FORM 20-F

Galmed Pharmaceuticals Ltd. - GLMD

Filed: March 31, 2015 (period: December 31, 2014)

Annual and transition report of foreign private issuers under sections 13 or 15(d)

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 20-F

£ REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934
Or
R ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2014
Or
£ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
Or
£ SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Commission File No. 001-36345

GALMED PHARMACEUTICALS LTD.

(Exact name of Registrant as specified in its charter)

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

State of Israel
(Jurisdiction of incorporation)

8 Shaul Hamelech Blvd., Amot Mishpat Bldg., Tel Aviv, Israel 6473307
(Address of principal executive offices)

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

Title of each class	*Name of each exchange on which registered*
Ordinary shares, par value NIS 0.01 per share	**Nasdaq Capital Market**

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. 11,100,453

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such a 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, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act. (Check one): Large accelerated filer ☐ Accelerated filer ☐ Non-accelerated filer ☒

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:
U.S. GAAP ☒ **International Financial Reporting Standards as issued by the International Accounting Standards Board ☐** **Other ☐**

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the Registrant has elected to follow: Item 17 ☐ Item 18 ☐

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

(APPLICABLE ONLY TO ISSUERS INVOLVED IN BANKRUPTCY PROCEEDINGS DURING THE PAST FIVE YEARS)

Indicate by check mark whether the registrant has filed all documents and reports required to be filed by Sections 12, 13 or 15(d) of the Securities Exchange Act of 1934 subsequent to the distribution of securities under a plan confirmed by a court. Yes ☐ No ☐

TABLE OF CONTENTS

PART I	4
ITEM 1. Identity of Directors, Senior Management and Advisers	4
ITEM 2. Offer Statistics and Expected Timetable	4
ITEM 3. Key Information	5
ITEM 4. Information on the Company	41
ITEM 4A. Unresolved Staff Comments	81
ITEM 5. Operating and Financial Review and Prospects	81
ITEM 6. Directors, Senior Management and Employees	91
ITEM 7. Major Shareholders and Related Party Transactions	111
ITEM 8. Financial Information	113
ITEM 9. The Offer and Listing	113
ITEM 10. Additional Information	114
ITEM 11. Quantitative and Qualitative Disclosures About Market Risk	132
ITEM 12. Description of Securities Other Than Equity Securities	133
PART II	134
ITEM 13. Defaults, Dividend Arrearages and Delinquencies	134
ITEM 14. Material Modifications to the Rights of Security Holders and Use of Proceeds	134
ITEM 15. Controls and Procedures	134
ITEM 16. [RESERVED]	135
ITEM 16A. Audit Committee Financial Expert	135
ITEM 16B. Code of Ethics	135
ITEM 16C. Principal Accountant Fees and Services	135
ITEM 16D. Exemptions from the Listing Standards for Audit Committees	136
ITEM 16E. Purchases of Equity Securities by the Issuer and Affiliated Purchasers	136
ITEM 16F. Change in Registrant's Certifying Accountant	136
ITEM 16G. Corporate Governance	136
ITEM 16H. Mine Safety Disclosure	137
PART III	137
ITEM 17. Financial Statements	137
ITEM 18. Financial Statements	137
ITEM 19. Exhibits	138

ABOUT THIS ANNUAL REPORT

All references to "we," "us," "our," "the Company" and "our Company", in this Annual Report on Form 20-F, or our annual report, are to Galmed Pharmaceuticals Ltd. and its subsidiaries, unless the context otherwise requires. All references to "shares" or "ordinary shares" are to our ordinary shares, NIS 0.01 nominal par value per share. All references to "Israel" are to the State of Israel. "U.S. GAAP" means the generally accepted accounting principles of the United States. Unless otherwise stated, all of our financial information presented in this annual report has been prepared in accordance with U.S. GAAP. Any discrepancies in any table between totals and sums of the amounts listed are due to rounding. Unless otherwise indicated, or the context otherwise requires, references in this annual report to financial and operational data for a particular year refer to the fiscal year of our company ended December 31 of that year.

Our reporting currency and financial currency is in the U.S. dollar. In this annual report, "NIS" means New Israeli Shekel, and "$," "US$" and "U.S. dollars" mean United States dollars.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 20-F contains forward-looking statements about our expectations, beliefs or intentions regarding, among other things, our product development efforts, business, financial condition, results of operations, strategies or prospects. In addition, from time to time, we or our representatives have made or may make forward-looking statements, orally or in writing. Forward-looking statements can be identified by the use of forward-looking words such as "believe," "expect," "intend," "plan," "may," "should," "anticipate," "could," "might," "seek," "target," "will," "project," "forecast," "continue" or their negatives or variations of these words or other comparable words or by the fact that these statements do not relate strictly to historical matters. These forward-looking statements may be included in, among other things, various filings made by us with the Securities and Exchange Commission, or the SEC, press releases or oral statements made by or with the approval of one of our authorized executive officers. Forward-looking statements relate to anticipated or expected events, activities, trends or results as of the date they are made. Because forward-looking statements relate to matters that have not yet occurred, these statements are inherently subject to risks and uncertainties that could cause our actual results to differ materially from any future results expressed or implied by the forward-looking statements. Many factors could cause our actual activities or results to differ materially from the activities and results anticipated in forward-looking statements, including, but not limited to, the factors summarized below:

- U.S. Food and Drug Administration, or FDA, approval of, or European Medicines Authority, or EMA, or other regulatory action with respect to, our product candidate, aramchol;
- the commercial launch and future sales of aramchol or any other future products or product candidates;
- our ability to achieve favorable pricing for aramchol;
- our expectations regarding the commercial market of Non-Alcoholic Steato-Hepatitis, or NASH, in patients who also suffer from obesity and insulin resistance and our expectations regarding the commercial market of patients with cholesterol gallstones;
- third-party payor reimbursement for aramchol;
- our estimates regarding anticipated capital requirements and our needs for additional financing;
- the timing and cost of Phase IIb and Phase III trials for aramchol or whether such trials will be conducted at all;
- completion and receiving favorable results of Phase IIb and Phase III trials for aramchol;
- patient market size and market adoption of aramchol by physicians and patients;

- the timing, cost or other aspects of the commercial launch of aramchol;
- the development and approval of the use of aramchol for additional indications or in combination therapy; and
- our expectations regarding licensing, acquisitions and strategic operations.

We believe these forward-looking statements are reasonable; however, 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. We discuss many of these risks in this annual report in greater detail under the heading "Risk Factors" and elsewhere in this annual report. Given these uncertainties, you should not rely upon forward-looking statements as predictions of future events.

All forward-looking statements attributable to us or persons acting on our behalf speak only as of the date hereof and are expressly qualified in their entirety by the cautionary statements included in this annual report. We undertake no obligations to update or revise forward-looking statements to reflect events or circumstances that arise after the date made or to reflect the occurrence of unanticipated events. In evaluating forward-looking statements, you should consider these risks and uncertainties.

EXPLANATORY NOTE

Market data and certain industry data and forecasts used throughout this Annual Report on Form 20-F were obtained from internal company surveys, market research, consultant surveys commissioned by the Company, publicly available information, reports of governmental agencies and industry publications and surveys. Industry surveys, publications, consultant surveys commissioned by the Company and forecasts generally state that the information contained therein has been obtained from sources believed to be reliable. However, this information may prove to be inaccurate because of the method by which some of the data for the estimates is obtained or because this information cannot always be verified with complete certainty due to the limits on the availability and reliability of raw data, the voluntary nature of the data gathering process and other limitations and uncertainties. As a result, the market and industry data and forecasts included or incorporated by reference in this Annual Report on Form 20-F, and estimates and beliefs based on that data, may not be reliable. We have relied on certain data from third-party sources, including internal surveys, industry forecasts and market research, which we believe to be reliable based on our management's knowledge of the industry. However, we have not ascertained the underlying economic assumptions relied upon therein. Forecasts are particularly likely to be inaccurate, especially over long periods of time. In addition, we do not necessarily know what assumptions regarding general economic growth were used in preparing the forecasts we cite. Statements as to our market position are based to the best of our knowledge on the most currently available data. While we are not aware of any misstatements regarding the industry data presented in this Annual Report on Form 20-F, our estimates involve risks and uncertainties and are subject to change based on various factors, including those discussed under the heading "Risk Factors" in this annual report.

PART I

ITEM 1. Identity of Directors, Senior Management and Advisers.

Not applicable.

ITEM 2. Offer Statistics and Expected Timetable.

Not applicable.

ITEM 3. Key Information.

A. Selected Financial Data.

The following table sets forth our selected consolidated financial data for the periods ended and as of the dates indicated, which reflects the financial data of Galmed Holdings Inc., a holdings company incorporated in the British Virgin Islands, or GHI, our predecessor, prior to the Reorganization (as defined below), as well as the financial data of the Company post Reorganization. The following selected consolidated financial data for our company should be read in conjunction with the financial information, "Item 5. Operating and Financial Review and Prospects" and other information provided elsewhere in this Annual Report on Form 20-F and our consolidated financial statements and related notes. The selected consolidated financial data in this section is not intended to replace the consolidated financial statements and is qualified in its entirety thereby. In the opinion of our management, our unaudited consolidated financial statements contain all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of our financial position, results of operations and cash flows as of and for the periods indicated therein.

We derived the selected consolidated financial statements as of and for the years ended December 31, 2014, 2013, 2012 and 2011, as applicable, from our audited consolidated financial statements included elsewhere in this Annual Report on Form 20-F.

	Year ended December 31,			
	2011	2012	2013	2014
	(in thousands)			
Research and development expenses	$ 1,326	$ 2,443	$ 7,207	$ 6,664
General and administrative expenses	151	694	7,355	2,478
Capital loss	—	—	10	—
Operating loss	1,477	3,137	14,572	9,142
Financial expenses	(3)	(6)	(2,912)	(10)
Financial income	—	—	—	50
Taxes on income	2	6	1	1
Net loss	1,482	3,149	17,485	9,103
Other comprehensive income:				
Net unrealized gain on available for sale securities	—	—	—	4
Comprehensive loss	1,482	3,149	17,485	9,099
Net loss per ordinary share (*)	$ 0.30	$ 0.63	$ 3.45	$ 0.88
Number of ordinary shares used in computing loss per ordinary share (*)	4,995,837	4,995,837	5,096,466	10,323,686

(*) Retroactively adjusted to reflect the 729:1 share split, which occurred upon the consummation of the Reorganization (as defined below).

Consolidated Balance Sheet data:	As of December 31,		
	2012	2013	2014
		(In thousands)	
Cash and cash equivalents	718	137	23,736
Other receivables	14	16	8,415
Fixed assets	30	13	774
Total assets	762	166	32,925
Total liabilities	2,741	2,117	1,518

B. Capitalization and Indebtedness.

Not applicable.

C. Reasons for the Offer and Use of Proceeds.

Not applicable.

D. Risk Factors.

Risks Related to Our Financial Position and Capital Requirements

We are a clinical-stage biopharmaceutical company with a history of operating losses. We expect to incur additional losses in the future and may never be profitable.

We are a clinical-stage biopharmaceutical company with an operating history limited to clinical development of one product and no approved products. To date, we have focused nearly exclusively on developing our product candidate, aramchol. We have funded our operations to date primarily through proceeds from the private placement of ordinary shares, convertible debt and our initial public offering on March 18, 2014. In addition, we have limited operating 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 currently have no products approved for marketing in the United States or any other jurisdiction and have not generated any revenue from product sales to date. We have incurred operating losses in each year since the inception of our predecessor in 2000. Our loss attributable to holders of our ordinary shares for the years ended December 31, 2013 and 2014 was approximately $17.5 million and $9.1 million, respectively. As of December 31, 2014, we had an accumulated deficit of $36.7 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 ability to become profitable depends upon our ability to generate revenue in excess of our expenses. To date, we have not generated any revenue as our lead product candidate, aramchol, is still in clinical development and has not been approved by the FDA, nor has any other product candidate. We do not know when, or if, we will generate any revenue. We do not expect to generate revenue unless and until we obtain regulatory and marketing approval of, and commercialize, aramchol, or any other product candidate. We will continue to incur research and development and general and administrative expenses related to our operations. We expect to continue to incur losses for the foreseeable future, and these losses will likely increase as we:

- initiate and manage additional clinical trials for aramchol, and initiate additional research and development programs;
- seek regulatory approvals for our product candidate, or future product candidates, if any;
- implement internal systems and infrastructures, including, without limitation, hiring of additional personnel as needed and developing sales and marketing functions if and when our product candidate receives applicable regulatory approval;

- seek to in-license additional products or technologies to develop;
- hire additional management and other personnel; and
- move towards commercialization of our product candidate and future product candidates, if any.

