014, the FASB issued Accounting Standards Update ("ASU") No. 2014-15, "Presentation of Financial Statements-Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern". The standard 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. This update was effective to for the Company in the fourth quarter of fiscal 2016. The adoption of the guidance did not impact the Company's consolidated financial statements.

## s. Impact of recently issued accounting standard not yet adopted:

In February 2016, the FASB issued ASU No. 2016-02, "Leases (Topic 842)". The standard requires that long-term lease arrangements be recognized on the balance sheet. The standard is effective for interim and annual periods beginning after December 15, 2018, and early adoption is permitted. The Company is currently evaluating the impact of adoption on its consolidated financial statements.

In March 2016, the FASB issued ASU No. 2016-09, "Compensation-Stock Compensation (Topic 718): Improvement to Employee Share-based Payment Accounting" to simplify the accounting for share-based payment transactions, including the income tax consequences, an option to recognize gross share-based compensation expense with actual forfeitures recognized as they occur, as well as certain classifications on the statement of cash flows. This guidance will be effective for the Company in the first quarter of 2017, and early adoption is permitted. The adoption of this ASU will not have an impact on the Company's consolidated financial statements.

In June 2016, the FASB issued ASU No. 2016-13, "Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments". This ASU provides guidance for recognizing credit losses on financial instruments based on an estimate of current expected credit losses model. For public business entities that are SEC filers, the amendments in this update are effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. All entities may adopt the amendments in this update earlier as of fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. The Company is in the process of assessing the impact that the adoption of this ASU will have on its consolidated financial statements.



## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

## NOTE 2:- SIGNIFICANT ACCOUNTING POLICIES (Cont.)

In November 2016, the FASB issued ASU No. 2016-18, "Statement of Cash Flows (Topic 230) Restricted Cash a consensus of the FASB Emerging Issues Task Force". The standard requires restricted cash and cash equivalents to be included with cash and cash equivalents on the statement cash flows. The new standard is expected to be effective for fiscal years, and interim periods within those years, beginning after December 15, 2017, with early adoption permitted. Accordingly, the new standard will result in the Company's restricted cash to be included with cash and cash equivalents to reflect total cash on the Company's statement of cash flows.

## NOTE 3:- MARKETABLE SECURITIES

The following is a summary of available-for-sale marketable securities:

	December 31, 2016			
	Amortized cost	Gross unrealized gains	Gross unrealized losses	Fair Value
<b>Available-for-sale – matures within one year:</b>				
Banks debentures	\$ 6,358	\$ *)	\$ -	\$ 6,358
Corporate debentures	6,933	*)	(6)	6,927
	<u>13,291</u>	<u>*)</u>	<u>(6)</u>	<u>13,285</u>
<b>Available-for-sale – matures after one year through two years:</b>				
Banks debentures	1,653	-	-	1,653
	<u>1,653</u>	<u>-</u>	<u>-</u>	<u>1,653</u>
Total	<u>\$ 14,944</u>	<u>\$ *)</u>	<u>\$ (6)</u>	<u>\$ 14,938</u>

\*) Represents an amount less than \$ 1.

All investments with an unrealized loss as of December 31, 2016, are with continuous unrealized losses for less than 12 months.

As of December 31, 2016, interest receivable amounted to \$ 58 and is included within other receivables in the balance sheet.

## NOTE 4:- FAIR VALUE MEASUREMENTS

In accordance with ASC 820, "Fair Value Measurements and Disclosures", the Company measures its money market funds and available-for-sale marketable securities at fair value. Money market funds and marketable securities are classified within Level 1 and Level 2. This is because these assets are valued using quoted market prices or alternative pricing sources and models utilizing market observable inputs.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

## NOTE 4:- FAIR VALUE MEASUREMENTS (Cont.)

The Company's financial assets measured at fair value on a recurring basis, excluding accrued interest components, consisted of the following types of instruments as of December 31, 2016:

	December 31, 2016		
	Fair value measurements using input type		
	Level 1	Level 2	Total
<b>Cash equivalents:</b>			
Money market funds	\$ 78	\$ -	\$ 78
<b>Marketable securities:</b>			
Foreign banks debentures	-	8,011	8,011
Corporate debentures	-	6,927	6,927
<b>Total financial assets</b>	<b>\$ 78</b>	<b>\$ 14,938</b>	<b>\$ 15,016</b>

## NOTE 5:- PREPAID EXPENSES AND OTHER RECEIVABLES

	December 31,	
	2016	2015
Government authorities	\$ 51	\$ 116
Prepaid expenses	362	1,084
Restricted cash	164	161
Interest receivable	470	212
Other current assets	10	93
	<u>\$ 1,057</u>	<u>\$ 1,666</u>

## NOTE 6:- PROPERTY AND EQUIPMENT, NET

	December 31,	
	2016	2015
<b>Cost:</b>		
Computers and electronic equipment	\$ 179	\$ 146
Office furniture and equipment	122	84
Clinical and medical equipment	15	15
Leasehold improvement	96	93
	<u>412</u>	<u>338</u>
<b>Accumulated depreciation:</b>		
Computers and electronic equipment	92	50
Office furniture and equipment	12	7
Clinical and medical equipment	13	12
Leasehold improvement	55	42
	<u>172</u>	<u>111</u>
<b>Depreciated cost</b>	<b>\$ 240</b>	<b>\$ 227</b>

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

## NOTE 6:- PROPERTY AND EQUIPMENT, NET (Cont.)

Depreciation expenses for the years ended December 31, 2016, 2015 and 2014, were \$ 61, \$ 51 and \$ 31, respectively.

## NOTE 7:- ACCRUED EXPENSES AND OTHER LIABILITIES

	December 31,	
	2016	2015
Employees and payroll accruals	\$ 1,292	\$ 1,277
Accrued expenses	2,520	888
Government authorities	-	59
Other liability	-	71
	<u>\$ 3,812</u>	<u>\$ 2,295</u>

## NOTE 8:- INCOME TAXES

a. Tax laws applicable to Alcobra Ltd. and the Subsidiary:

1. Taxable income of Israeli companies is subject to tax at a rate of 25% in 2016 and a rate of 26.5% in 2015 and in 2014.

On January 5, 2016, the Israeli Parliament officially published the Law for the Amendment of the Israeli Tax Ordinance (Amendment 216), that reduces the corporate tax rate from 26.5% to 25%.

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

2. The Subsidiary is taxed under U.S. tax law. The federal tax rates applicable to the Company whose place of incorporation is within the United States are corporate (progressive) tax at the rate of up to 35%, excluding state tax, which rates depend on the state in which the Subsidiary conducts its business.

b. Net operating losses carry forward:

Alcobra Ltd. has accumulated losses for tax purposes in Israel as of December 31, 2016 in the amount of approximately \$ 72,000 which may be carried forward and offset against taxable income in the future for an indefinite period.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

## NOTE 8:- INCOME TAXES (Cont.)

## 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,	
	2016	2015
Operating loss carry forward	\$ 16,676	\$ 12,791
Reserves and allowances	4,190	4,688
Deferred tax assets before valuation allowance	20,866	17,479
Valuation allowance	(20,866)	(17,479)
Net deferred tax assets	<u>\$ -</u>	<u>\$ -</u>

All deferred taxes are domestic. 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, 2016 and 2015.
- 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.
- f. Net loss before taxes is comprised as follows:

	December 31,		
	2016	2015	2014
Domestic (Israel)	\$ 24,128	\$ 19,003	\$ 31,154
Foreign (U.S.)	402	395	1,697
	<u>\$ 24,530</u>	<u>\$ 19,398</u>	<u>\$ 32,851</u>

- g. Taxes on income relate solely to the foreign Subsidiary.

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

U.S. dollars in thousands, except share data

**NOTE 9:- CONTINGENT LIABILITIES AND COMMITMENTS**

## a. Legal Proceedings:

On November 19, 2014, a class action lawsuit was filed against the Company and certain of its current and former officers and directors in the United States District Court for the Southern District of New York (the "Court"). The complaint, brought by a putative class of investors, alleges, among other things, that the Company's officers and directors made false or misleading statements relating to the results of the Phase III study for its MDX drug candidate. On May 20, 2015, the Company moved to dismiss the complaint. On March 30, 2016, the Court accepted the motion to dismiss all charges against the Company.

On February 17, 2017, a class action lawsuit was filed against the Company and certain of its current officers (one of whom also is a director) in the United States District Court for the Southern District of New York. The case was filed on behalf of a putative class of investors who purchased or acquired the Company's publicly-traded securities between August 13, 2015 and January 17, 2017. The complaint asserted violations of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 thereunder. The complaint alleged, among other things, that the Company and the individual defendants made false or misleading statements relating to the results of the Company's second Phase III clinical trial for its MDX drug candidate. At this preliminary stage the Company cannot assess the exposure under such complaint.

## b. Lease commitments:

Facilities of the Company are rented under operating lease agreements, which expire on various dates, the latest of which is in 2018. The Company recognizes rent expense under such arrangements on a straight-line basis.

In June 2016, the Company entered into a new operating lease agreement for its vehicles until 2019.