We may out-license aramchol before it is approved by any applicable regulatory agency, commercialized and/or generates revenue, depending on a number of factors, including our ability to:

- obtain favorable clinical results from and progress the clinical development of aramchol;
- develop and obtain regulatory approvals in the countries and for the uses we intend to pursue for aramchol;
- subject to successful completion of registration, clinical trials and perhaps additional clinical trials of aramchol, apply for and obtain marketing approval in the countries we intend to pursue for aramchol;
- contract for the manufacture of commercial quantities of aramchol at acceptable cost levels if marketing approval is received; and
- establish external, and potentially in the future, internal, sales and marketing capabilities to effectively market and sell aramchol in the United States and other countries.

Even if aramchol is approved for commercial sale for the treatment of NASH, or any other indications, it may not gain market acceptance or achieve commercial success. In addition, we anticipate incurring significant costs associated with seeking regulatory approval and 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 additional funding.

We expect our research and development expenses to increase in connection with our planned clinical trials and potential initiation of clinical trials for other indications. In addition, if we obtain marketing approval for aramchol, we will likely initially incur significant expenses associated with sales, marketing and manufacturing by third parties, as well as continued research and development expenses. Furthermore, we expect to incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and 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.

Our limited operating history makes it difficult to evaluate our business and prospects.

Our operating history is limited to clinical development of one product, and our operations to date have been limited primarily to research and development, raising capital and recruiting scientific and management personnel and third-party partners. Therefore, it may be difficult to evaluate our business and prospects. We have not yet demonstrated an ability to commercialize or obtain regulatory approval for any product candidate. Consequently, any predictions about our future performance may not be accurate, and you may not be able to fully assess our ability to complete development and/or commercialize our product candidate, or any future product candidate, obtain regulatory approvals or achieve market acceptance or favorable pricing for our product candidate or any future product candidate.

We have not yet commercialized any products and we may never be able to do so, and even if we do, the products may not gain market acceptance.

We have not yet commercialized any products and we may never be able to do so. We do not know when or if we will complete any of our product development efforts, obtain regulatory approval for any product candidates or successfully commercialize any approved products. Even if we are successful in developing products that are approved for marketing, we will not be successful unless these products gain market acceptance for appropriate indications at favorable reimbursement rates. The degree of market acceptance of these products will depend on a number of factors, including:

- the timing of regulatory approvals in the countries, and for the uses, we intend to pursue with respect to the commercialization of our product candidates;
- the competitive environment;
- the acceptance by the medical community of the safety and clinical efficacy of our products and their potential advantages over other therapeutic products;
- the development of a non-invasive diagnostic biomarker for the detection of NASH and ongoing management of the condition;
- the adequacy and success of distribution, sales and marketing efforts, including through strategic agreements with pharmaceutical and biotechnology companies; and
- the pricing and reimbursement policies of government and third-party payors, such as insurance companies, health maintenance organizations and other plan administrators.

Physicians, patients, third-party payors or the medical community in general may be unwilling to accept, utilize or recommend, and in the case of third-party payors, cover any of our planned future products. As a result, we are unable to predict the extent of future losses or the time required to achieve profitability, if at all. Even if we successfully develop one or more products, we may not become profitable.

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

We currently estimate that our cash position will support our current clinical trials and operations into 2017, although there is no assurance of this. We will likely need to raise substantial additional capital to fund our operations and to develop aramchol beyond its current development stage, and ultimately commercialize it. In addition, we may choose to expand our current research and development focus, or other clinical operations, which may also require additional capital. As of December 31, 2014, we had a net working capital of $31.8 million and cash and cash equivalents of $23.7 million. Our future capital requirements may be substantial and will depend on many factors including:

- our clinical trial results;
- exploration of the possibility to develop aramchol for the treatment of other conditions or indications, or possible label expansion of aramchol once its approved, if at all, for the treatment of other conditions or indications;
- the cost of filing and prosecuting patent applications and the cost of defending our patents;
- the cost of prosecuting infringement actions against third parties;
- the cost, timing and outcomes of seeking marketing approval of aramchol;
- the costs associated with commercializing aramchol if we receive marketing approval, including the cost and timing of establishing external, and potentially in the future, internal, sales and marketing capabilities to market and sell aramchol;
- 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 future product candidates or products, if any;

- the demand for our products;
- the costs associated with developing and/or in-licensing other research and development programs;
- 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, into 2017, although there is no assurance of this. We believe these funds will enable us to complete any preparatory clinical and non-clinical work, as well as our planned Phase IIb clinical trial of aramchol for the treatment of patients with NASH in patients suffering from obesity and insulin resistance, which we refer to as our ARREST Study, and Phase IIa clinical trial of aramchol for the treatment of patients with cholesterol gallstones. We will require significant additional funds to initiate and complete additional clinical trials, including but not limited to a possible Phase III pivotal trial for the treatment of patients with NASH, and the FDA and EMA approval processes. However, changing circumstances may cause us to consume capital significantly faster than we currently anticipate, such as losing our Small and Medium Enterprise status at the EMA, which entitles us to significant fee reductions. Because there are numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amount of increased capital outlays and operating expenditures associated with our anticipated clinical trials. 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 and additional financing may cause significant dilution to our existing shareholders. If adequate funds are not available to us on a timely basis, or at all, we may be required to terminate or delay planned or ongoing clinical trials or other development activities for aramchol.

Raising additional capital may be costly or difficult to obtain and will dilute current shareholders' ownership interests.

Any debt or equity financing that we may need may not be available on terms favorable to us, or at all. If we obtain funding through a strategic collaboration or licensing arrangement, we may be required to relinquish our rights to certain of our technologies, products or marketing territories. If we are unable to obtain required additional capital, we may have to curtail our growth plans or cut back on existing business, and we may not be able to continue operating if we do not generate sufficient revenues from operations needed to stay in business.

We may incur substantial costs in pursuing future capital financing, including investment banking fees, legal fees, accounting fees, securities law compliance fees, printing and distribution expenses and other costs. We may also be required to recognize non-cash expenses in connection with certain securities we issue, such as convertible notes and warrants, which may adversely impact our financial condition and results of operations.

Any additional capital raised through the sale of equity or equity-linked securities may dilute our current shareholders' ownership in us and could also result in a decrease in the market price of our ordinary shares. The terms of those securities issued by us in future capital transactions may be more favorable to new investors and may include the issuance of warrants or other derivative securities, which may have a further dilutive effect.

We are unable to estimate our long-term capital requirements due to uncertainties associated with the development and commercialization of our product candidate. If we fail to obtain necessary funds for our operations, we will be unable to maintain and improve our intellectual property and technology, and we will be unable to develop and commercialize our product candidate.

Our long-term capital requirements are expected to depend on many potential factors, including, among others:

- the number of product candidates in development;
- the size, duration and scope of future clinical trials;

- the regulatory path of our lead product candidate;
- the results of our clinical tests, which can be unpredictable in product candidate development;
- our ability to successfully commercialize our product candidates, including securing commercialization and out-licensing agreements with third parties and favorable pricing and market share;
- the progress, success and cost of our clinical trials and research and development programs, including those associated with milestones and royalties;
- the costs, timing and outcome of regulatory review and obtaining regulatory approval of our lead product candidate and addressing regulatory and other issues that may arise post-approval;
- the breadth of the labeling, assuming that our product candidate is approved for commercialization by a relevant regulatory authority, which may not occur;
- our need, or decision, to acquire or in-license complementary technologies or new platform technologies or product candidate targets;
- the costs of enforcing our issued patents and defending intellectual property-related claims;
- the costs of investigating patents that might block us from developing potential product candidates;
- the costs of recruiting and retaining qualified personnel;
- our revenue, if any; and
- our consumption of available resources more rapidly than currently anticipated, resulting in the need for additional funding sooner than anticipated.

If we are unable to obtain the funds necessary for our operations, we will be unable to maintain and improve our intellectual property and technology, and we will be unable to develop and commercialize aramchol, or other product candidates, which would materially and adversely affect our business, liquidity and results of operations.

We may become subject to the payment of taxes in connection with the Reorganization.

On February 2, 2014, we underwent a reorganization, or the Reorganization, pursuant to which all of our current business (including our intellectual property) was transferred to us. The Reorganization was effected by way of share transfers and asset transfers, as follows: First, GHI, our predecessor, transferred the entire share capital of Galmed 2000 Inc., a holdings company incorporated in the British Virgin Islands, or GTTI, to the Company; next, GTTI transferred the entire share capital of Galmed International Limited, a company incorporated in Malta, a European Union, or EU, member state, or GIL, to the Company; then, GIL transferred and assigned all of its intellectual property to Galmed Research and Development Ltd., a newly formed Israeli company, or GRD. GIL held all of the equity rights in and to Galmed Medical Research Ltd., an Israeli company, or GMR. In connection with the Reorganization, we obtained a tax pre-ruling, or the Tax Pre-Ruling, from the Israeli Tax Authority. The Tax Pre-Ruling confirms that the transfer of shares and assets resulting in the Company as the parent company and 100% equity-owner of GRD, which holds all of the Group's intellectual property, including the Company's patent portfolio, GIL and GTTI, is not taxable pursuant to the provisions of Sections 131 and 132 of the Income Tax Ordinance (New Version) — 1961, or the Israeli Tax Ordinance, as long as certain requirements are met. However, we have not obtained a tax pre-ruling from the tax authorities in the British Virgin Islands with respect to the transfer of the shares of GTTI and the transfer of the shares of GIL to the Company, or from the tax authorities in Malta with respect to the transfer of the intellectual property of GIL to GRD. We believe that such transfers of shares and assets are not taxable in the British Virgin Islands and Malta, respectively. However, there can be no assurance that we will not become subject to the payment of taxes in the British Virgin Islands, with respect to the transfers of shares as aforesaid, or in Malta, in connection with the transfer of the intellectual property as mentioned above. See also "Item 4. Information on the Company—Historical Background and Corporate Structure" below.

Risks Related to Our Business, Industry and Regulatory Requirements

We depend largely on the success of our product candidate, aramchol, and we may not obtain regulatory approval of aramchol.

We have invested almost all of our efforts and financial resources in the research and development of aramchol, which is currently our only product candidate. As a result, our business is largely dependent on our ability to complete the development of, obtain regulatory approval for and successfully commercialize aramchol in a timely manner. The process to develop, obtain regulatory approval for and commercialize aramchol is long, complex, costly and uncertain as to its outcome.

The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drugs are subject to extensive regulation by the FDA and other regulatory agencies in other countries. These regulations differ from jurisdiction to jurisdiction. We are not permitted to market aramchol, or any other product candidate, in the United States until we receive approval of a New Drug Application, or NDA, from the FDA, or in any foreign countries until we receive the requisite approval from the respective regulatory agencies in such countries. We have not received regulatory clearance to conduct the clinical trials that are necessary to file an NDA with the FDA or comparable applications to other regulatory authorities in other countries or received marketing approval for aramchol. The results of clinical trials may be unsatisfactory, even if we believe those clinical trials to be successful, the FDA, or other regulatory authorities, 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 receives 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 jurisdiction does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one jurisdiction 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 aramchol. This would reduce our target market and limit the full commercial potential of aramchol.

We may be forced to abandon development of aramchol, or other future product candidates, which will significantly impair our ability to generate product revenues.