Aggregate minimum lease commitments, net of sub-lease proceeds in the amount of \$ 22 in 2017, under non-cancelable operating leases as of December 31, 2016, were as follows:

Year ended December 31,	Minimum Facilities Lease Payments	Minimum Vehicles Lease Payments	Total
2017	\$ 457	13\$	\$ 470
2018	287	-	287
	\$ 744	\$ 13	\$ 757

Facilities rent expense, not including sublease income, was \$ 488, \$ 498 and \$ 179 for the years ended December 31, 2016, 2015 and 2014, respectively. Sublease rental income for the years ended December 31, 2016 and 2015 was \$ 47 and \$ 17, respectively.

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS****U.S. dollars in thousands, except share data**

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**NOTE 9:- CONTINGENT LIABILITIES AND COMMITMENTS (Cont.)**

The vehicle rent expenses for the years ended December 31, 2016, 2015 and 2014, amounted to \$ 100, \$ 110 and \$ 67, respectively.

In August 2015, the Company moved its headquarters to new offices. The previous lease agreement for the headquarters office was terminated on March 31, 2016 and the Company recognized a loss of \$ 71, net in 2015 in respect with this contract.

In connection with the Company's facilities lease agreements, the Company established letters of credit for a total amount of \$ 164, which has automatic annual extensions and are fully secured by restricted cash.

c. Royalty bearing Government grants:

The Company partially financed its research and development expenditures under programs sponsored by the Israeli Office of Chief Scientist ("OCS") (the OCS has since been replaced by the Israel Innovation Authority ("IIA")) for the support of certain research and development activities conducted in Israel.

In connection with the participation payments received from the OCS in previous years, the Company is committed to pay royalties at a rate of 3%-5% of sales of the developed product linked to U.S dollars, up to 100% of the amount of grants received (100% plus interest at LIBOR). The Company's total commitment for royalties payable with respect to future sales, based on OCS participations received or accrued, net of royalties paid or accrued, totaled approximately \$122 as of December 31, 2016. In addition, the OCS (today the IIA) may impose certain conditions on any arrangement under which it permits the Company to transfer technology or development out of Israel.

**NOTE 10:- SHAREHOLDERS' EQUITY**

a. 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.

b. Issuances of shares:

1. During January 2015, the Company completed a public offering and issued 7,475,000 ordinary shares in consideration of \$ 27,903, net.
2. During November 2015, the Company completed a public offering and issued 6,379,197 ordinary shares in consideration of \$ 38,556, net.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

## NOTE 10:- SHAREHOLDERS' EQUITY (Cont.)

## c. 2010 incentive option plan:

In February 2010, the Company authorized through its 2010 incentive option plan (the "2010 Plan") the grant of options to officers, directors, advisors, management and other key employees. The Company reserved for grants of options up to 3,078,102 of the Company's ordinary shares. The options granted have generally four year vesting terms and expire between five to ten years after the grant date. As of December 31, 2016, 97,946 options were still available for future grants under the Plan.

In March 2017, the Company increased its option pool for grants of options to 4,487,334 and granted 1,507,178 options to employees and directors with an exercise price of \$ 1.19 per share. Please also refer to Note 13.

A summary of the Company's options activity (for employees and directors) under the 2010 Plan is as follows:

	Year ended December 31,			
	2016		2015	
	Number of options	Weighted average exercise price	Number of options	Weighted average exercise price
Outstanding at beginning of year	1,824,369	\$ 5.83	1,540,869	\$ 7.30
Granted	1,015,571	\$ 4.60	445,000	\$ 5.70
Exercised	(1,875)	\$ 3.29	(4,000)	\$ 3.29
Cancelled *)	-	\$ -	(112,500)	\$ 23.85
Forfeited	(90,125)	\$ 7.75	(45,000)	\$ 10.39
Outstanding at end of year	<u>2,747,940</u>	<u>\$ 5.31</u>	<u>1,824,369</u>	<u>\$ 5.83</u>
Vested and expected to vest	<u>2,747,940</u>	<u>\$ 5.31</u>	<u>1,824,369</u>	<u>\$ 5.83</u>
Options exercisable at the end of the year	<u>1,200,823</u>	<u>\$ 6.17</u>	<u>843,661</u>	<u>\$ 6.50</u>

\*) On March 31, 2015 the Company granted to its Chief Executive Officer ("CEO") options to purchase 400,000 of the Company's ordinary shares. On the same date, the Company cancelled 112,500 of the CEO's out-of-money options. The Company accounted for the cancellation of options, accompanied by the concurrent grant of options in accordance with ASC 718-20-35-8, "Cancellation and Replacement," and calculated the incremental compensation cost as the excess of the fair value of the replacement award over the fair value of the cancelled award at the cancellation date.

The weighted average fair values at grant date of options granted for the years ended December 31, 2016, 2015 and 2014, with an exercise price equal to the market value at the date of grant, were \$ 2.56, \$ 4.10 and \$ 1.67, respectively.

As of December 31, 2016, the weighted-average remaining contractual term of the outstanding and exercisable options is 4.16 and 4.42 years, respectively.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

## NOTE 10:- SHAREHOLDERS' EQUITY (Cont.)

The aggregate intrinsic value represents the total intrinsic value (the difference between the Company's closing share price on the last trading day of the fiscal year 2016 and the exercise price, multiplied by the number of in-the-money options) that would have been received by the option holders had all option holders exercised their options on December 31, 2016. This amount may change based on the fair market value of the Company's share.

As of December 31, 2016, the aggregate intrinsic value of outstanding and exercisable options is \$ 603. As of December 31, 2016, the unrecognized compensation cost is \$ 2,020 to be recognized from 2017 through 2020, excluding cost of \$ 440 for options with vesting subject to certain performance conditions, which are not probable.

The options outstanding as of December 31, 2016, have been separated into ranges of exercise price, as follows:

Exercise price \$	Number of options	Outstanding		Exercisable		
		Weighted average remaining contractual life (years)	Weighted average exercise price \$	Number of options	Weighted average remaining contractual life (years)	Weighted average exercise price \$
0.33-3.29	887,805	3.31	2.15	589,132	3.49	1.58
4.15-4.55	929,570	4.28	4.55	-	-	-
5.53-8.00	716,494	4.39	6.40	410,557	4.86	6.92
12.99-18.49	171,571	7.00	16.69	160,196	6.98	16.62
23.00-23.48	42,500	3.61	23.75	40,938	3.47	23.78
0.33-23.48	<u>2,747,940</u>	4.16	5.31	<u>1,200,823</u>	4.42	6.17

## d. Options granted to consultants:

The Company granted options to certain service providers and accounted for these options in accordance with ASC 505-50, "Equity-Based Payments to Non-Employees".

The outstanding options granted to the Company's consultants are as follows:

Grant date	Number of options	Exercise price	Expiration date
February 28, 2010	8,805	\$ 2.184	February 28, 2020
February 17, 2011	3,804	\$ 0.0005	February 17, 2021
	<u>12,609*)</u>		

\*) All options were fully vested on grant date.



**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

U.S. dollars in thousands, except share data

**NOTE 10:- SHAREHOLDERS' EQUITY (Cont.)**

## e. Share-based payment:

The share-based expense recognized in the consolidated financial statements for services received from employees and directors is shown in the following table:

	<b>Year ended December 31,</b>		
	<b>2016</b>	<b>2015</b>	<b>2014</b>
Research and development expenses	\$ 707	\$ 768	\$ 1,773
Pre-commercialization expenses	390	308	616
General and administrative expenses	1,403	1,289	1,700
	<u>\$ 2,500</u>	<u>\$ 2,365</u>	<u>\$ 4,089</u>

**NOTE 11:- RELATED PARTY BALANCES AND TRANSACTIONS**

## Related parties' expenses:

	<b>Year ended December 31,</b>		
	<b>2016</b>	<b>2015</b>	<b>2014</b>
Amounts charged to:			
General and administrative expense	<u>\$ -</u>	<u>\$ -</u>	<u>\$ 332</u>

On March 1, 2008, the Company signed an agreement with a consultant, who is also one of the Company's shareholders, as a contractor to render management, finance and operation services. The Company paid the consultant an amount of \$ 7 per month. During May 2013, the monthly fee was increased to an amount of \$ 12. The amendment was effective upon consummation of the Company's initial public offering in May 2013. In February 2014, the general meeting of the Company's shareholders approved the grant of an annual bonus to the consultant, in the amount of \$ 200. The agreement was terminated in May 2014.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

U.S. dollars in thousands, except share data

## NOTE 12:- FINANCIAL INCOME, NET

	Year ended December 31,		
	2016	2015	2014
Financial expenses:			
Amortization of premium on marketable securities	\$ 123	\$ -	\$ -
Exchange rate	19	31	2
Bank fees	19	7	10
	<u>161</u>	<u>38</u>	<u>12</u>
Financial income:			
Exchange rate	-	-	2
Interest income	798	338	237
	<u>798</u>	<u>338</u>	<u>239</u>
Financial income, net	<u>\$ (637)</u>	<u>\$ (300)</u>	<u>\$ (227)</u>

## NOTE 13:- SUBSEQUENT EVENTS

In January 2017, the Company's Board of Directors resolved to grant 712,500 options to employees and directors with an exercise price of \$ 2.26 per share. Following the changes in the stock price and the Company's will to retain its employees, in March 2017, the Company's Board of Directors decided to cancel the previous resolution to grant options and instead grant 1,507,178 options to employees and directors with an exercise price of \$ 1.19 per share. As part of March 2017 resolution, 55,000 of unvested options granted on March 2, 2016 were also cancelled to certain officers. In addition, the Board of Directors resolved to increase the Company's option pool to 4,487,334 options.