Upon the completion of any clinical trial, the results might not support the claims sought by us. Further, success in earlier clinical trials does not ensure that later clinical trials will be successful, and the results of later clinical trials may not replicate the results of prior clinical trials and preclinical testing. The clinical trial process may fail to demonstrate that aramchol is safe, tolerable and effective for the indicated uses. Any such failure may cause us to abandon aramchol and may delay development of other product candidates. Any delay in, or termination or suspension of, our clinical trials will delay the requisite filings with the FDA or other regulatory agencies and, ultimately, our ability to commercialize our product candidates and generate product revenues. If the clinical trials do not support our product claims, the completion of development of such product candidate may be significantly delayed or abandoned, which will significantly impair our ability to generate revenues and will materially adversely affect our results of operations.

If we acquire or in-license additional technologies or product candidates, we may incur a number of costs, may have integration difficulties and may experience other risks that could harm our business and results of operations.

We may acquire and in-license additional product candidates and technologies. Any product candidate or technologies we in-license or acquire will likely require additional development efforts prior to commercial sale, including extensive preclinical or clinical testing, or both, and approval by the FDA and applicable foreign regulatory authorities, if any. All product candidates are prone to risks of failure inherent in pharmaceutical product development, including the possibility that the product candidate, or product developed based on in-licensed technology, will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any product candidate that we develop based on acquired or in-licensed technology that is granted regulatory approval will be manufactured or produced economically, successfully commercialized or widely accepted or competitive in the marketplace. Moreover, integrating any newly acquired or in-licensed product candidates could be expensive and time-consuming. If we cannot effectively manage these aspects of our business strategy, our business may not succeed.

The clinical trial process is complex and expensive, and 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, a Marketing Authorization Application, or MAA, to the EMA or any similar submission to regulatory authorizes in other countries. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our clinical trials. The fact that the FDA, EMA or other regulatory authorities permit a company to conduct human clinical trials is no guarantee that the trial will be successful. On the contrary, most candidate drugs that enter clinical trials do not prove to be successful and do not result in the filing of an NDA, MAA or similar filing. Drug candidates that prove successful at one clinical trial phase may prove unsuccessful at a subsequent phase. Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements and in part because the results of clinical trials are inherently uncertain and unpredictable. Regulatory authorities, such as the FDA, may decline to permit a clinical trial to proceed or may suspend a clinical trial that it has previously cleared. Additionally, the clinical trial process is time-consuming, and failure can occur at any stage of the trials. We may encounter problems that cause us to abandon or repeat clinical trials. The commencement and completion of clinical trials may be delayed by several factors, including:

- difficulties obtaining regulatory clearance or approval to commence a clinical trial or complying with conditions imposed by a regulatory authority regarding the scope or duration of a clinical trial;
- delays in reaching or failing to reach agreement on acceptable terms with prospective contract research organizations, or CROs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- insufficient or inadequate supply or quality of a product candidate or other materials necessary to conduct our clinical trials;
- difficulties in obtaining institutional review board, or IRB, approval to conduct a clinical trial at a prospective site;
- delays resulting from a decision of the FDA not to review an NDA for aramchol as a Breakthrough Therapy;
- challenges in recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including size and nature of patient population, proximity of patients to clinical sites, eligibility and exclusion 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.

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

- irregularities in conducting a clinical trial, including by way of example, failure to conduct the clinical trial in accordance with regulatory requirements or the FDA-cleared clinical protocols;
- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities;
- unforeseen safety issues or lack of effectiveness; and
- lack of adequate funding to continue the clinical trials.

Although we have not experienced many of the risks involved with conducting clinical trials, including but not limited to, increased expense and material delay, to date, there can be no assurance that we will not experience such risks in the future as we progress with our planned clinical trials. To date, we have experienced a slight delay of approximately three months in the beginning of enrollment of our ARREST Study. Accordingly, we now expect to release the interim results of our ARREST Study in the first half of 2016, instead of in the second half of 2015 as originally planned.

Furthermore, positive results in previous clinical studies of aramchol may not be predictive of similar results in future clinical trials. Also, interim results during a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage development. Accordingly, the results from the completed preclinical studies and clinical trials for aramchol may not be predictive of the results we may obtain in later stage trials. Our clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain FDA or EMA, or other regulatory agency, approval for their products.

In addition, we or regulatory authorities may suspend our clinical trials at any time if it appears that we are exposing participants to unacceptable health risks or if the regulatory authorities find deficiencies in our regulatory submissions or the conduct of such trials. Any suspension of clinical trials will delay possible regulatory approval, if any, and adversely impact our ability to develop products and generate revenue.

Lack of a reliable non-invasive method for the diagnosis of NASH is likely to present a major challenge to our product candidate's market penetration, if ever commercialized.

Liver biopsy is the standard approach for the diagnosis of inflammation and fibrosis associated with NASH. However, the procedure-related morbidity, sample errors, costs and lack of patient interest in participating in such studies limit its use. As such, only patients with a high risk of NASH, which includes patients with metabolic syndrome and an indication of Non-Alcoholic Fatty Liver Disease, or NAFLD, are sent for liver biopsy. Because NASH tends to be asymptomatic, until the disease progresses, many individuals with NASH go undiagnosed until the disease has reached its late stages. The lack of a reliable non-invasive method for the diagnosis of NASH is likely to present a major challenge to aramchol's market penetration, as many practitioners and patients may not be aware that a patient suffers from NASH and requires treatment. As such, use of aramchol might not be as wide-spread as our actual target market and this may limit the commercial potential of aramchol.

A further challenge to aramchol's market penetration is that currently a liver biopsy is the standard approach for measuring improvement in NASH patients. Because it would be impractical to subject all aramchol users to regular and repeated liver biopsies, it will be difficult to demonstrate aramchol's effectiveness to practitioners and patients unless and until a reliable non-invasive method for the diagnosis and monitoring of NASH becomes available, as to which there can be no assurance.

Obtaining approval of an NDA, or other regulatory approval, even after clinical trials that are believed to be successful, is an uncertain process.

Even if we complete our planned clinical trials and believe that the clinical data confirms that the drug is both safe and effective for its intended use, obtaining approval of an NDA, or similar regulatory application, is an extensive, lengthy, expensive and uncertain process, and the FDA and other regulatory agencies may delay, limit or deny approval of aramchol for many reasons, including, without limitation, the fact that:

- we may not be able to demonstrate to the satisfaction of the applicable regulatory agencies that aramchol is safe and effective for any indication;
- the results of clinical trials may not meet the level of statistical significance or clinical significance required by the applicable regulatory agencies for approval;
- the applicable regulatory agencies may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the applicable regulatory agencies may not find the data from preclinical studies and clinical trials sufficient to demonstrate that aramchol's clinical and other benefits outweigh its safety risks;
- the applicable regulatory agencies may disagree with our interpretation of data from preclinical studies or clinical trials;
- the applicable regulatory agencies may not accept data generated at our clinical trial sites;
- the data collected from preclinical studies and clinical trials of aramchol may not be sufficient to support the submission of an NDA or similar regulatory application;
- the applicable regulatory agencies may not schedule an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the applicable regulatory agencies require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the applicable regulatory agencies may require development of a risk evaluation and mitigation strategy as a condition of approval;
- the applicable regulatory agencies may require simultaneous approval for both adults and children, which would delay required approvals, or we may have successful clinical trial results for adults, but not children, or vice versa;
- the applicable regulatory agencies may change their approval policies or adopt new regulations that may impede consideration or approval of our NDA, or similar regulatory application;
- the applicable regulatory agencies may identify deficiencies in the manufacturing processes or facilities of third-party manufacturers, or suppliers of active pharmaceutical ingredients, or APIs, with which we enter into agreements for clinical and commercial supplies; and
- the applicable regulatory agencies may require post-marketing approval studies, such as Phase IV clinical trials, in connection with aramchol.

Before we can submit an NDA, or similar regulatory application, to the FDA, or other regulatory authorities, as applicable, we must conduct a Phase IIb clinical trial and pivotal Phase III clinical trials that will be substantially broader than our Phase IIa trial. We will also need to agree on a protocol with the FDA for both the Phase IIb and Phase III clinical trials before commencing those trials in the United States. Phase III clinical trials frequently produce unsatisfactory results even though prior clinical trials were successful. Therefore, the results of these additional Phase IIb or Phase III clinical trials that we conduct may or may not be successful. The applicable regulatory agencies may suspend all clinical trials or require that we conduct additional clinical, nonclinical, manufacturing, validation or drug product quality studies and submit data from these additional studies before considering or reconsidering the NDA or similar regulatory application. 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 applicable regulatory agencies to provide regulatory approval. If any of these outcomes occur, we would not receive approval for aramchol and may be forced to cease operations.

Even if we obtain regulatory approval for aramchol, the approval might contain significant limitations related to the intended uses for which the drug is approved, use restrictions including, without limitation, for certain labeled populations, 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 aramchol, we may be forced to cease operations.

Aramchol may produce undesirable side effects that we may not detect in our clinical trials, which could prevent us from achieving or maintaining market acceptance of this product candidate and could substantially increase commercialization costs or even force us to cease operations.

Even if aramchol receives marketing approval, we or others may later identify undesirable side effects caused by the product, and in that event, a number of potentially significant negative consequences could result, including, without limitation:

- regulatory authorities may suspend or withdraw their approval of the product;
- regulatory authorities may require the addition of labeling statements, such as warnings, so-called “black box warnings,” contraindications or restrictions on the product’s intended use;
- 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 preclinical studies or clinical trials or restrict or cease the distribution or use of the product; and
- we could be sued and held liable for harm caused to patients.

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.

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 adversely affect the cost, timing or successful completion of a clinical trial. If we experience delays in the completion of, or if we terminate, any of our clinical trials, the commercial prospects for aramchol would be harmed and our ability to generate product revenue would be delayed, possibly materially.

We cannot be certain that the results of our potential Phase III clinical trials, even if all endpoints are met, will support regulatory approval of aramchol for the treatment of NASH.

Although progress has been made as indicated below, currently, the FDA and other regulatory agencies do not have any clear guidance on which endpoints of a Phase III clinical trial would be sufficient for approval of a drug for the treatment of NASH. Therefore, notwithstanding this progress, the development pathway for aramchol is not entirely clear beyond Phase IIb, as no official guidelines have been published to date.

For example, the FDA recognizes that because NASH is characterized by a long asymptomatic natural history, it may be difficult to demonstrate efficacy in a Phase III clinical trial. However, it is precisely this type of demonstration, evidencing the "substantive evidence of effectiveness" of a drug that is required for drug approval.

In certain limited and rare circumstances, the FDA permits drug developers to use a "surrogate endpoint" to demonstrate the clinical benefits of their drugs in the short term, the demonstration of which is sufficient for initial marketing approval. A surrogate endpoint is defined as a biomarker that is intended to substitute for a clinical endpoint, and which is expected to predict the clinical benefit or harm associated with a drug.

Although the FDA has indicated at a workshop held in association with the American Association for the Study of Liver Diseases, or AASLD, and in the subsequent joint publication, that an acceptable surrogate endpoint for drugs targeting the early stages of NASH (i.e., fat infiltration and inflammation, as opposed to fibrosis) is resolution of NASH in liver biopsy, this has not been confirmed by any formal guidelines. It is possible that even if the results of our Phase III clinical trial demonstrate resolution of NASH in liver biopsy, the FDA will require longer-term studies of aramchol, such as Phase IV studies, prior to granting marketing approval.

Even if aramchol, or any other product candidate that we may develop, receives marketing approval, we will continue to face extensive regulatory requirements and any such product may still face future regulatory risks or new requirements.