As part of a process of adjusting the Company's resources to the new business strategy, the Company is undergoing a reduction in force.

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# Alcobra Ltd.

## The Amended and Restated 2010 Incentive Option Plan

### 1. PURPOSE OF THE PLAN

The purpose of this 2010 Amended and Restated Incentive Option Plan (the “**Plan**”) is to advance the interests of Alcobra Ltd. (the “**Company**”) and its shareholders by attracting and retaining the best available personnel for positions of substantial responsibility, providing additional incentive to employees, office holders and service providers and promoting a close identity of interests between those individuals and entities and the Company.

### 2. DEFINITIONS

As used herein, the following definitions shall apply:

- 2.1. “**Administrator**” means the Board or the Committee, as shall administer the Plan, as set forth herein.
- 2.2. “**Articles**” mean the Company’s Articles of Association, as amended from time to time.
- 2.3. “**Board**” means the Board of Directors of the Company.
- 2.4. “**Committee**” means the Company’s compensation committee, or in the case there is no such committee, a committee appointed in order to administer the Plan, and until such committee is appointed, the Board.
- 2.5. “**Companies Law**” means the Israeli Companies Law 5759 - 1999.
- 2.6. “**Employee**” means: (I) any person, employed by the Company or employed by any Related Entity; and (II) any Office Holder (as such term is defined in the Companies Law), officer or Director of the Company or a Related Entity.
- 2.7. “**Exercise Price**” means the price that is to be paid in order to exercise an Option.
- 2.8. “**Group**” means the Company and the Related Entities taken together.
- 2.9. “**IPO**” means an initial public offering of the Company’s Shares.
- 2.10. “**Option**” means an option to purchase a Share according to the provisions of this Plan.
- 2.11. “**Option Grant**” means a single grant of Options to a certain Participant as determined by the Board or the Committee.
- 2.12. “**Option Grant Letter Agreement**” means the notice letter attached to this Plan as Exhibit A.
- 2.13. “**Participant**” means a person or entity that has been granted Options.
- 2.14. “**Related Entity**” means any parent or subsidiary of the Company. In addition, Related Entity shall include any business, corporation, partnership, limited liability company or other entity in which the Company, or the Company’s parent or a subsidiary holds a substantial ownership and/or interest, directly or indirectly, and is determined by the Board to be a Related Entity.

- 2.15. “**Service Provider**” means a person or entity who is engaged by the Company or any Related Entity to render services (e.g., consulting services, advisory services, development services, marketing and sale services or any other services, including suppliers) to the Company or a Related Entity.
- 2.16. “**Share**” means the Company’s Ordinary Share of NIS 0.01 par value, or that was issued following an exercise of an Option.
- 2.17. “**Total Option Amount**” means the amount of Options granted to a Participant in a single Option Grant.

### 3. ADMINISTRATION OF THE PLAN

- 3.1. Subject to the provisions of the Plan, any applicable law, the Articles and any other binding commitments taken by the Company, the Board or the Committee shall have the power and authority to administer the Plan. Such power and authority shall include, but not be limited to: (i) approval of Option Grants and the determination of the terms and provisions of respective Option Grants, including, the vesting schedules of the Options; the Exercise Price thereof; provisions concerning the time or times when and the extent to which Options may be exercised; the nature and duration of restrictions as to transferability; or any other special conditions relating to an Option Grant; (ii) the acceleration of any Participant’s right to exercise Options, in whole or in part; (iii) the interpretation of the provisions of the Plan; (iv) altering, amending or rescinding any resolution or act previously taken by the Committee; and (v) the determination of any other matter which is necessary or desirable for, or incidental to, the administration of the Plan, as set forth in the Plan.
- 3.2. Notwithstanding the above, the Board shall have the power and authority to take any act the Committee is empowered and authorized to take, and to alter amend or rescind any act or resolution taken by the Committee.
- 3.3. The Committee shall consist of such number of directors as may be appointed by the Board.
- 3.4. The Board shall have the exclusive discretion and power to grant Options. Such power may be delegated by the Board to the Committee subject to the provisions of the Companies Law.
- 3.5. All Committee resolutions and decisions, including the interpretation and construction of any provision of the Plan, shall be final and conclusive unless otherwise determined by the Board.
- 3.6. No member of the Board or of the Committee shall be held liable for any act or determination made in good faith with respect to the Plan or any Option Grant.

### 4. SHARES RESERVED FOR THE PLAN

- 4.1. Subject to adjustments, as set forth in Section 9 below, a total of 4,487,334 Ordinary Shares, of NIS 0.01 par value each, from the Company’s authorized share capital shall be reserved and subject to the Plan (the “**Reserved Shares**”).
- 4.2. Until termination of the Plan the Company shall at all times reserve sufficient number of Ordinary Shares in its authorized share capital to cover for all Reserved Shares that were not issued.

4.3. Without derogating from Section 4.2 above:

4.3.1. The Company need not reserve Shares with respect to Options that terminated, expired or were canceled for any reason prior to exercise thereof.

4.3.2. In the case that there are certain Reserved Shares, which remain unissued and which are not subject to outstanding Options, then the Board may resolve that such Reserved Shares shall cease to be reserved.

**5. DESIGNATION OF PARTICIPANTS; OPTION GRANTS**

5.1. The Board may grant Option Grants to the following persons and entities:

5.1.1. Employees.

5.1.2. Service Providers and their employees.

5.2. Unless determined otherwise by the Board or Committee, a Participant shall not be required to pay any consideration for an Option Grant.

**6. VESTING; EXERCISE PERIOD**

6.1. Unless determined otherwise by the Committee or Board, upon approval of the Option Grant or thereafter, Options underlying an Option Grant shall vest over four years, commencing on the vesting commencement date (the "**Vesting Commencement Date**") as determined by the Committee.

6.2. The vesting schedule of each Option Grant shall be as determined by the Committee. However, unless determined otherwise by the Committee or Board, upon approval of the Option Grant or thereafter, the following shall apply:

25% of the Total Option Amount shall vest on the first anniversary of the Vesting Commencement Date, and additional 6.25% of the Total Option Amount shall vest on the last day of each three months period immediately after the first anniversary of the Vesting Commencement Date.

In the case that as a consequence of the vesting schedule mentioned above a fraction of vested Option is created, then such fraction shall be rounded up or down, as determined by the Board.

6.3. Notwithstanding anything to the contrary in this Plan, all Options shall terminate and not bestow any rights on their owner after ten years from the date the Options were granted. All Options that have not been exercised by such date shall expire immediately and the Participants shall not have any claim against the Company with respect thereto.

6.4. The period within which Options are exercisable shall be called the "**Exercise Period**". Options which have not been exercised during the Exercise Period shall expire immediately, and will be automatically returned to the Options pool and may be re-allocated.

**7. TERMINATION OF EMPLOYMENT WITH THE GROUP**

In the event that the Participant is an Employee at the time of the Option Grant, whose employment with the Group was subsequently terminated, for whatever reason but subject to Section 7.6 (including but not limited to (i) dismissal of a Participant or (ii) a Participant's resignation, or (iii) death of a Participant or (iv) disability of a Participant), then the following provisions shall apply:

- 7.1. The date on which employment was terminated under applicable labor laws, or, in the case an Employee is not an employee under applicable labor laws the date in which such Employee ceases to be an Employee as defined in the Plan, shall be deemed the date in which such Employee's employment was terminated ("**Employment Termination Date**").
- 7.2. On the Employment Termination Date all Options that are not vested shall immediately expire.
- 7.3. In the event that the Participant's termination of employment is not due to the Participant's death (but does include termination due to Disability), then the Participant will be entitled to exercise all, or part of, the vested Options that have not expired, for a period of thirty (30) days after the Employment Termination Date. After such thirty days period, all unexercised Options will automatically expire.
- For purposes of this Section 7.3, "Disability" shall mean the inability in 100%, due to illness or injury, to engage in any gainful occupation for which the individual is suited by education, training or experience, which condition continues for at least six (6) months.
- 7.4. Notwithstanding the above, in the event of termination of employment due to the Participant's death or Disability, the Participant (if applicable) or Participant's estate, or other person who acquired the right to exercise the Options by way of bequest or inheritance, may, but only within six (6) months after the date of such death or the Employment Termination Date (in the case of Disability), exercise all, or part of, the vested Options that have not expired. After such six (6) months period, all unexercised options shall automatically expire.
- 7.5. Notwithstanding Section 7.3 above, all Options granted to a certain Employee (whether vested or unvested) will immediately expire if the termination of the Participant's employment is due to Participant's breach of his/her employment agreement (whether written or oral) including without limitation, a breach of non compete obligations, or breach of his/her fiduciary duties towards the Company or a Related Entity as determined by the Committee or the Board, in their sole discretion, or in the case that competent court or other authority resolves that such employee is not entitled to discharge compensation.
- 7.6. For the purposes of this Plan, the Committee or Board is authorized to determine if and when a Participant terminated his/her employment with the Company, and due to what reason, subject to the provisions of Israeli labor laws with respect to Israeli employees.
- 7.7. The Committee or the Board shall be entitled, prospectively and retroactively, to extend the periods in which Options (either vested or unvested) do not expire and remain exercisable after the Employment Termination Date.

## **8. TERMINATION OF ENGAGEMENT WITH THE GROUP**

In the event that a Participant is not an Employee, and the agreement of such Participant with the Group is terminated, then, unless otherwise specified in the Option Grant Letter Agreement, or otherwise determined by the Committee, on the date of such termination, all Options that have not vested by then shall expire and the vested options shall remain exercisable as specified in sections 7.3, 7.4 or 7.5, as the case may be, which shall apply *mutatis mutandis* to such Participant (where if such Participant has more than one agreement with the Group, then the foregoing shall apply to the Options underlying the terminated agreement or issued in connection therewith).

## 9. ADJUSTMENTS

### 9.1. Merger, Sale of the Company or Sale of the Company's Assets.

In the event of a merger of the Company into another corporation, in a way that the Company shall no longer continue to exist as a legal entity subsequent to such merger, the sale of all, or substantially all of the Company's issued and outstanding shares to a third party or the sale of all, or substantially all of the assets of the Company (each of them, a "**Transaction**"), then the following provisions shall apply:

- 9.1.1. Each outstanding Option shall be assumed by, or an equivalent option shall be substituted by the successor corporation or a parent or subsidiary of the successor corporation.
- 9.1.2. In the event that the successor corporation does not agree to assume the Options or to substitute them with equivalent options, the Committee may in lieu of such assumption or substitution, provide for the Participant to have the right to exercise the Options as to all, or part of the Shares, including certain Shares as to which it would not otherwise be exercisable.
- 9.1.3. In addition to Section 9.1.2 above, and if Section 9.1.1 does not apply, the Committee may notify the Participants that all Options that are exercisable shall remain so for a period of no less than seven (7) days from the date of such notice, and that all Options will terminate upon the expiration of such period. In any case, the Committee may condition the termination of all said Options upon consummation of the Transaction.

### 9.2. Bonus Shares

In the event that the Company issues any of its shares as bonus shares to all its shareholders, on a pro rata basis, then the number of Shares received upon exercise of certain Options shall be increased to the number of Shares the Participant would have held after the issuance of the bonus shares had such Participant exercised such Options immediately before the issuance of the bonus shares.

### 9.3. Reorganization; Separation

If the Company is separated, reorganized, or consolidated with another corporation (other than as part of a Transaction) while Options which were not yet exercised remain outstanding under this Plan, the Company shall use reasonable efforts to maintain the rights of each Participant through such separations, reorganizations or consolidations, or compensate the Participant for such event in lieu of the Options such Participant holds. The Committee, at its sole discretion, shall determine what steps shall be taken according to this section 9.3.

### 9.4. Changes in Capitalization

If the outstanding shares of the Company shall at anytime be changed or exchanged by declaration of a share split, reverse share split, combination or reclassification of Ordinary Shares, or any other increase or decrease in the number Company's Ordinary Shares effected without receipt of consideration by the Company from the shareholders, then the number, class and kind of Shares subject to this Plan or subject to any Options therefore granted, and the Exercise Prices of the Options, shall be appropriately and equitably adjusted so as to maintain the proportionate number of Shares without changing the aggregate Exercise Prices of the Options (except in case the Exercise Price is equal to the par value of the shares, in which case the Exercise Price will be increased respectively). However no adjustment shall be made by reason of the distribution of subscription rights on outstanding shares, or conversion of securities into shares of the Company.

9.5. Other terms and conditions

- 9.5.1. The allocation of each Option Grant hereunder is subject to the relevant Participant's agreement to sign any document he/she is required to sign pursuant to the provisions of this section 9. If a Participant refuses to sign any such documents, the Committee or Board may determine that the Options held by the Participant or by a trustee for such Participant's benefit shall immediately expire.
- 9.5.2. Such adjustments as mentioned in this Section 9 shall be made by the Committee, whose determination in such respect shall be final, binding and conclusive.
- 9.5.3. Anything herein to the contrary notwithstanding, if prior to an IPO, there is a bona fide offer to purchase all or substantially all of the issued and outstanding shares of the Company, or upon a reorganization separation or the like, all or substantially all of the shares of the Company are to be exchanged for securities of another company, then each Participant shall be obliged to sell or exchange (in accordance with the value of such Participant's Options and Shares pursuant to the terms of such transaction) as the case may be, any Shares such Participant purchases hereunder, in accordance with the instructions issued by the Board in connection with such transaction, which will be given according to a policy of the Board concerning all of the Participants under the Plan.

**10. ASSIGNABILITY AND SALE OF OPTIONS**

No Option shall be assignable, transferable, given as collateral, hypothecated pledged or encumbered and no right with respect to the Options shall be given to any third party whatsoever, and during the lifetime of each Participant, each and all of such Participant's rights to purchase Shares hereunder shall be exercisable only by such Participant.

**11. TERM AND EXERCISE OF OPTIONS**

- 11.1. Options shall be exercised by a Participant by giving written notice to the Company, in the form substantially attached hereto as **Exhibit B** or such other form(s) and method as may be determined by the Company from time to time (the "**Exercise Notice**").
- 11.2. The Exercise Price and applicable withholding taxes, if any, shall be payable upon the exercise of the Option in either: (i) cash or by check; (ii) by delivery (on a form prescribed by the Company) of an irrevocable direction to a securities broker approved by the Company to sell Shares and to deliver all or part of the sales proceeds to the Company or the Trustee; or (iii) Payment may be made by any other method approved or accepted by the Committee in its discretion, which may include procedures for net exercise.
- 11.3. The Exercise Price will be paid in NIS, or if the Exercise Price is fixed in U.S. dollars, in U.S. dollars or in accordance with the representative rate of exchange of the U.S. dollar, last published by the Bank of Israel at the time of actual payment, or as provided for by the Company.
- 11.4. Each Participant will be entitled to exercise, upon signing the Exercise Notice and any additional documents as required by the Company, and paying the Exercise Price, all, or part of the Options that are vested at the Exercise Period.



- 11.5. Options shall not be deemed exercised unless: (I) the Company receives duly signed Exercise Notice including all relevant details; and (II) the Company receives the Exercise Price.
- 11.6. The Options may be exercised only to purchase whole Shares, and in no case may a fraction of a Share be purchased. If any fractional Shares would be deliverable upon exercise, such fraction shall be rounded up or down, to the nearest whole number. Half of a Share will be rounded up.
- 11.7. Each Option granted under this Plan shall be exercisable during the Exercise Period. Subject to adjustments, as set forth in Section 9 above, the exercise of one Option shall entitle the Participant to hold one Share.
- 11.8. Without derogating from any restrictions mentioned hereinabove, the exercise of the Options is being subject to the following terms, restrictions and conditions as may be in effect on the time of the exercise of the Options is requested: (i) any applicable law or regulation; (ii) any order or limitation set by any stock exchange in which the Company's securities may be traded (e.g., blackout periods, and lock up after an IPO); and (iii) any limitation undertaken by the Company with respect of the shares of the Company, including limitations set forth by Company's underwriters. Such period of restriction of sale or exercise shall not be counted as part of the applicable exercise period.
- 11.9. Notwithstanding the foregoing, starting as of the Employment Termination Date of a certain Participant and during the period that the vested Options are exercisable, the Company shall be entitled (subject to the provisions of applicable law) to purchase the vested Options held by such Participant by sending the Participant a purchase notice (the "**Purchase Notice**"). The purchase price of each Option shall be the Market Value of an Ordinary Share less the Exercise Price of the Option. The Market Value of an Ordinary Share shall be determined as follows: (i) in case the Company's shares are listed on a stock exchange, the Market Value shall be the average price of the Shares during 5 days prior to the Purchase Notice; or (ii) in case the Company's shares are not traded, the Market Value shall be the value determined in good faith unanimously by the Board and in the event the Board members are unable to reach an agreement with respect to the Market Value within 10 days of the Purchase Notice to the Participant, the Board will refer to an external expert. The Committee or the Board shall be entitled to establish further processes for the purchase of the Options as set forth above, provided, however, that if the Company receives the Participant's Exercise Notice prior to the receipt of the Purchase Notice from the Company, then the Company's right to purchase the said Options shall become null and void and the Participant may exercise the vested Options pursuant to their terms.

## 12. RIGHTS AND OBLIGATIONS ATTACHED TO THE SHARES

- 12.1. No Participant shall have any of the rights or privileges of a shareholder of the Company with respect to any of the Shares, unless and until, following exercise, the registration of the Participant as holder of such Shares in the Company's register of members is duly completed.
- 12.2. The rights and obligations attached to the Shares will be as set forth in the Articles. The Shares may be subject to rights of first refusal, co-sale rights and other rights specified in the Articles.
- 12.3. The Participant waives any of the following rights to the extent such rights are attached to the Shares: (i) pre-emptive rights in relation to issuance of new securities in the Company; (ii) rights of first refusal in relation with any sale of shares of the Company; (iii) co-sale rights in relation with any sale of shares of the Company.