Even if we receive regulatory approval to market a particular product candidate, any such product will remain subject to extensive regulatory requirements, including requirements relating to manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion, distribution and recordkeeping. Even if regulatory approval of a product is granted, the approval may be subject to limitations on the uses for which the product may be marketed or the conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product, which could negatively affect us by reducing revenues or increasing expenses, and cause the approved product candidate not to be commercially viable. In addition, as clinical experience with a drug expands after approval, typically because it is used by a greater number and more diverse group of patients after approval than during clinical trials, side effects and other problems may be observed over time after approval that were not seen or anticipated during pre-approval clinical trials or other studies. Any adverse effects observed after the approval and marketing of a product candidate could result in limitations on the use of the approved product, withdrawal of FDA approval of the previously approved product, or voluntary withdrawal from the marketplace of the approved product. Absence of long-term safety data may also limit the approved uses of our products, if any. If we fail to comply with the regulatory requirements of the FDA, and other applicable U.S. and foreign regulatory authorities, or previously unknown problems with any approved commercial products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions or other setbacks, including the following:

- suspension or imposition of restrictions on operations, including costly new manufacturing requirements;
- refusal to approve pending applications or supplements to applications;
- suspension of any ongoing clinical trials;
- suspension or withdrawal of marketing approval;
- an injunction or imposition of civil or criminal penalties or monetary fines;
- seizure or detainment of products;
- banning or restriction of imports and exports;
- issuance of warning letters or untitled letters;

- suspension or imposition of restrictions on operations, including costly new manufacturing requirements; or
- refusal to approve pending applications or supplements to applications.

In addition, various aspects of our operations are subject to federal, state or local laws, rules and regulations, any of which may change from time to time. Costs arising out of any regulatory developments could be time-consuming and expensive and could divert management resources and attention and, consequently, could adversely affect our business operations and financial performance.

Delays in regulatory approval, limitations in regulatory approval and withdrawals of regulatory approval may have a material adverse effect on the Company. If we experience significant delays in testing or receiving approvals or sign-offs to conduct clinical trials, our product development costs will increase and our ability to out-license product candidates may be impeded.

If we obtain approval to commercialize aramchol outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If aramchol is approved for commercialization outside the United States, we will likely enter into agreements with third parties to commercialize aramchol outside the United States. We expect that we will be subject to additional risks related to entering into or maintaining international business relationships, including, without limitation:

- 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 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;
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters; and
- risks associated with clinical co-development agreements in other jurisdictions prior to or post-regulatory approval.

A failure to timely and effectively address the additional risks related to entering into or maintaining international business relationships could have a material adverse effect on our business, liquidity operating results and financial condition.

If we receive marketing approval for aramchol, sales will be limited unless the product achieves broad market acceptance.

The commercial success of aramchol and any other future product candidate for which we obtain marketing approval from the FDA, or other regulatory authorities, will depend on the breadth of its approved labeling and 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, without limitation:

- demonstration of clinical safety and efficacy compared to other products;
- ability of physicians to accurately diagnose NASH in its early stages;
- 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 other regulatory agencies, or agreed to by us as part of a mandatory or voluntary risk management plan;
- availability of alternative treatments, including, in the case of aramchol, a number of 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 aramchol 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 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 as reflected in the product's approved labeling. In particular, any labeling approved by FDA or other foreign regulatory agencies for aramchol necessarily limits its use for certain conditions in certain patient populations. Also, regulatory agencies may impose further requirements or restrictions on the distribution or use of aramchol 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 aramchol, physicians may nevertheless prescribe aramchol to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses or knowingly acquiesced in such off-label uses, we may become subject to significant liability. In particular, the U.S. 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.

We may be subject to extensive environmental, health and safety, and other laws and regulations in multiple jurisdictions.

Our business involves the controlled use, through our service providers, of hazardous materials, various biological compounds and chemicals, and as such, we, our agents and our service providers may be subject to various environmental, health and safety laws and regulations, including those governing air emissions, water and wastewater discharges, noise emissions, the use, management and disposal of hazardous, radioactive and biological materials and wastes and the cleanup of contaminated sites. The risk of accidental contamination or injury from these materials cannot be eliminated. If an accident, spill or release of any regulated chemicals or substances occurs, we could be held liable for resulting damages, including for investigation, remediation and monitoring of the contamination, including natural resource damages, the costs of which could be substantial. We may incur substantial capital costs and operating expenses and may be required to obtain consents to comply with any environmental and health laws or regulations and the terms and conditions of any permits required pursuant to such laws and regulations, including costs incurred by us to install new or updated pollution control equipment for our service providers, modify our operations or perform other corrective actions at our facilities or the facilities of our service providers. In addition, fines and penalties may be imposed on us, our agents and/or our service providers for noncompliance with environmental, health and safety and other laws and regulations or for the failure to have, or comply with the terms and conditions of, required environmental or other permits or consents.

We expect the healthcare industry to face increased limitations on reimbursement, rebates and other payments as a result of healthcare reform, which could adversely affect third-party coverage of our products and how much or under what circumstances healthcare providers will prescribe or administer our products.

In both the United States and other countries, sales of our products will depend in part upon the availability of reimbursement from third-party payors, which include governmental authorities, managed care organizations and other private health insurers. Third-party payors are increasingly challenging the price and examining the cost effectiveness of medical products and services.

Increasing expenditures for healthcare have been the subject of considerable public attention in the United States. Both private and government entities are seeking ways to reduce or contain healthcare costs. Numerous proposals that would effect changes in the U.S. healthcare system have been introduced or proposed in U.S. Congress, or Congress, and in some state legislatures, including reducing reimbursement for prescription products and reducing the levels at which consumers and healthcare providers are reimbursed for purchases of pharmaceutical products.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or Modernization Act, changed the way Medicare covers and pays for most pharmaceutical products in a number of ways. Medicare is the single largest third-party payment program and is administered by the Centers for Medicare & Medicaid Services, or CMS. Medicare traditionally covered prescription drugs administered by physicians. The Modernization Act introduced a new reimbursement methodology based on average sales prices for many of these drugs. The Modernization Act also established a new competitive acquisition program for the purchase of Part B drugs. This program, when fully implemented, will likely reduce the prices of these drugs. While the Medicare provisions of the Modernization Act apply only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from federal legislation or regulation may result in a similar reduction in payments from private payors.

Most notably, the Modernization Act also expanded coverage through a new Part D to include ordinary self-administered outpatient drugs. Medicare part D though operates through private insurers, and these insurers negotiate prices with pharmacies and with manufacturers. Intense negotiations can result in reduced revenues to manufacturers.

Increasing expenditures for healthcare have been the subject of considerable public attention in the United States. Both private and government entities are seeking ways to reduce or contain healthcare costs. Numerous proposals that would effect changes in the U.S. healthcare system have been introduced or proposed in U.S. Congress, or Congress, and in some state legislatures, including reducing reimbursement for prescription products and reducing the levels at which consumers and healthcare providers are reimbursed for purchases of pharmaceutical products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act and the Health Care and Education Affordability Reconciliation Act of 2010, or the Affordable Care Act, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers and impose additional health policy reforms. The Affordable Care Act expanded manufacturers' Medicaid rebate liability to include covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, increased the minimum rebate due for innovator drugs from 15.1% of average manufacturer price, or AMP, to 23.1% of AMP. The rebate on innovator drugs is the greater of 23.1% of the AMP per unit or the difference between the AMP and the best price per unit and adjusted by the Consumer Price Index-Urban (CPI-U) based on a launch date and current quarter AMP. The total rebate amount for innovator drugs is capped at 100.0% of AMP. The Affordable Care Act and subsequent legislation also narrowed the definition of AMP. Furthermore, the Affordable Care Act imposes a significant annual, nondeductible fee on companies that manufacture or import certain branded prescription drug products. Substantial new provisions affecting compliance were also been enacted, which may affect our business practices with healthcare practitioners. Although it is too early to determine the effect of the Affordable Care Act, it appears likely to continue to put pressure on pharmaceutical pricing, especially under the Medicare and Medicaid programs, and may also increase our regulatory burdens and operating costs.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. More recently, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of an amount greater than $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to healthcare providers of up to 2.0% per fiscal year, starting in 2013. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several categories of healthcare providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. If we ever obtain regulatory approval and commercialization of aramchol, these new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and accordingly, our financial operations. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of aramchol may be. Further, the Deficit Reduction Act of 2010, directed CMS to contract a vendor to determine "retail survey prices for covered outpatient drugs that represent a nationwide average of consumer purchase prices for such drugs, net of all discounts and rebates (to the extent any information with respect to such discounts and rebates is available)." This survey information can be used to determine the National Average Drug Acquisition Cost, or NADAC. Some states have indicated that they will reimburse based on the NADAC and this can result in further reductions in the prices paid for various outpatient drugs.

Although we cannot predict the full effect on our business of the implementation of existing legislation or the enactment of additional legislation pursuant to healthcare and other legislative reform, we believe that legislation or regulations that would reduce reimbursement for, or restrict coverage of, our products could adversely affect how much or under what circumstances healthcare providers will prescribe or administer our products. This could materially and adversely affect our business by reducing our ability to generate revenue, raise capital, obtain additional collaborators and market our products. In addition, we believe the increasing emphasis on managed care in the United States has and will continue to put pressure on the price and usage of pharmaceutical products, which may adversely impact product sales.

It will be difficult for us to profitably sell aramchol, if reimbursement for the product is limited by government authorities and third-party payor policies.

In addition to any healthcare reform measures which may affect reimbursement, market acceptance and sales of aramchol will depend on the reimbursement policies of government authorities and third-party payors. It will be difficult for us to profitably sell aramchol if reimbursement for the product is limited by government authorities or third-party payors. 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 coverage or reimbursement will be available for aramchol and, if coverage and reimbursement are available, the extent of coverage and the level of reimbursement. Reimbursement may affect 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 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 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 products 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 our future products. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our future products. If reimbursement is not available, or is available only to limited levels, we may not be able to commercialize our product candidate, or any future product candidates, profitably, or at all, even if approved. In addition, if physicians, government agencies and other third-party payors do not accept the use or efficacy of aramchol, we will not be able to generate significant revenue, if any.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the countries of the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

We are subject to federal anti-kickback laws and regulations. Our failure to comply with these laws and regulations could have adverse consequences to us.

There are extensive U.S. federal and state laws and regulations prohibiting fraud and abuse in the healthcare industry that can result in significant criminal and civil penalties. These federal laws include: The anti-kickback statute, which prohibits certain business practices and relationships, including the payment or receipt of remuneration for the referral of patients whose care will be paid by Medicare or other federal healthcare programs; the physician self-referral prohibition, commonly referred to as the Stark Law; the anti-inducement law, which prohibits providers from offering anything to a Medicare or Medicaid beneficiary to induce that beneficiary to use items or services covered by either program; the False Claims Act, which prohibits any person from knowingly presenting or causing to be presented false or fraudulent claims for payment by the federal government, including the Medicare and Medicaid programs; and the Civil Monetary Penalties Law, which authorizes the U.S. Department of Health and Human Services to impose civil penalties administratively for fraudulent or abusive acts. In addition, the Affordable Care Act requires drug manufacturers to report to the government any payments to physicians and certain hospitals for consulting services and the like.

Sanctions for violating these federal laws include criminal and civil penalties that range from punitive sanctions, damage assessments, monetary penalties, imprisonment, denial of Medicare and Medicaid payments or exclusion from the Medicare and Medicaid programs, or both, and debarment. As federal and state budget pressures continue, federal and state administrative agencies may also continue to escalate investigation and enforcement efforts to root out waste and to control fraud and abuse in governmental healthcare programs. Private enforcement of healthcare fraud has also increased, due in large part to amendments to the civil False Claims Act in 1986 and again in 2009 and 2010 that were designed to encourage private persons to sue on behalf of the government. A violation of any of these federal and state fraud and abuse laws and regulations could have a material adverse effect on our liquidity and financial condition. An investigation into the use by physicians of any of our products, once commercialized, may dissuade physicians from either purchasing or using them, and could have a material adverse effect on our ability to commercialize those products.

If we or our manufacturers fail to comply with manufacturing regulations, our financial results and financial condition could be adversely affected.

Before an NDA is approved, and before we begin the commercial manufacture of aramchol, contract 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 at all.