- 12.4. Unless provided otherwise by the Committee, until an IPO, all voting rights, and rights to receive information from the Company with respect to the Shares shall be granted to the Board or as determined by the Board, in accordance with **Exhibit C** attached hereto.
- 12.5. Without derogating from any restrictions mentioned hereinabove, by accepting an Option Grant, each Participant agrees that the sale or disposal of Shares is subject to the following terms, restrictions and conditions as may be in effect on the time when such sale or disposal is requested: (i) any applicable law or regulation; (ii) any order or limitation set by any stock exchange in which the Company's securities may be traded (e.g., blackout periods, and lock up after an IPO); and (iii) any limitation undertaken by the Company with respect of the shares of the Company, including limitations set forth by Company's underwriters.
- 12.6. Until an IPO the Company shall have the authority to endorse upon the certificate or certificates representing the Shares such legends referring to the foregoing restrictions, and any other applicable restrictions, as it may deem appropriate (and which do not violate the Participant's rights according to this Agreement).
- 12.7. By accepting an Option Grant, each Participant agrees that in the case of an IPO or after registering the Company's securities for trading, to sign any document and approve any resolution or restriction upon the Shares, or modify the terms of allocation of the Shares, if such Participant's signature or approval or such restriction or modification were reasonably required, in the Committee's discretion, in order to facilitate the Company in meeting all the underwriters and stock exchange demands and all applicable securities and corporate laws and regulations.
- 12.8. The Participant shall not sell, pledge, transfer or otherwise dispose of any Shares in transactions which violate, according to the Company's sole discretion, any applicable laws, rules and regulations, or the Articles.
- 12.9. No transfer of Shares shall be effective if the Committee determines that the transferee is a competitor of the Company (either directly or indirectly).
- 12.10. Notwithstanding anything to the contrary in this Section 12, as long as Shares are held by a trustee for the benefit of a Participant (if applicable) the Shares shall not be sold, pledged, transferred or otherwise disposed of, by the Participant until an IPO, or until such time or event as determined by the Committee, either individually or with respect to all Participants.

### **13. TERM OF THE PLAN**

This Plan shall be effective as of January 1, 2010, which is the day it was adopted by the Board and shall terminate when all the Options are exercised into Shares or expired in accordance with the provisions of this Plan or such other date as shall be determined by the Board, which date shall be no later than January 1, 2020.

### **14. AMENDMENTS; TERMINATION**

- 14.1. The Board may, at any time and from time to time, amend, alter or terminate the Plan, provided, however, that the rights of the Participants shall not be adversely affected, unless such Participants agreed to such amendment, alteration or termination.
- 14.2. The Plan may be terminated at any time by an action of the Board, but any such termination will not terminate any Options granted under this Plan, which are then outstanding, without the consent of the Participant that is holding such Options.

**15. BINDING EFFECT**

The provisions of the Plan shall be binding upon the heirs, executors, administrators, and successors of the Participants.

**16. GOVERNMENT REGULATIONS AND OTHER RESTRICTIONS**

- 16.1. This Plan, the Option Grant Letter Agreements, the grant and exercise of Options hereunder, the obligation of the Company to issue the Shares, and any other act or obligation of the Company or any related individual or entity acting in connection with this Plan are all subject to the Articles, all applicable laws, rules, and regulations, whether of the State of Israel or of the United States or any other state having jurisdiction over the Company and any Participant.
- 16.2. By accepting an Option Grant, each Participant agrees not to sell, pledge, transfer or otherwise dispose of any of the Shares such Participant may hold except in compliance with: (I) the United States Securities Act of 1933, as amended, and the rules and regulations thereunder if applicable; and (II) the Israeli Securities Law 5728 – 1968; and (III) any other applicable securities law, regulations or other rules set by any stock exchange in which the Company's securities may be traded; and to further agree that certificates evidencing any of such Shares shall bear appropriate legend to reflect such restrictions. The Company does not obligate itself to register any shares under the United States Securities Act of 1933, as amended or any other securities laws.

**17. TAX CONSEQUENCES, INDEMNIFICATION**

- 17.1. Any tax consequences (pursuant to Israeli or any other applicable law that the relevant Participant is subject to), including tax consequences due to adjustments, made in accordance with Section 9 above, arising from the grant or exercise of any Option, the payment for Shares covered thereby, or any other event or act (of the Company or any Participant) relating to the Plan, shall be borne solely by each Participant.
- 17.2. The Company and/or the Board and/or the Committee and/or a trustee for the Plan shall not be required to release any Share certificates or transfer any Shares to a Participant until all required tax payments have been fully made.
- 17.3. The Company may withhold taxes according to the requirements under the applicable laws, rules, and regulations, including withholding taxes at source. In the case that applicable law requires so, the Company shall deduct taxes at source. Such deduction may be made from any proceeds attributed to the exercise of the Options and sale of Shares, or from any proceeds the Participant is entitled to receive from the Group or other proceeds such Participant owns and are held by the Group, including from Participant's salary or other proceeds he/she is entitled to receive from the Company or a Related Entity. It is explicitly stated herein that each Participant who is an Employee, by accepting an Option Grant agrees to the deduction from his/her salary of any amounts that in the Company's determination are required to be deducted under applicable law in connection with the Plan. In any such case, the Company shall be entitled to offset any amounts due to such Participant on account of such taxes.
- 17.4. In the case that the Company, or any other person on its behalf is required to pay taxes, that under applicable law should have been paid by the Participant, then such Participant shall immediately either pay such tax, or, if such tax was already paid, reimburse the Company, or such other person for the total amount paid.

- 17.5. Neither the Company, nor any Related Entity nor anyone on their behalf, shall give, or be deemed to be giving any Participant, or a potential Participant, advice regarding tax consequences relating to the Plan and issuance of securities thereunder. Each Participant shall rely solely, while considering participation in the Plan, on the advice of such Participant's consultants.

**18. CONTINUANCE OF EMPLOYMENT OR ENGAGEMENT**

Neither the Plan nor any Option Grant shall be construed to impose any obligation on any entity included in the Group to continue any Participant's employment with it (in the case that the Participant is an Employee) or to maintain any business engagement with such Participant. Nothing in the Plan or in any Option Grant shall confer upon any Participant any right to continue to be employed by the Group or to maintain any other business engagement with it, or restrict the right of any entity included in the Group to terminate such employment or business engagement at any time.

**19. RULES PARTICULAR TO SPECIFIC COUNTRIES**

- 19.1. Notwithstanding anything herein to the contrary, the terms and conditions of the Plan may be amended with respect to particular types of Participants as determined by the Board (for example, Israeli employees, employees that are subject to US taxation) by an addendum to the Plan (the "Appendix").
- 19.2. The Company may adopt one or more Appendixes. Each Appendix shall be approved by the Board and as required or advisable under applicable law.
- 19.3. The terms of an Appendix shall govern only with respect to the types of Participants specified in such Appendix.
- 19.4. In the case that the terms and conditions set forth in an Appendix conflict with any provisions of the Plan, the provisions of the Appendix shall govern with respect to Participants that are subject to such Appendix, provided, however, that such Appendix shall not be construed to grant the Participants rights not consistent with the terms of the Plan, unless specifically provided in such Appendix.

**20. NON-EXCLUSIVITY OF THE PLAN**

- 20.1. The adoption of the Plan by the Board shall not be construed as amending, modifying or rescinding any previously approved incentive arrangements or as creating any limitations on the power of the Board to adopt such other incentive arrangements as it may deem desirable, including, without limitation, the granting of Options other than under this Plan, and such arrangements may be either applicable generally or only in specific cases.
- 20.2. The grant of Options hereunder shall neither entitle the recipient thereof to participate, nor disqualify him from participating in, any other grant of Options pursuant to this Plan or any other option or stock plan of the Company.

**21. MULTIPLE AGREEMENTS; OTHER CORPORATE ACTIONS**

- 21.1. The terms of each Option Grant may differ from other Options Grants granted under the Plan at the same time, or at any other time. The Board may also grant more than one Option Grant to a certain Participant during the term of this Plan, either in addition to, or in substitution for, one or more Option Grants previously granted to such Participant.

- 21.2. Under no circumstances shall the Plan be construed to grant any right to a Participant, or any other third party, to postpone, delay or affect any corporate action resolved by the Company.

## 22. GOVERNING LAW & JURISDICTION

This Plan shall be governed by, construed and enforced in accordance with the laws of the State of Israel, without giving effect to the principles of conflict of laws. Any dispute or claim shall be put to the Board's resolution. Subject to the above, the competent courts of Tel-Aviv, Israel shall have sole jurisdiction in any matter pertaining to this Plan, and any other issue related to it.

## 23. NO WAIVER

The failure of the Company or any other party acting on its behalf or assisting it in implementing the Plan to enforce at any time any provisions of the Plan shall not be construed to constitute a waiver of such provision or of any other provision hereof.

## 24. NOTICES

- 24.1. Any notice, request, demand or other communication required or permitted under the Plan shall be in writing and shall be deemed to have been duly given, made and received only by personal delivery or if sent by certified mail, postage prepaid, return receipt requested, overnight delivery service, facsimile transmission (with confirmation of delivery), or confirmed e-mail to the address of the Company (if sent to the Company), or to the address of the Participant as such was provided by him in the Option Grant Letter Agreement, unless such address is changed by written notice received by the Company.
- 24.2. Except as otherwise set forth herein, any notice sent by mail shall be deemed to be given six days after deposit with the relevant post service; any notice sent by overnight delivery service shall be deemed given the first business day after deposited with the delivery service; and any notice sent by facsimile transmission or e-mail, shall be deemed given when transmitted if sent during normal business hours or if not, on the next business day; and any notice given by personal delivery shall be deemed given on the date of delivery.
- 24.3. In the case a certain Participant changes his or her contact details, in a way that the contact details provided to the Company by him do not enable the Company to provide notices and other communications to such Participant, then such Participant shall be deemed to have waived his or her right to receive any notices, and the Committee shall have the right, in its sole discretion, to take any appropriate action under the circumstances.

### Appendixes

Appendix A: Terms of grant of options to Israeli employees

Appendix B: Terms of Options granted to United States Employees and Service Providers

### Exhibits:

Exhibit A: Option Grant Letter Agreement

Exhibit B: Form of Exercise Notice

## Appendix A

### Terms of grant of Options to Israeli employees

#### 1. Purpose of the Appendix

- 1.1. This Appendix (the “**Appendix**”) is made as part of the Plan (as defined herein whereas all terms not otherwise defined herein shall have the meaning ascribed to them in the Plan) and pursuant to the provisions of Section 102 of the Income Tax Ordinance (as defined herein).
- 1.2. This Appendix governs grants of Options to Israeli Employees, either by a Trustee, or without a Trustee.

#### 2. Definitions

As used herein, the following definitions shall apply:

- 2.1. “**Capital Gain Method**” means choosing the alternative of capital gain method under Section 102.
- 2.2. “**Eligible Participant**” means any employee as such term is defined in Section 102. Without derogating from the foregoing Eligible Participant shall include any employee or Office Holder (as such term is defined in the Companies Law) of the Company or any Subsidiary except for such persons that are deemed to be ‘*Ba’al Shlita*’ under Section 32 to the Income Tax Ordinance.
- 2.3. “**Deposit Date**” means the date in which options were deposited with the Trustee for the benefit of a certain Participant.
- 2.4. “**Income Tax Authorities**” mean the Israeli income tax authorities that are authorized to give approvals in relation with this Appendix and Option Grants to Eligible Participants.
- 2.5. “**Income Tax Ordinance**” means the Israeli Income Tax Ordinance (New Version) 1961, as amended from time to time.
- 2.6. “**Labor Income Method**” means choosing the alternative of labor income method under Section 102.
- 2.7. “**Participant**” means any Eligible Participant who is granted with Options.
- 2.8. “**Plan**” means the Amended and Restated 2010 Incentive Option Plan this Appendix is attached to.
- 2.9. “**Realization Event**” means, with respect to each Option Grant granted to a certain Participant, the earlier to occur of: (I) transfer of Securities from the Trustee to such Participant; or (II) the sale of Shares by the Trustee; or (III) one day before such Participant is no longer an Israeli resident (as provided for in Section 100A to the Income Tax Ordinance).
- 2.10. “**Release Term**” means: (i) in the case of Capital Gains Method, a period ending twenty four (24) months after the Deposit Date; (ii) In the case of Labor Income Method ‘Release Term’ shall mean a period ending twelve (12) months after the Deposit Date.

- 2.11. “**Section 102**” means Section 102 to the Income Tax Ordinance as amended from time to time, and / or as superseded and any rules regulations or instructions promulgated or enacted under such Section 102.
- 2.12. “**Securities**” mean Options subject to a certain Option Grant and Shares received subsequent exercise of such Options.
- 2.13. “**Tax Method**” means either Capital Gains Method or Labor Income Method.
- 2.14. “**Trust**” means a trust, maintained under the Trust Agreement entered into between the Company and the Trustee for administration of grant of Options under Section 102.
- 2.15. “**Trust Agreement**” means the agreement between the Company and the Trustee as may be in effect from time to time specifying the duties and authorities of the Trustee.
- 2.16. “**Trust Assets**” mean all Securities and other assets held in Trust for the benefit of the Participants pursuant to this Appendix and the Trust Agreement
- 2.17. “**Trustee**” means ESOP Trust Company Ltd. (and any successor Trustee) who was, or shall be appointed by the Board of Directors of the Company and approved by the Income Tax Authorities to hold the Trust Assets.

### **3. Provisions of the Appendix shall govern**

The provisions of the Appendix shall supersede and govern in the case of any inconsistency or conflict arising between the provisions of the Appendix and the provisions of the Plan, provided, however, that this Appendix shall not be construed to grant Participant rights not consistent with the terms of the Plan, unless specifically provided herein.

### **4. Selection of Tax Method – Capital Gains Method**

The Company chooses the Capital Gain Method (*‘Maslul Revach Hon’*). This choice may be changed in the future, by a Board resolution, provided, however, that the change in selection is permissible under the provisions of Section 102.

### **5. Holding of Securities by the Trustee**

- 5.1. All Securities shall be issued to the Trustee to be held in the Trust for the benefit of the relevant Participants. All certificates representing Securities issued to the Trustee under this Appendix shall be deposited with the Trustee, and shall be held by the Trustee until such time that such Options or Shares are released from the Trust as herein provided.
- 5.2. After the Release Term is over, a Participant shall be entitled to instruct the Trustee to transfer the Shares held for such Participant’s benefit to such Participant, provided, however, that the Trustee confirms that all applicable tax as set in Section 102 was actually paid and the Trustee holds a confirmation to that effect from Income Tax Authorities.
- 5.3. In the case that the Company distributes dividends, than the amount of dividends with respect of Shares held in Trust shall be paid to the Participants that are the beneficial holders of such Shares, subject to deduction at source of the applicable tax.

**6. Provisions governing this Appendix and Plan**

Notwithstanding anything to the contrary in the Plan or elsewhere in this Appendix:

- 6.1. The Plan shall have one, sole, Trustee.
- 6.2. The Appendix shall be subject to one Tax Method, unless the provisions of Section 102 allow otherwise.
- 6.3. The Participants shall not be entitled to cause a Realization Event to occur unless the Release Term is fulfilled.
- 6.4. All rights or benefits that are received subsequent to the grant or exercise the Options or the Shares underlying such Options (including and not limited to bonus shares) shall be deposited with the Trustee until the end of the Release Term, and all such rights and benefits shall be subject to the Tax Method selected by the Company.

**7. Effectiveness of the Appendix.**

This Appendix shall become effective, and Option Grants may be granted hereunder only after receipt the required approvals under Section 102 from the Income Tax Authorities.

**8. Additional limitations**

- 8.1. The Company shall not issue Options to a Participant unless such Participant confirmed in writing that he/she is aware of the provisions of Section 102 and the applicable Tax Method, and such Participant agreed in writing to the terms of the Trust Agreement, and that he/she shall not cause a Realization Event to occur before the Release Term is over. The form for the above confirmation shall be determined by the Committee, and shall be attached to the Plan as Exhibit A.
- 8.2. By accepting an Option Grant, each Participant agrees irrevocably to discharge the Trustee, the Company and any other office holder, employee or agent thereof from any liability with respect of any action or decision duly taken and *bona fide* executed in relation with the Plan, or relating to any Option Grant or Shares.
- 8.3. The Trustee shall use the voting rights vested in any such shares issued upon the exercise of any Options granted under the Plan, in accordance with Exhibit C of the Plan.

**9. Grant of Options not by a Trustee**

Notwithstanding the above, the Company shall be entitled to allocate Option Grants not according to the Tax Methods, but by direct grant to Participants, provided, however, that the requirements of Section 102 are met.



## Appendix B - Addendum

### Terms of Options granted to United States Employees and Service Providers

#### 1. Purpose of the Addendum

This Addendum (also referred to as the "**Addendum**") is part of the Amended and Restated 2010 Incentive Option Plan of Alcobra Ltd. (the "**Plan**"). All terms not otherwise defined herein shall have the meaning ascribed to them in the Plan. This Addendum governs grants of Options to United States Employees and other Service Providers.

#### 2. Provisions of the Addendum

The provisions of the Addendum shall supersede and govern in the case of inconsistency between the provisions of the Addendum and the provisions of the Plan, provided, however, that this Addendum shall not be construed to grant to any Participant rights not consistent with the terms of the Plan, unless specifically provided herein.

#### 3. Eligibility

The individuals who shall be eligible to receive Option Grants under the Plan that are subject to the provisions of this Addendum shall be employees, directors and other individuals and entities who are United States citizens or who are resident aliens of the United States for United States federal tax purposes (collectively, "**U.S. Persons**"), and who render services to the management, operation or development of the Company or a Subsidiary and who have contributed or may be expected to contribute materially to the success of the Company or a Subsidiary. ISOs (as defined in Section 4 below) shall not be granted to any individual who is not an employee of a corporation for United States federal tax purposes. The term "**Subsidiary**" as used in this Addendum means a corporation or other business entity of which the Company owns, directly or indirectly through an unbroken chain of ownership, fifty percent or more of the total combined voting power of all classes of stock.

#### 4. Terms and Conditions of Options

Every Option granted to a U.S. Person shall be evidenced by a written stock option agreement (the "**Stock Option Agreement**") in such form as the Committee shall approve from time to time, specifying the number of Shares that may be purchased pursuant to the Option, the time or times at which the Option shall become exercisable in whole or in part, whether the Option is intended to be an incentive stock option ("**ISO**") or a nonqualified stock option ("**NSO**") and such other terms and conditions as the Committee shall approve, and containing or incorporating by reference the following terms and conditions. The Plan and this Addendum shall be administered in such a manner as to permit those Options granted hereunder and specially designated as an ISO to qualify as incentive stock options as described in Section 422 of the Internal Revenue Code of 1986, as amended (the "**Code**").

(a) Duration. Each Option shall expire no later than ten (10) years from its grant date; provided, however, that no ISO granted to an Employee who owns (directly or under the attribution rules of Section 424(d) of the Code) stock possessing more than ten percent of the total combined voting power of all classes of stock of the Company or any Subsidiary shall expire later than five (5) years from its date of grant.