The FDA and foreign regulators require manufacturers to register manufacturing facilities. The FDA and foreign regulators also inspect these facilities to confirm compliance with requirements that the FDA or foreign regulators establish. We do not intend to engage in the manufacture of our products other than for preclinical and clinical studies, but we or our materials suppliers may face manufacturing or quality control problems causing product production and shipment delays or a situation where we or the supplier may not be able to maintain compliance with the FDA's or foreign regulators' requirements necessary to continue manufacturing our product candidate. Drug manufacturers are subject to ongoing periodic unannounced inspections by the FDA, the U.S. Drug Enforcement Agency, or DEA, and corresponding foreign regulators to ensure strict compliance with requirements and other governmental regulations and corresponding foreign standards. Any failure to comply with DEA, FDA or foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop and market our product candidate and any future product candidates.

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 could adversely affect our financial results and financial condition.

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

There are a number of products in development for NASH in patients who also suffer from obesity and insulin resistance, most of which are being developed by pharmaceutical companies that are far larger than us, with significantly greater resources and more experience than us. Further, our industry is highly competitive and subject to rapid and significant technological change. Our potential competitors include large, fully-integrated 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 aramchol or other product candidates. 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 aramchol. Key competitive factors affecting the commercial success of aramchol and any other product candidates that we develop 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. Accordingly, our competitors may be more successful than us 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 aramchol or any other product candidates 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 aramchol, or any other product candidate that we develop, non-competitive or obsolete. If we cannot successfully compete with new or existing products, our marketing and sales will suffer and we may never be profitable.

Our competitors currently include companies with marketed products and/or an advanced research and development pipeline. The majority of competitors in the liver disease therapeutic field include Intercept Pharmaceuticals, Inc., Genfit S.A. and Gilead Sciences, Inc. See also "Item 4. Information on the Company—Competition." Moreover, several companies have reported the commencement of research projects related to NASH, including those mentioned in the preceding sentence. However, we are not aware if such projects are ongoing or have been completed and, to the best of our knowledge, there is no approved drug currently on the market which is similar to aramchol, nor are we aware of any product candidate targeting NASH similar to aramchol with respect to chemical profile and mechanism of action.

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

Our products and product candidates could cause adverse events. These adverse events may not be observed in clinical trials, but may nonetheless occur in the future. If any of these adverse events occur, they may render our product candidates ineffective or harmful in some patients, and our sales would suffer, materially adversely affecting our business, financial conditions and results of operations.

In addition, potential adverse events caused by our product candidates, or products, could lead to product liability claims. Product liability claims might be brought against us by consumers, healthcare providers or others 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, among other things:

- decreased demand for aramchol 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 aramchol or any other product candidate for which we obtain marketing approval.

Although our clinical studies to date indicate that aramchol is safe and well-tolerated at single doses up to 900 mg, at doses up to 600mg administered once-daily for up to ten days and at doses up to 300 mg administered once-daily for up to three months, there were incidences of non-serious adverse events in four completed and fully analyzed clinical trials. Those four studies enrolled 168 patients.

In our Phase Ia clinical trial we enrolled 17 healthy volunteers. A total of 34 adverse events were reported in nine subjects. All adverse events were mild or moderate and transient and resolved without sequelae. There were no serious adverse events, deaths or other significant adverse events observed in this study.

In our Phase Ib placebo-controlled clinical trial with 25 healthy and mildly overweight male volunteers a total of 64 adverse events were reported by 80% of the patients. A higher proportion of patients reported drug-related adverse events in the placebo group (88.9%) compared to the 30 mg active group (55.6%) and the 300 mg active group (71.4%). All adverse events were mild or moderate and resolved without sequelae. There were no serious adverse events, deaths or other significant adverse events.

We completed a pharmacokinetic, or PK, and food effect study in 66 healthy male volunteers consisting of three parts. Overall, over the three parts of the study, the vast majority of adverse events were mild and unrelated to aramchol and all of the adverse events were transient and gave no indication of target organ toxicity. All doses of aramchol administered during the study were safe and well-tolerated. No serious adverse events or deaths occurred during the study. No clinically significant abnormalities related to any aramchol dose were noted in electrocardiograms, or ECGs, laboratory results, vital signs or physical examinations.

In our Phase IIa placebo-controlled trial with 60 patients with steatosis due to NAFLD or NASH, most adverse events were mild and transient, except for three (mild asthenia, mild nausea and moderate back pain), which were initially considered to be related to the study drug; however, after unblinding the study results it was found that the three adverse events occurred in the placebo group. There was one serious adverse event reported, acute appendicitis that was unrelated to study drug, which occurred in a patient taking the placebo. The patient fully recovered from the serious adverse event without sequelae and completed the study treatment. There were no deaths or other significant adverse events reported in this study.

If we are unable to obtain adequate insurance to protect our business and property against damage, and from any losses or claims from third parties, our financial condition could be adversely affected in the event of uninsured or inadequately insured loss or damage. We may not be able to obtain insurance policies on terms affordable to us that would adequately insure our business and property against damage, loss or claims by third parties. To the extent our business or property suffers any damages, losses or claims by third parties, which are not covered, or adequately covered, by insurance, our financial condition may be materially adversely affected.

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

We have obtained insurance coverage for our clinical trials in accordance with market standards and in compliance with applicable Israeli law. However, our insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly 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 aramchol, 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.

We manage our business through a small number of senior executive officers. We depend on them even more than similarly- situated companies.

Our future growth and success depends on our ability to recruit, retain, manage and motivate our senior executive officers. The loss of the services of our President and Chief Executive Officer, Chief Medical Officer, Dr. Maureen Graham and Dr. Antony Appleyard 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.

Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified senior executive officers with scientific and technical experience. In particular, the loss of one or more of our senior executive officers 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.

Additionally, our ability to effectively recruit and retain qualified officers and directors could also be adversely affected if we experience difficulty in obtaining adequate directors' and officers' liability insurance. We may be unable to maintain sufficient insurance as a public company to cover liability claims made against our officers and directors. If we are unable to adequately insure our officers and directors, we may not be able to retain or recruit qualified officers and directors to manage the Company.

Failure to build our finance infrastructure and improve our accounting systems and controls could impair our ability to comply with the financial reporting and internal control requirements for publicly traded companies.

As a public company, we will operate in an increasingly challenging regulatory environment which requires us to comply with the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and the related rules and regulations of the SEC and securities exchanges, expanded disclosures, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes-Oxley Act include establishing corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud. However, 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, or Section 404, until the date we are no longer an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, because we are taking advantage of the exemptions contained in the JOBS Act. We will remain an emerging growth company until, subject to certain conditions, the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of our initial public offering, (b) in which we have total annual gross revenue of at least $1.0 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our ordinary shares that is held by non-affiliates exceeds $700.0 million as of the prior June 30, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

To date, our independent public accountant has never conducted a review of our internal control for the purpose of providing the reports required by these rules. During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall.

To build our finance infrastructure, we will need to improve our accounting systems, disclosure policies, procedures and controls. If we are unsuccessful in building an appropriate accounting infrastructure, we may not be able to prepare and disclose, in a timely manner, our financial statements and other required disclosures, or comply with existing or new reporting requirements. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from the Nasdaq Capital Market or other adverse consequences that would materially harm our business. If we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed and investors could lose confidence in our reported financial information.

We will need to significantly increase the size of our organization, and we may experience difficulties in managing growth.

We may experience rapid and substantial growth in order to achieve our operating plans, which will place a strain on our human and capital resources. Successful implementation of our business plan will require management of growth, which will result in an increase in the level of responsibility for management personnel. We currently have a minimum number of employees and in order to continue the development and the commercialization of our products, we will need to substantially increase our operations, including expanding our employee base of managerial, operational and financial personnel. We currently intend to establish our infrastructure in the United States and therefore we may require additional funds. Any future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. To that end, we must be able to, among other things:

- manage our clinical trials and the regulatory process effectively;
- develop our administrative, accounting and management information systems and controls;
- hire and train additional qualified personnel; and
- integrate current and additional management, administrative, financial and sales and marketing personnel.

If we are unable to establish, scale-up and implement improvements to our control systems in an efficient or timely manner, or if we encounter deficiencies in existing systems and controls, investors may choose not to invest in us, which could cause our share price to decline and negatively impact our ability to successfully commercialize our product candidate and future product candidates.

Failure to attract and retain sufficient numbers of talented employees will further strain our human resources and could impede our growth or result in ineffective growth. If we are unable to manage our growth effectively, our losses could materially increase and it will have a material adverse effect on our business, results of operations and financial condition.

Our business, including our ability to raise capital, may be affected by macroeconomic conditions.

A deterioration in global economic conditions and uncertainties may have an adverse effect on our business. For instance, interest rates, the liquidity of the credit markets and the volatility of the capital markets could also affect the value of our investments, if any, and our ability to liquidate such investments in order to fund our operations. Interest rates and the ability to access credit markets could also adversely affect the ability of patients and distributors to purchase, pay for and effectively distribute our products.

Moreover, in past years, the U.S. and global economies have taken a downturn as the result of the deterioration in the credit markets and related financial crisis as well as a variety of other factors including, among other things, extreme volatility in security prices, diminished liquidity and credit availability, ratings downgrades of certain investments and declining valuations of others. The U.S. and certain foreign governments have recently taken actions in an attempt to address and rectify these extreme market and economic conditions by providing liquidity and stability to the financial markets. If the actions taken by these governments are not successful, the continued economic decline may cause a significant impact on our ability to raise capital, if needed, on a timely basis and on acceptable terms or at all. In addition, we rely and intend to rely on third-parties, including our clinical research organizations, third-party manufacturers and second source suppliers, and certain other important vendors and consultants. As a result of the current volatile and unpredictable global economic situation, there may be a disruption or delay in the performance of our third-party contractors and suppliers. If such third-parties are unable to satisfy their contractual commitments to us, our business could be severely adversely affected.

The Israeli Ministry of Health may not permit us to conduct multiple biopsies as contemplated in our ARREST Study of aramchol in Israel.

On March 9, 2015, we announced that we had begun the enrollment stage of our Phase IIb ARREST Study of aramchol in 240 biopsy-diagnosed NASH patients. While the primary endpoint of the study is a significant reduction of liver fat, as measured by magnetic resonance spectroscopy, or MRS, the main secondary endpoint of the ARREST Study is resolution of NASH on biopsies, which can be assessed only at the completion of the study and by repeated liver biopsies. We are conducting a portion of our ARREST Study in Israel. While, the Israeli Ministry of Health has granted us approval to conduct our ARREST Study in 14 centers in Israel, it has taken exception to the necessity of conducting a second biopsy at the end of the trial period, as specified by the trial protocol. As this position is inconsistent with the already established guidance by the FDA and the EMA, it was unexpected. We are not expecting that the Israeli Ministry of Health will reverse its preliminary position, and as such, we reconfigured our recruitment targets in Israel to include patients who have undergone liver biopsies no more than six months prior to enrolling in the ARREST Study. However, there is still a possibility of the Israeli Ministry of Health reversing its preliminary position as multiple parties unrelated to us, including leading Israeli hematologists and gastroenterologists, are conducting ongoing discussions with the Israeli Ministry of Health to attempt to convince it to reconsider its original position for a variety of reasons. Notwithstanding the foregoing, we will also continue a close dialogue with the Israeli Ministry of Health, especially after we obtain the interim results from the ARREST Study, to continuously assess the Israeli Ministry of Health's willingness to allow a second biopsy.

Contemporaneously, we also announced on March 9, 2015 that we had expanded our clinical activities to include patient recruitment for the ARREST Study in the United States. Professor Vlad Ratziu, from the University Pierre et Marie Curie in Paris, an internationally acclaimed key opinion leader, is the ARREST Study's global principal investigator, and Professor Rohit Loomba, from the University of California San Diego School of Medicine, is the ARREST Study's U.S.-based principal investigator. We expanded our patient recruitment into the United States because we believe that U.S.-based patient recruitment will shorten the recruitment time for our ARREST Study, especially considering the Israeli Ministry of Health's current position on the requirement of a second liver biopsy. We also believe that expanding our clinical activities into the United States will improve the ARREST Study's breadth and relevance, including potentially allowing us to immediately commence Phase III clinical trials in NASH in the United States without any addition clinical requirements, although there is no assurance.

Phase IIb clinical operations in the United States may divert a significant amount of Company resources and may ultimately be unsuccessful.

We are expanding our clinical operations for Phase IIb to the United States, which will require significant time, funds and Company resources. We believe that the United States has a larger population of potential patients from which we can recruit for our ARREST Study than Israel, and we believe that the FDA is more likely to accept our trial protocol, which requires repeated liver biopsies, than the Israeli Ministry of Health. In March 2015, we submitted to the FDA an update of our existing Investigational New Drug, or IND, filing, in order to initiate the ARREST Study in the United States. However, there is no assurance that the FDA will clear our updated IND request. Furthermore, even if the FDA clears our updated IND request, we may not have the time, funds or resources necessary to complete the ARREST Study in the United States. Moreover, even to the extent the ARREST Study is conducted, such study may ultimately prove to be unsuccessful.

Risks Related to Our Reliance on Third Parties

We have no manufacturing capacity and anticipate reliance on third-party manufacturers for our products.

We do not currently operate manufacturing facilities for the production of aramchol or its API. We still have not, and may never, develop facilities for the manufacture of product candidates or products for clinical trials or commercial purposes. We rely, and for the foreseeable future, will continue to rely, on third-party manufacturers to produce bulk drug products required for our clinical trials. We plan to initially rely upon contract manufacturers and, potentially, collaboration partners, to manufacture commercial quantities of our product candidates, if and when approved for marketing by the applicable regulatory authorities. Our contract manufacturers have not completed process validation for aramchol or the aramchol API manufacturing processes. If our contract manufacturers and their facilities, as applicable, are not approved by the FDA, or other applicable regulatory authorities, our commercial supply of the drug substance will be significantly delayed and may result in significant additional costs. We purchase finished aramchol from a third-party under a clinical supply agreement. If we need to identify an additional finished product manufacturer, we would not be able to do so without significant delay and likely significant additional cost.

Our contract manufacturer's failure to achieve and maintain high manufacturing standards, in accordance with applicable regulatory requirements, or the incidence of manufacturing errors, could result in patient injury or death, product shortages, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously harm our business. Contract manufacturers often encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel.

Our existing manufacturers and any future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business. In the event of a natural disaster, business failure, strike or other difficulty, we may be unable to replace a third-party manufacturer in a timely manner and the production of aramchol would be interrupted, resulting in delays and additional costs.

We intend to rely primarily on third parties to market and sell aramchol.

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

Although we may ultimately develop a marketing and sales force with technical expertise and supporting distribution capabilities in the longer term, we do not currently intend to do so and as such, we will be unable to market our product candidate directly in the near future. To promote any of our potential products through third parties, we will have to locate acceptable third parties for these functions and enter into agreements with them on acceptable terms, and we may not be able to do so. Any third-party arrangements we are able to enter into may result in lower revenues than we could achieve by directly marketing and selling our potential products. In addition, to the extent that we depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, as well as the terms of our agreements with such third parties, which cannot be predicted in most cases at this time. As a result, we might not be able to market and sell our products in the United States or overseas, which would have a material adverse effect on us.

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 intend to seek collaboration arrangements with pharmaceutical or biotechnology companies for the development and commercialization of our current and potential future product candidates. 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. 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. Moreover, collaborations with pharmaceutical or biotechnology companies and other third parties are often terminated or allowed to expire by the other party. Any lack of effort or ability by our collaborators or any such disagreement, termination or expiration could adversely affect us financially and could harm our business reputation.

We depend on third parties to conduct our clinical trials.

We rely on third parties, such as contract research organizations, medical institutions, clinical investigators and contract laboratories to oversee most of the operations of our clinical trials and to perform data collection and analysis. As a result, 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 aramchol 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

The failure to obtain or maintain patents, licensing agreements and other intellectual property rights that are sufficiently broad and protective could impact our ability to compete effectively.

To compete effectively, we must develop and maintain a proprietary position with regard to our own technologies, intellectual property, licensing agreements, product candidates and business. Legal standards relating to the validity and scope of claims in the biotechnology and biopharmaceutical fields are still evolving. We cannot predict the scope and extent of patent protection for aramchol because the patent positions of pharmaceutical products are complex and uncertain. Therefore, the degree of future protection for our proprietary rights in our core technologies and any product candidates or products that might be developed using these technologies is also uncertain. The risks and uncertainties that we face with respect to our patents and other proprietary rights include, but are not limited to, the following:

- while the patents we own have been issued, pending patent applications we have filed may not result in issued patents or may take longer than we expect to result in issued patents;
- we may be subject to interference or reexamination proceedings;
- we may be subject to opposition proceedings in foreign countries;
- any patents that are issued may not provide meaningful protection for any significant period of time, if at all;
- any issued patents may not be broad or strong enough to prevent competition from other products including identical or similar products;
- we may not be able to develop additional proprietary technologies that are patentable;
- 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 or pending patent applications existing in the patent landscape for aramchol that will affect our freedom to operate;
- other companies may challenge and invalidate patents licensed or issued to us or our customers;

- a court could determine that a competitor's technology or product does not infringe our patents;
- other companies may independently develop similar or alternative technologies, or duplicate our technologies;
- other companies may design around technologies we have licensed or developed;
- if we are not awarded patents or if issued patents expire or are declared invalid or not infringed, there may be no protections against competitors making generic equivalents;
- enforcement of patents is complex, uncertain and expensive, and our patents may be found invalid or enforceable;
- our patents 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 cannot be certain that patents will be issued as a result of any of our pending applications, and we cannot be certain that any of our issued patents, whether issued pursuant to our pending applications or licensed from third parties, will give us adequate protection from competing products. For example, issued patents may be circumvented or challenged, declared invalid or unenforceable, or narrowed in scope. In addition, because publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain that we were the first to make our inventions or to file patent applications covering those inventions. If any of our composition of matter patents, or pending applications, was subject to a successful challenge or failed to issue, our business and competitive advantage could be significantly affected. Our current patents will expire or they may otherwise cease to provide meaningful competitive advantage, and we may be unable to adequately develop new technologies and obtain future patent protection to preserve our competitive advantage or avoid adverse effects on our business.

The composition of matter patents pertaining to aramchol will expire on March 25, 2019 worldwide outside of Israel and on April 8, 2018 in Israel. We do not expect that we will be able to submit an NDA seeking approval of aramchol prior to the composition of matter patents' expiration date. However, because aramchol may be a new chemical entity, or NCE, following approval of an NDA, if we are the first applicant to obtain NDA approval, we may be entitled to five years of data and market exclusivity in the United States with respect to such NCE**.** Analogous data and market exclusivity provisions, of varying duration, may be available in Europe and other foreign jurisdictions. The Company also has rights under its pharmaceutical use issued patents with respect to aramchol, which provide patent exclusivity within the Company's field of activity until the last of such patents expires in 2030. While the Company believes that it may be able to protect its exclusivity in its field of activity through such use patent portfolio and such period of exclusivity, the lack of composition of matter patent protection may diminish the Company's ability to maintain a proprietary position for its intended uses of aramchol. Moreover, the Company cannot be certain that it will be the first applicant to obtain an FDA approval for any indication of aramchol and it cannot be certain that it will be entitled to NCE exclusivity. Such diminution of aramchol's proprietary position could have a material adverse effect on our business, results of operation and financial condition.

Others may obtain issued patents that could prevent us from commercializing our product candidates or require us to obtain licenses requiring the payment of significant fees or royalties in order to enable us to conduct our business. As to those patents that we have licensed, our rights depend on maintaining our obligations to the licensor under the applicable license agreement, and we may be unable to do so.

In addition to patents and patent applications, we depend upon trade secrets and proprietary know-how to protect our proprietary technology. We require our employees, consultants, advisors and collaborators to enter into confidentiality agreements that prohibit the disclosure of confidential information to any other parties. We also require our employees and consultants to disclose and assign to us their ideas, developments, discoveries and inventions. These agreements may not, however, provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure.

Our potential development of aramchol salts may not result in improved bioavailability compared to the existing form of aramchol. Furthermore, although we have submitted patent applications for our aramchol salts in development, there is no assurance that we will receive any patents for them, and even if we receive one or more patents for our aramchol salts in development, they may be of little or no commercial value.

As part of our ongoing pre-formulation studies, we have confirmed that several aramchol salts have improved solubility and intestinal permeability as compared to the existing form of aramchol. We have recently submitted new patent applications to protect such salts. In addition, we intend to plan and conduct further formulation development in order to test the possibility of using aramchol salts in future clinical studies. If we decide to develop the formulations of aramchol salts due to the improvement in solubility and bioavailability and longer patent protection, we may conduct an appropriate bioequivalence study, or studies of the biological equivalence of two proprietary preparations of a drug, prior to administering an aramchol salt formulation to patients in our clinical studies.

If we commence animal PK studies and formulation development in order to test the bioavailability of the aramchol salt compounds, the results might not support the claims sought by us. Success in our earlier pre-formulation studies does not ensure that later studies will be successful, and the results of later studies may not replicate the results of our prior pre-formation studies. Furthermore, either or both of the animal PK and formulation development studies may fail to demonstrate that the aramchol salts result in an improvement in solubility and bioavailability. Any such failure may cause us to abandon the aramchol salt compounds and may delay development of other product candidates. If the animal PK studies do not support our claims, the completion of development of such potential product candidates may be significantly delayed or abandoned, which will significantly impair our ability to generate revenues and will materially adversely affect our results of operations.

There can be no assurance that the U.S. Patent and Trademark Office, or the USPTO, will issue any patents based on the patent applications that we submitted to protect our aramchol salts, nor, should the USPTO issue any patents to us with respect to the aramchol salts, that we will be provided with adequate protection against potentially competitive products. Furthermore, if the USPTO issues us one or more patents for the aramchol salts, there can be no assurance that the issued patents will be of any commercial value, or that private parties or competitors will not successfully challenge these patents or circumvent these patents in the United States or abroad. In the absence of adequate patent protection, our business may be adversely affected by competitors who develop comparable technology or products.

We may not be able to enforce our intellectual property rights throughout the world. This risk is exacerbated for us because we expect aramchol will be manufactured and used in a number of foreign countries.

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 we expect aramchol will be manufactured and used in a number of foreign countries.

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 our other intellectual property rights. For example, several foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, some 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.

Although most jurisdictions in which the Company has applied for, intends to apply for, or has been issued patents have patent protection laws similar to those of the United States, some of them do not. For example, the Company expects to do business in South America, Eurasia, China and Indochina in the future and the countries in these regions may not provide the same or similar protection as that provided in the United States. Additionally, due to uncertainty in patent protection law, the Company has not filed applications in many countries where significant markets exist, including South American countries, Eurasian countries, African countries and Taiwan.

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 be unable to protect the intellectual property rights of the third parties from whom we may license certain of our intellectual property or with whom we have entered into other strategic relationships, which could have a material adverse effect on our business, results of operations and financial condition.

Certain of our intellectual property rights may be licensed from third parties, including universities and/or strategic partners. Such third parties may determine not to or fail to protect the intellectual property rights that we license from them and we may be unable to defend such intellectual property rights on our own or we may have to undertake costly litigation to defend the intellectual property rights of such third parties. There can be no assurances that we will continue to have proprietary rights to any of the intellectual property that we license from such third parties or otherwise have the right to use through similar strategic relationships. Any loss or limitations on use with respect to such intellectual property licensed from third parties or otherwise obtained from third parties with whom we have entered into strategic relationships could have a material adverse effect on our business, results of operations and financial condition.

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 product candidates or products unless we obtained a license under the applicable patents, or until the patents expire. In addition to litigation proceedings which may be filed against us, 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.

We may be unable to adequately prevent disclosure and unauthorized use of trade secrets and other proprietary information by third parties.