(b) Exercise Price. The exercise price of each Option shall be as specified by the Committee in its discretion; provided, however, that the price shall be at least 100 percent of the Fair Market Value (as hereinafter defined) of the Shares on the date on which the Board grants the Option (or shareholders resolution to grant such options, if such resolution is required), which shall be considered the date of grant of the Option for purposes of fixing the price; and provided, further, that the price with respect to an ISO granted to an Employee who at the time of grant owns (directly or under the attribution rules of Section 424(d) of the Code) stock representing more than ten percent (10%) of the voting power of all classes of stock of the Company or of any Subsidiary shall be at least 110 percent of the Fair Market Value of the Shares on the date of grant of the ISO. For purposes of the Plan, except as may be otherwise explicitly provided in the Plan or in any Stock Option Agreement, the “**Fair Market Value**” of a Share at any particular date shall be determined according to the following rules: (i) if the Shares are not at the time listed or admitted to trading on a stock exchange, the Fair Market Value shall be the closing price of the Shares on the date in question in the over-the-counter market, as such price is reported in a publication of general circulation selected by the Board and regularly reporting the price of the Shares in such market; provided, however, that if the price of the Shares is not so reported, the Fair Market Value shall be determined in good faith by the Board, which may take into consideration (1) the price paid for the Shares in the most recent trade of a substantial number of shares known to the Board to have occurred at arm’s length between willing and knowledgeable investors, (2) an appraisal by an independent party or (3) any other method of valuation undertaken in good faith by the Board, or some or all of the above as the Board shall in its discretion elect; or (ii) if the Shares are at the time listed or admitted to trading on any stock exchange, then the Fair Market Value shall be the last known closing price of the Shares when the relevant Option Grant is approved by the Company. Notwithstanding Subsection (ii) above, the Administrator may adopt any other method in order to determine the Fair Market Value of a Share, as long as use of such method will not give rise to adverse tax consequences under Internal Revenue Code Section 409A.

(c) Notice of ISO Stock Disposition. The Participant must notify the Company promptly in the event that he sells, transfers, exchanges or otherwise disposes of any Shares issued upon exercise of an ISO before the later of (i) the second anniversary of the date of grant of the ISO or (ii) the first anniversary of the date the shares were issued upon his exercise of the ISO.

(d) Effect of Cessation of Employment or Service Relationship. The Committee shall determine in its discretion and specify in each Stock Option Agreement the effect, if any, of the termination of the Participant’s employment with or performance of services for the Company or any Subsidiary on the exercisability of the Option.

(e) No Rights as Stockholder. A Participant shall have no rights as a stockholder with respect to any Shares covered by an Option until the date of issuance of a stock certificate to him for the Shares. No adjustment shall be made for dividends or other rights for which the record date is earlier than the date the stock certificate is issued, other than as required or permitted by the Plan.

(f) Transferability of Options. Except as permitted by the Committee, and set forth in the terms of a Participant’s Stock Option Agreement, an Option shall not be assignable or transferable by the Participant except by will or by the laws of descent and distribution. During the life of the Participant, an Option shall be exercisable only by him, by a conservator or guardian duly appointed for him by reason of his incapacity or by the person appointed by the Participant in a durable power of attorney acceptable to the Company’s counsel.

## 5. **Requirements of Law**

(a) The Company shall not be required to transfer Shares or to sell or issue any Shares upon the exercise of any Option if the issuance of such Shares will result in a violation by the Participant or the Company of any provisions of any law, statute or regulation of any governmental authority. Specifically, in connection with the Securities Act of 1933, as amended from time to time (the “**Securities Act**”), upon the exercise of any Option, the Company will not be required to issue Shares unless the Committee has received evidence satisfactory to it to the effect that the holder of the Option will not transfer such shares except pursuant to a registration statement in effect under the Securities Act or unless an opinion of counsel satisfactory to the Company has been received by the Company to the effect that registration is not required. Any determination in this connection by the Committee shall be conclusive. The Company shall not be obligated to take any other affirmative action in order to cause the exercise of an Option to comply with any law or regulations of any governmental authority, including, without limitation, the Securities Act or applicable state securities laws.

- (b) All other provisions of this Addendum and the Plan notwithstanding, this Addendum and the Plan shall be administered and construed so as to avoid any person who receives an Option Grant incurring any adverse tax consequences under Internal Revenue Code Section 409A. The Administrator shall suspend the application of any provisions of the Plan which could, in its sole determination, result in an adverse tax consequence to any person under Internal Revenue Code Section 409A.

**6. Forfeiture for Dishonesty or Termination for Cause**

Notwithstanding any provision of the Plan to the contrary, if the Committee determines, after full consideration of the facts, that:

(a) the Participant has been engaged in fraud, embezzlement, theft or commission of a felony in the course of his or her employment by or involvement with the Company, a Subsidiary or a parent corporation as defined in Section 424 of the Code or any direct or indirect subsidiary of such parent (an “**Affiliate**”) or has made unauthorized disclosure of trade secrets or other proprietary information of the Company, a Subsidiary, an Affiliate or of a third party who has entrusted such information to the Company, a Subsidiary or an Affiliate; or

(b) the Participant has violated the terms of any employment, noncompetition, nonsolicitation or proprietary information agreement to which he is a party; or

(c) the Participant’s employment or involvement with the Company, a Subsidiary or an Affiliate was terminated for “cause,” as defined in any employment agreement with the Participant, if applicable, or if there is no such agreement, as determined by the Committee, which may determine that “cause” includes among other matters the willful failure or refusal of the Participant to perform and carry out his or her assigned duties and responsibilities diligently and in a manner satisfactory to the Committee;

then the Participant’s right to exercise an Option shall terminate as of the date of such act (in the case of (a) or (b)) or such termination (in the case of (c)), the Participant shall forfeit all unexercised Options and shall be required to sell to the Company or, in the case the Company is not allowed to repurchase its own shares, to a third party approved by the Company, all or any part of the Shares acquired by the Participant prior to such event, at a price equal to the lesser of their Fair Market Value or the amount paid to the Company upon such transfer or exercise. If a Participant whose behavior the Company asserts falls within the provisions of (a), (b) or (c) above has exercised or attempts to exercise an Option prior to consideration of the application of this Section 6 or prior to a decision of the Committee, the Company shall not be required to recognize such exercise until the Committee has made its decision and, in the event any exercise shall have taken place, it shall be of no force and effect (and shall be void ab initio) if the Committee makes an adverse determination, provided, however, that if the Committee finds in favor of the Participant then the Participant will be deemed to have exercised the Option retroactively as of the date he or she originally gave notice of his or her attempt to exercise or actual exercise, as the case may be. The decision of the Committee as to the cause of a Participant’s discharge and the damage done to the Company shall be final, binding and conclusive. No decision of the Committee, however, shall affect in any manner the finality of the discharge of such Participant by the Company. For purposes of this Section 6, reference to the Company shall include any Subsidiary or Affiliate.

**7. Tax Withholding**

To the extent required by law, the Company may withhold or cause to be withheld income and other taxes with respect to any income recognized by a Participant by reason of the exercise of an Option, and as a condition to the receipt of any Option the Participant shall agree that if the amount payable to him by the Company and any Subsidiary in the ordinary course is insufficient to pay such taxes, then he shall upon the request of the Company pay to the Company an amount sufficient to satisfy its tax.

**Exhibit A**

**Option Grant Letter Agreement**

This letter agreement (the “**Agreement**”) is made as of \_\_\_\_\_, 20\_\_\_\_, by and among Alcobra Ltd. (the “**Company**”), an Israeli Company with main place of business at [Address], Israel, and \_\_\_\_\_, an [Israeli citizen], I.D number \_\_\_\_\_ (the “**Participant**”).

**Whereas** The Company adopted an Incentive Option Plan (together with applicable Appendixes, the “**Plan**”), a copy of which was reviewed by the Participant; and

**Whereas** The Company resolved to grant to the Participant an Option Grant, subject to the terms and conditions herein; and

**NOW, THEREFORE**, it is agreed as follows:

1. All terms not defined herein shall have the meaning ascribed to them in the Plan.
2. The Company resolved to grant certain options (the “**Option Grant**”) to purchase the Company’s Ordinary Shares to the Participant.
3. The terms of the Option Grant are as follows:
  - 3.1. Number of Options: \_\_\_\_\_ (\_\_\_\_\_).
  - 3.2. Vesting Schedule – as defined in the Plan / \_\_\_\_\_. [Choose the relevant alternative]
  - 3.3. Vesting Commencement Date: \_\_\_\_\_, 200\_.
  - 3.4. Exercise Price per options: US\$\_\_\_\_\_ per share.
  - 3.5. [Acceleration Terms: \_\_\_\_\_]
4. The grant of the Option Grant is conditioned upon, and shall not become effective unless and until the Participant agreeing to the terms of this Agreement.
5. Contact details and personal details of the Participant as supplied by it:
  - 5.1. Full name: \_\_\_\_\_.
  - 5.2. Identification / registration number: \_\_\_\_\_. [For Israeli citizens or entities]
  - 5.3. Address: \_\_\_\_\_.
  - 5.4. Telephone (home): \_\_\_\_\_.
  - 5.5. Cellular Phone: \_\_\_\_\_.