Our ability to obtain and maintain patent protection and trade secret protection for our intellectual property and proprietary technologies, our products and their uses is important to our commercial success. We rely on a combination of patent, copyright, trademark and trade secret laws, non-disclosure and confidentiality agreements, licenses, assignment of inventions agreements and other restrictions on disclosure and use to protect our intellectual property rights.

We also 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 product candidates or products or cause additional material adverse effects upon our competitive business position.

We cannot be certain that the steps that we have taken will prevent the misappropriation or other violation of our confidential information and other intellectual property, particularly in foreign countries in which laws may not protect our proprietary rights as fully as in the United States and other developed economies. Moreover, if we lose any key personnel, we may not be able to prevent the unauthorized disclosure or use of our technical knowledge or other trade secrets by those former employees. If we are unable to maintain the security of our proprietary technology, this could materially adversely affect our competitive advantage, business and results of operations.

Under applicable U.S. and Israeli law, 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. In addition, employees may be entitled to seek compensation for their inventions irrespective of their agreements with us, which in turn could impact our future profitability.

We generally enter into non-competition agreements with our employees and certain key consultants, or our employment and consulting agreements contain non-competition provisions. These agreements, to the extent they are in place and in effect, 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.

In addition, Chapter 8 to the Israeli Patents Law, 5727-1967, or the Patents Law, deals with inventions made in the course of an employee's service and during his or her term of employment, whether or not the invention is patentable, or service inventions. Section 134 of the Patents Law provides that if there is no agreement that explicitly determines whether the employee is entitled to compensation for the service inventions and the extent and terms of such compensation, such determination will be made by the Compensation and Rewards Committee, a statutory committee of the Israeli Patents Office. Although our employees have agreed to assign to us service invention rights, we may face claims demanding remuneration in consideration for assigned inventions. Recent decisions by the Compensation and Rewards Committee and Israeli courts have created some uncertainty in this area, as it was held that employees may be entitled to remuneration for their service inventions despite having specifically waived any such rights. As a consequence of such claims, we could be required to pay additional remuneration or royalties to our current and/or former employees, or be forced to litigate such claims, which could negatively affect our business.

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

We may be required 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 and who claim that their rights are infringed by aramchol or any of our 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.

A third-party may claim that we are using inventions claimed by their patents and may go to court to stop us from engaging in our normal operations and activities, such as research, development and the sale of any future products. Such lawsuits are expensive and would consume time and other resources. There is a risk that such court will decide that we are infringing the third-party's patents and will order us to stop the activities claimed by the patents, redesign our products or processes to avoid infringement or obtain licenses, which may not be available on commercially reasonable terms. In addition, there is a risk that a court will order us to pay the other party damages for infringement.

Moreover, there is no guarantee that any prevailing patent owner would offer us a license so that we could continue to engage in activities claimed by the patent, or that such a license, if made available to us, could be acquired on commercially acceptable terms. In addition, third parties may, in the future, assert other intellectual property infringement claims against us with respect to our product candidates, technologies or other matters.

In addition, our patents and patent applications 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 patents 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 patent law could diminish the value of patents 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 particular, the United States has recently enacted, and is currently implementing, wide-ranging patent reform legislation. The United States Supreme Court has ruled on several patent cases in recent years, and could do so again in the future, 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 applicable courts and legislatures in the countries in which we may pursue patent protection, including those of the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents and the interpretations of such laws 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, documentary, 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 USPTO 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.

Risks Related to Ownership of Our Ordinary Shares

The market price of our ordinary shares is volatile and you may sustain a complete loss of your investment.

Since our initial public offering, the trading price of our ordinary shares has been volatile and is likely to continue to be volatile. In addition, the trading volume is and has been volatile and sometimes relatively illiquid. The following factors, some of which are beyond our control, in addition to other risk factors described in this section, may have a significant impact on the market price and trading volume of our ordinary shares:

- inability to obtain the approvals necessary to commence further clinical trials;
- delays in existing clinical trials due to an inability to enroll patients at the expected pace, among other factors;
- unsatisfactory or inconclusive 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 aramchol;
- any adverse changes to our relationship with manufacturers or suppliers;
- any product liability actions or 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 our Board, management or other key personnel;
- legislation in the United States, Europe and other foreign countries relating to the sale or pricing of pharmaceuticals;
- announcements by us of significant strategic partnerships, out-licensing, in-licensing, joint ventures, acquisitions or capital commitments;
- expiration or terminations of licenses, research contracts or other collaboration agreements;
- public concern as to the safety of drugs we, our licensees or others develop;
- success of research and development projects;
- variations in our and our competitors' results of operations;
- changes in earnings estimates or recommendations by securities analysts, if our ordinary shares are covered by analysts;
- developments by our licensees, if any; and
- future issuances of ordinary shares or other securities.

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

In addition, the stock market in general, and the Nasdaq Capital Market and the market for biotechnology companies 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. Price volatility of our ordinary shares might be worse if the trading volume of our ordinary shares is low. Following periods of market volatility, shareholders may institute securities class action litigation. If we were involved in securities litigation, it could have a substantial cost and divert resources and attention of management from our business, even if we are successful. Future sales of our ordinary shares could also reduce the market price of such stock. Any adverse determination in litigation could also subject us to significant liabilities.

Moreover, the liquidity of our ordinary shares is limited, not only in terms of the number of shares that can be bought and sold at a given price, but by delays in the timing of transactions and reduction in security analysts' and the media's coverage of us, if any. These factors may result in lower prices for our ordinary shares than might otherwise be obtained and could also result in a larger spread between the bid and ask prices for our ordinary shares. In addition, without a large float, our ordinary shares are less liquid than the stock of companies with broader public ownership and, as a result, the trading prices of our ordinary shares are more volatile. In the absence of an active public trading market, an investor may be unable to liquidate its investment in our ordinary shares. Trading of a relatively small volume of our ordinary shares may have a greater impact on the trading price of our stock than would be the case if our public float were larger. We cannot predict the prices at which our ordinary shares will trade in the future.

Our principal shareholders, President and Chief Executive Officer and directors currently own approximately 39.7% of our outstanding ordinary shares on a fully diluted basis. They will therefore be able to exert significant control over matters submitted to our shareholders for approval.

Our President and Chief Executive Officer, directors and shareholders that own more than 5% of our outstanding ordinary shares own approximately 39.7% of our ordinary shares on a fully diluted basis. As a result, these shareholders, if they acted together, could significantly influence or even unilaterally approve matters requiring approval by our shareholders, including the election of directors and the approval of mergers or other business combination transactions. The interests of these shareholders may not always coincide with our interests or the interests of other shareholders. This significant concentration of share ownership may adversely affect the trading price for our ordinary shares because investors often perceive disadvantages in owning stock in companies with controlling shareholders.

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. Prior to the consummation of our initial public offering and in accordance with the terms of the Tax Pre-Ruling, the holders of substantially all of our then-outstanding ordinary shares and options agreed, not to sell or dispose of our ordinary shares for a period of two years following the consummation of the Reorganization, subject to certain exceptions. Substantially all of our outstanding shares will become eligible for unrestricted sale upon expiration of such lockup period. In addition, shares issued or issuable upon exercise of options and warrants vested as of the expiration of the lock-up period will be eligible for sale at that time. Sales of shares by these shareholders could have a material adverse effect on the trading price of our ordinary shares.

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

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

Our U.S. shareholders may suffer adverse tax consequences due to our classification as a passive foreign investment company, or PFIC.

Generally, if for any taxable year 75% or more of our gross income is passive income, or at least 50% of our assets are held for the production of, or produce, passive income, we would be characterized as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes. Based upon our review of our financial data, we have determined that we are currently a PFIC, and we likely will continue to be a PFIC, at least until we develop a source of significant operating revenues. If we were to be characterized as a PFIC for U.S. federal income tax purposes in any taxable year during which a U.S. Holder, as defined in "Item 10. Additional Information—E. Taxation— Certain U.S. Federal Income Tax Considerations," owns ordinary shares, such U.S. Holder could face adverse U.S. federal income tax consequences. For example, such U.S. Holder could be liable to additional taxes and interest charges upon certain distributions by us and any gain recognized on a sale, exchange or other disposition of our shares, whether or not we continue to be characterized as a PFIC. One way in which certain of the adverse consequences of PFIC status can be mitigated is for a U.S. Holder to make an election to treat us as a qualified electing fund, or QEF. A shareholder making the QEF election is required for each taxable year to include in income a pro rata share of the ordinary earnings and net capital gain of the QEF, subject to a separate election to defer payment of taxes, which deferral is subject to an interest charge. An election to treat us as a QEF will not be available if we do not provide the information necessary to make such an election. It is not expected that a U.S. Holder will be able to make a QEF election because we do not intend to provide U.S. Holders with the information necessary to make a QEF election. See also "Item 10. Additional Information—E. Taxation— Certain U.S. Federal Income Tax Considerations."

If we are unable to satisfy the requirements of Section 404 as they apply to a foreign private issuer and emerging growth company, or our internal controls over financial reporting are not effective, the reliability of our financial statements may be questioned and our share price may suffer.

We became subject to the requirements of the Sarbanes-Oxley Act when our ordinary shares were listed on the Nasdaq Capital Market. Section 404 requires companies subject to the reporting requirements of the U.S. securities laws to do a comprehensive evaluation of its and its subsidiaries' internal controls over financial reporting. To comply with this statute, we will be required to document and test our internal control procedures and our management will be required to assess and issue a report concerning our internal controls over financial reporting. Pursuant to the JOBS Act, we will be classified as an "emerging growth company." Under the JOBS Act, emerging growth companies are exempt from certain reporting requirements, including the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act. Under this exemption, our auditor will not be required to attest to and report on management's assessment of our internal controls over financial reporting during a five year transition period. We will need to prepare for compliance with Section 404 by strengthening, assessing and testing our system of internal controls to provide the basis for our report. However, the continuous process of strengthening our internal controls and complying with Section 404 is complicated and time-consuming. Furthermore, as our business continues to grow both domestically and internationally, our internal controls will become more complex and will require significantly more resources and attention to ensure our internal controls remain effective overall. During the course of its testing, our management may identify material weaknesses or significant deficiencies, which may not be remedied in a timely manner to meet the deadline imposed by the Sarbanes-Oxley Act. If our management cannot favorably assess the effectiveness of our internal controls over financial reporting, or our independent registered public accounting firm identifies material weaknesses in our internal controls, investor confidence in our financial results may weaken, and the market price of our securities may suffer. Nevertheless, as a foreign private issuer that is an emerging growth company, we are not be required to comply with the auditor attestation requirements of Section 404 for up to five fiscal years after the date of our initial public offering. See "Item 5. Operating and Financial Review and Prospects—Jumpstart Our Business Startups Act of 2012" for more detail regarding our status as an emerging growth company.

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 be negatively impacted.

The trading market for our ordinary shares is influenced by the research and reports that industry or securities analysts may publish about us, our business, our market or our competitors. We do not have any control over these analysts and we cannot provide any assurance that analysts will cover us or provide favorable coverage. If any of the analysts who may cover us adversely change their recommendation regarding our 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 negatively impact our share price or trading volume.

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, as amended, or the Companies Law, imposes certain restrictions on our ability to declare and pay dividends. See "Item 8. Financial Information—Consolidated Financial Statements and Other Financial Information—Dividend Policy" 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 Securities Exchange Act of 1934, or the Exchange Act, the Sarbanes-Oxley Act, the listing requirements of the Nasdaq Capital Market, on which our ordinary shares are traded, 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 Capital Market may also impose various additional requirements on public companies. As a result, we incurred and will continue to incur additional legal, accounting and other expenses that we did not incur as a privately-held company, particularly after we are no longer an "emerging growth company" as defined in the JOBS Act. Further, the need to establish the corporate infrastructure demanded of a public company may divert management's attention from implementing our development plans. We have made and will continue to make changes to our corporate governance standards, compensation policy, disclosure controls and financial reporting and accounting systems to meet our reporting obligations and applicable law. The measures we take, however, may not be sufficient to satisfy our obligations as a public company, which could subject us to delisting of our ordinary shares, fines, sanctions and other regulatory action and potentially civil litigation.