5.6. Facsimile: \_\_\_\_\_.

5.7. E-mail: \_\_\_\_\_.

6. The grant is made in accordance with the terms of the Plan.
7. Prior to signing this Agreement Participant had the reasonable opportunity to review the Plan and consult with his / her advisors (such advisors shall not include the Company or anyone on the Company's behalf) as Participant deemed fit.
8. Participant hereby confirms that he /she received reasonable opportunity to review the Plan and understand its terms, and that Participant agrees to the terms and provisions of the Plan.
9. The Participant acknowledges and agrees that the Company may be merged, or acquired or sold to a third party, and in such case, by signing this Agreement, the Participant grants the Board, or anyone on behalf of the Board, the right to sign on behalf of such Participant any document or agreement reasonably necessary, in the Board's discretion, in order to consummate such acquisition, merger or sale.
10. Participant hereby confirms that he /she is aware of the provisions of Section 102 (the updated Section 102 is attached hereto as Schedule A) and the applicable Tax Method.
11. Participant shall not exercise shares (as such term is defined in Section 102) before the Release Term.
12. Participant agrees to the terms in the Trust Agreement (attached hereto as Schedule B).

[Sections 10 – 12 are applicable only to grants under Appendix A]

Sincerely yours,

\_\_\_\_\_  
**Alcobra Ltd.**

\_\_\_\_\_  
**[Participant]**

By: \_\_\_\_\_  
Title: \_\_\_\_\_

Name: \_\_\_\_\_

[for consultant use this form]

**Option Grant Letter Agreement**

This letter agreement (the “**Agreement**”) is made as of \_\_\_\_\_, 20\_\_\_\_, by and among Alcobra Ltd. (the “**Company**”), an Israeli Company with main place of business at [Address], Israel, and \_\_\_\_\_, an [Israeli citizen], I.D number \_\_\_\_\_ (the “**Participant**”).

**Whereas** The Company adopted an Incentive Option Plan (together with applicable Appendixes, the “**Plan**”), a copy of which was reviewed by the Participant; and

**Whereas** The Company resolved to grant to the Participant an Option Grant, subject to the terms and conditions herein; and

**NOW, THEREFORE**, it is agreed as follows:

1. All terms not defined herein shall have the meaning ascribed to them in the Plan.
2. The Company resolved to grant certain options (the “**Option Grant**”) to purchase the Company’s Ordinary Shares to the Participant.
3. The terms of the Option Grant are as follows:
  - 3.1. Number of Options: \_\_\_\_\_ (\_\_\_\_\_).
  - 3.2. Vesting Schedule – as defined in the Plan / \_\_\_\_\_. [Choose the relevant alternative]
  - 3.3. Vesting Commencement Date: \_\_\_\_\_, 200\_.
  - 3.4. Exercise Price per options: US\$\_\_\_\_\_ per share.
  - 3.5. [Acceleration Terms: \_\_\_\_\_]
4. The grant of the Option Grant is conditioned upon, and shall not become effective unless and until the Participant agreeing to the terms of this Agreement.
5. Contact details and personal details of the Participant as supplied by it:
  - 5.1. Full name: \_\_\_\_\_.
  - 5.2. Identification / registration number: \_\_\_\_\_. [For Israeli citizens or entities]
  - 5.3. Address: \_\_\_\_\_.
  - 5.4. Telephone (home): \_\_\_\_\_.

5.5. Cellular Phone: \_\_\_\_\_.

5.6. Facsimile: \_\_\_\_\_.

5.7. E-mail: \_\_\_\_\_.

6. The grant is made in accordance with the terms of the Plan.

7. Prior to signing this Agreement Participant had the reasonable opportunity to review the Plan and consult with his / her advisors (such advisors shall not include the Company or anyone on the Company's behalf) as Participant deemed fit.

8. Participant hereby confirms that he /she received reasonable opportunity to review the Plan and understand its terms, and that Participant agrees to the terms and provisions of the Plan.

9. The Participant acknowledges and agrees that the Company may be merged, or acquired or sold to a third party, and in such case, by signing this Agreement, the Participant grants the Board, or anyone on behalf of the Board, the right to sign on behalf of such Participant any document or agreement reasonably necessary, in the Board's discretion, in order to consummate such acquisition, merger or sale.

Sincerely yours,

\_\_\_\_\_  
**Alcobra Ltd.**

\_\_\_\_\_  
**[Participant]**

By: \_\_\_\_\_  
Title: \_\_\_\_\_

Name: \_\_\_\_\_

\_\_\_\_\_  
*Alcobra Ltd. – Amended and Restated 2010 Incentive Option Plan*

**Exhibit B**

**Form of Exercise Notice**

**To: Alcobra Ltd. (the "Company")**

Attention: **Secretary, CFO**

1. Exercise of Option. Effective as of today, \_\_\_\_\_, 200\_, I the undersigned ("**Participant**") hereby elects to exercise Participant's option to \_\_\_\_\_ Shares, each 0.01 NIS par value of the Company (hereinafter the: "**Shares**"), under and pursuant to the Company's Amended and Restated 2010 Incentive Option Plan (the "**Plan**") and the Option Grant Letter Agreement dated \_\_\_\_\_, 200\_ (the "**Option Agreement**").

2. Delivery of Payment. Participant herewith delivers to the Company the full payment for the Shares/Participant herewith delivers to the Company an irrevocable direction to a securities brokers approved by the Company to sell Shares and to deliver all or part of the sales proceeds to the Company or to the Trustee][Cross out the irrelevant options], as set forth in the Option Agreement.

3. Representations of Participant. Participant acknowledges that Participant has received, read and understood the Plan and the Option Agreement and agrees to abide by and be bound by their terms and conditions.

4. Rights as Shareholder. Until the issuance of the Shares (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company), no right to receive dividends or any other rights as a shareholder shall exist with respect to the Optioned Shares, notwithstanding the exercise of the Option. The Shares shall be issued to Participant as soon as practicable after the Option is exercised. No adjustment shall be made for a dividend or other right for which the record date is prior to the date of issuance of the Shares.

5. Waiver of Rights. The Participant hereby waives any of the following rights to the extent such rights are attached to the Shares: (i) preemptive rights in relation to issuance of new securities in the Company; (ii) rights of first refusal in relation with any sale of shares of the Company; (iii) co-sale rights in relation with any sale of shares of the Company

5. Tax Consultation. Participant understands that Participant may suffer adverse tax consequences as a result of Participant's purchase or disposition of the Shares. Participant represents that Participant has consulted with any tax consultants Participant deems advisable in connection with the purchase or disposition of the Shares and that Participant is not relying on the Company or any Related Entity for any tax advice.

Submitted by:  
PARTICIPANT

Signature: \_\_\_\_\_

Print Name: \_\_\_\_\_

Address:



**Exhibit 12.1**

**CERTIFICATION PURSUANT TO EXCHANGE ACT RULE 13a-14(a) or 15d-14(a)**

I, Dr. Yaron Daniely, certify that:

1. I have reviewed this annual report on Form 20-F of Alcobra Ltd.;
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The Company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:
  - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c) Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d) Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and
5. The Company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's board of directors (or persons performing the equivalent function):
  - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: April 28, 2017

\_\_\_\_\_  
/s/ Dr. Yaron Daniely  
Dr. Yaron Daniely  
Chief Executive Officer

**Exhibit 12.2**

**CERTIFICATION PURSUANT TO EXCHANGE ACT RULE 13a-14(a) or 15d-14(a)**

I, Dr. Tomer Berkovitz, certify that:

1. I have reviewed this annual report on Form 20-F of Alcobra Ltd.;
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The Company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:
  - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c) Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d) Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and
5. The Company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's board of directors (or persons performing the equivalent function):
  - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: April 28, 2017

\_\_\_\_\_  
/s/ Dr. Tomer Berkovitz  
Dr. Tomer Berkovitz  
Chief Financial Officer and Chief Operating Officer

**Exhibit 13.1**

**CERTIFICATION PURSUANT TO  
18 U.S.C. Section 1350**

In connection with the filing of the Annual Report on Form 20-F for the period ended December 31, 2016 (the "Report") by Alcobra Ltd. (the "Company"), the undersigned, as Chief Executive Officer of the Company, hereby certifies pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

- (1) the Report fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Dr. Yaron Daniely  
Dr. Yaron Daniely  
Chief Executive Officer  
April 28, 2017

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**Exhibit 13.2**

**CERTIFICATION PURSUANT TO  
18 U.S.C. Section 1350**

In connection with the filing of the Annual Report on Form 20-F for the period ended December 31, 2016 (the "Report") by Alcobra Ltd. (the "Company"), the undersigned, as Chief Financial Officer of the Company, hereby certifies pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

- (1) the Report fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Dr. Tomer Berkovitz

Dr. Tomer Berkovitz  
Chief Financial Officer and Chief Operating Officer  
April 28, 2017

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**CONSENT OF INDEPENDENT REGISTERED ACCOUNTING FIRM**

We consent to the incorporation by reference in the Registration Statement on Form F-3 (Registration No. 333-209960) and Registration Statements on Form S-8 (Registration No. 333-194875, Registration No. 333-202394 and Registration No. 333-209947) of Alcobra Ltd. of our report dated April 27, 2017 with respect to the consolidated financial statements of Alcobra Ltd. and its subsidiary for the year ended December 31, 2016 included in this Annual Report on Form 20-F for the year ended December 31, 2016.

Tel Aviv, Israel  
April 27, 2017

/s/ Kost, Forer, Gabbay & Kasierer  
KOST, FORER, GABBAY & KASIERER  
A Member of EY Global

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