The JOBS Act 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;
- the "say on pay" provisions of the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, or the Dodd-Frank Act, requiring a non-binding shareholder vote to approve compensation of certain executive officers, and the Dodd-Frank Act's "say on golden parachute" provisions requiring a non-binding shareholder vote to approve golden parachute arrangements for certain executive officers in connection with mergers and certain other business combinations and some of the disclosure requirements of the Dodd-Frank Act relating to compensation of our President and Chief Executive Officer;
- any rules that may be adopted by the Public Company Accounting Oversight Board, or the PCAOB, requiring mandatory audit firm rotation or a supplement to the auditor's report on the financial statements; and
- our ability to furnish two rather than three years of income statements and statements of cash flows in various required filings.

We 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 become more volatile and decline.

As a "foreign private issuer," we are permitted to and currently do follow certain home country corporate governance practices instead of otherwise applicable SEC and Nasdaq Capital Market 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 to, and currently do, follow certain home country corporate governance practices instead of those otherwise required under the Listing Rules of the Nasdaq Capital Market for domestic U.S. issuers. For instance, we currently follow home country practice in Israel with regard to, among other things, director nomination procedures, quorum requirements and approval of compensation of officers. In addition, we may follow our home country law instead of the Listing Rules of the Nasdaq Capital 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 the Nasdaq Capital Market may provide less protection to you than what is accorded to investors under the Listing Rules of the Nasdaq Capital Market applicable to domestic U.S. issuers. See "Item 16G. Corporate Governance."

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 certain individual executive compensation information, 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. Furthermore, as a "foreign private issuer," we are also not subject to the requirements of Regulation FD (Fair Disclosure) promulgated under the Exchange Act. These exemptions and leniencies reduce the frequency and scope of information and protections to which you are entitled as an investor.

Because our ordinary shares may be a "penny stock," it may be more difficult for investors to sell their ordinary shares, and the market price of our ordinary shares may be adversely affected.

Our ordinary shares may be a "penny stock" if, among other things, the stock price is below $5.00 per share, it is not listed on a national securities exchange or we have not met certain net tangible asset or average revenue requirements. Broker-dealers who sell penny stocks must provide purchasers of these stocks with a standardized risk-disclosure document prepared by the SEC. This document provides information about penny stocks and the nature and level of risks involved in investing in the penny-stock market. A broker must also give a purchaser, orally or in writing, bid and offer quotations and information regarding broker and salesperson compensation, make a written determination that the penny stock is a suitable investment for the purchaser, and obtain the purchaser's written agreement to the purchase. Broker-dealers must also provide customers that hold penny stock in their accounts with such broker-dealer a monthly statement containing price and market information relating to the penny stock. If a penny stock is sold to an investor in violation of the penny stock rules, the investor may be able to cancel its purchase and get its money back.

If applicable, the penny stock rules may make it difficult for investors to sell their ordinary shares. Because of the rules and restrictions applicable to a penny stock, there is less trading in penny stocks and the market price of our ordinary shares may be adversely affected. Also, many brokers choose not to participate in penny stock transactions. Accordingly, investors may not always be able to resell their ordinary shares publicly at times and prices that they feel are appropriate and the market price of our ordinary shares may be adversely affected.

Our ordinary shares are listed on the Nasdaq Capital Market. As such, we must meet the Nasdaq Capital Market's continued listing requirements and other Nasdaq rules, or we may risk delisting. Delisting could negatively affect the price of our ordinary shares, which could make it more difficult for us to sell securities in a financing and for you to sell your ordinary shares.

Our ordinary shares are listed on the Nasdaq Capital Market. As such, we are required to meet the continued listing requirements of the Nasdaq Capital Market and other Nasdaq rules, including those regarding director independence and independent committee requirements, minimum stockholders' equity, minimum share price and certain other corporate governance requirements. In particular, we are required to maintain a minimum bid price for our listed ordinary shares of $1.00 per share. If we do not meet these continued listing requirements, our ordinary shares could be delisted. Delisting of our ordinary shares from the Nasdaq Capital Market would cause us to pursue eligibility for trading on other markets or exchanges, or on the pink sheets. In such case, our shareholders' ability to trade, or obtain quotations of the market value of, our ordinary shares would be severely limited because of lower trading volumes and transaction delays. These factors could contribute to lower prices and larger spreads in the bid and ask prices for our securities. There can be no assurance that our ordinary shares, if delisted from the Nasdaq Capital Market in the future, would be listed on a national securities exchange, a national quotation service, the Over-The-Counter Markets or the pink sheets. Delisting from the Nasdaq Capital Market, or even the issuance of a notice of potential delisting, would also result in negative publicity, make it more difficult for us to raise additional capital, adversely affect the market liquidity of our ordinary shares, reduce security analysts' coverage of us and diminish investor, supplier and employee confidence. In addition, as a consequence of any such delisting, our share price could be negatively affected and our shareholders would likely find it more difficult to sell, or to obtain accurate quotations as to the prices of, our ordinary shares.

Risks Related to Israeli Law and Our Operations in Israel

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

Our executive offices are located in Tel-Aviv, Israel. In addition, the majority of our officers and directors are residents of Israel. Accordingly, political, economic and military conditions in Israel may directly affect our business. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its neighboring countries. Any hostilities involving Israel or the interruption or curtailment of trade between Israel and its trading partners could adversely affect our operations and results of operations. During the winter of 2008-2009, the autumn of 2012 and the summer of 2014, Israel was engaged in armed conflicts with Hamas, a militia group and political party operating in the Gaza Strip. The last conflict, as well as the previous round of escalation, involved missile strikes against civilian targets in various parts of Israel, including areas in which our employees, service providers and some of our consultants are located. During the summer of 2006, Israel was also engaged in armed conflicts with Hezbollah, a Lebanese Islamist Shiite militia group and political party, which also involved missile strikes against civilian targets in the northern part of Israel. The continuation of such strikes may negatively affect business conditions in Israel.

Since February 2011, riots and uprisings in several countries in the Middle East and neighboring regions have led to severe political instability in several neighboring states and to a decline in the regional security situation. Such instability may affect the local and global economy, could negatively affect business conditions and, therefore, could adversely affect our operations. To date, these matters have not had any material effect on our business and results of operations; however, the regional security situation and worldwide perceptions of it are outside our control, and there can be no assurance that these matters will not negatively affect us in the future. In addition, the political and security situation in Israel may result in parties with whom we have agreements involving performance in Israel claiming that they are not obligated to perform their commitments under those agreements pursuant to force majeure provisions in such agreements.

Our commercial insurance does not cover losses that may occur as a result of an event associated with the security situation in the Middle East. Although the Israeli government is currently committed to covering the reinstatement value of direct damages that are caused by terrorist attacks or acts of war, we cannot assure you that this government coverage will be maintained, or if maintained, will be sufficient to compensate us fully for damages incurred. Any losses or damages incurred by us could have a material adverse effect on our business. 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 subjects of 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 condition or the expansion of our business.

Our operations may be disrupted as a result of the obligation of Israeli citizens to perform military service.

Many Israeli citizens are obligated to perform several days, and in some cases more, of annual military reserve duty until they reach the age of 40 (or older, for reservists who are officers or who have certain occupations) and, in the event of a military conflict, may be called to active duty. In response to increases in terrorist activity, there have been periods of significant call-ups of military reservists. It is possible that there will be military reserve duty call-ups in the future. Our operations could be disrupted by such call- ups, which may include the call-up of our employees or the employees of our Israeli business partners. Such disruption could materially adversely affect our business, financial condition and results of operations.

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

Our functional currency is the U.S. dollar. We incur expenses in U.S. dollars, Euros and New Israeli Shekels, or NIS. As a result, we are exposed to the risks that the Euro and the NIS may appreciate relative to the U.S. dollar, or, if either the Euro and the NIS devalue relative to the U.S. dollar, that the inflation rate in the EU and in Israel may exceed such rate of devaluation of the Euro and the NIS, or that the timing of such devaluation may lag behind inflation in the EU and in Israel. In any such event, the U.S. dollar cost of our operations in the EU and in Israel would increase and our U.S. dollar-denominated results of operations would be adversely affected. The average exchange rate for the year ended December 31, 2014 was $1.00 = Euro 0.83 and $1.00 = NIS 3.89. We cannot predict any future trends in the rate of inflation in the EU and in Israel or the rate of devaluation, if any, of either the Euro or the NIS against the U.S. dollar. As of the date hereof, neither the inflation rate in the EU nor in Israel has exceeded the rate of devaluation of the Euro or the NIS, respectively, during the calendar years 2012, 2013 or 2014.

The Tax Pre-Ruling imposes restrictions and limitations that may adversely affect our ability to raise funds by selling our ordinary shares and our ability to commercialize our product candidate.

The Tax Pre-Ruling we obtained from the Israeli Tax Authority in connection with the Reorganization includes certain restrictions and limitations. Under the Tax Pre-Ruling, during the two year period following the consummation of the Reorganization, which ends in February 2016, or the Restriction Period, we may not sell or otherwise dispose of our intellectual property, other than in the ordinary course of business, which may prevent us from completing collaboration arrangements with pharmaceutical or biotechnology companies necessary for the commercialization of our product candidate.

Pursuant to the Tax Pre-Ruling, at any time following our initial public offering and until the end of the Restriction Period, we may not issue more than 49% of our share capital in a public or private offering, including the shares sold in our initial public offering. Such restrictions and limitations may limit our ability to raise funds by selling and issuing our ordinary shares, which in turn could delay the development and commercialization of our product candidate or could force us to cease our operations.

In addition, pursuant to the Tax Pre-Ruling, our shareholders and optionholders as of immediately after the consummation of the Reorganization may not sell or otherwise transfer or dispose of more than 10% of their respective shares and options, subject to a certain exemptions. Substantially all of such shareholders and option holders agreed, in accordance with the terms of the Tax Pre-Ruling, not to sell or dispose of our ordinary shares for a period of two years following the consummation of the Reorganization.

If during the Restriction Period, we or our shareholders or optionholders who held rights immediately after the consummation of the Reorganization, or the Rights Holders, violate one or more of the restrictions described under "Item 10. Additional Information—E. Taxation—Certain Israeli Tax Considerations—Pre-Ruling Regarding a Reorganization of Our Corporate Structure" below, or a Violation, the transfer of shares and assets in connection with the Reorganization will become subject to taxation based on the greater of the transferred assets' fair market value on the day of such Violation or taxes that, but for the Tax Pre-Ruling, would be payable in connection with the transfer of such assets and shares plus Israeli consumer price index linkage differentials and interest from the day of the actual transfer of such assets and shares until the day of payment of such taxes, unless the Israeli Tax Authority is satisfied that such Violation was a result of special circumstances beyond our control.

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

Israeli corporate law regulates mergers, requires tender offers for acquisitions of shares above specified thresholds, requires special approvals for transactions involving directors, officers or significant shareholders and regulates other matters that may be relevant to such types of transactions. For example, a merger may not be consummated unless at least 50 days have passed from the date on which a merger proposal is filed by each merging company with the Israel Registrar of Companies and at least 30 days have passed from the date on which the shareholders of both merging companies have approved the merger. In addition, a majority of each class of securities of the target company must approve a merger. Moreover, a tender offer for all of a company's issued and outstanding shares can only be completed if the acquirer receives positive responses from the holders of at least 95% of the issued share capital. Completion of the tender offer also requires approval of a majority of the offerees that do not have a personal interest in the tender offer, unless, following consummation of the tender offer, the acquirer would hold at least 98% of the Company's outstanding shares. Furthermore, the shareholders, including those who indicated their acceptance of the tender offer, may, at any time within six months following the completion of the tender offer, 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. Additional Information—E. Taxation—Certain Israeli Tax Considerations" for additional information.

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

- no cumulative voting in the election of directors, which limits the ability of minority shareholders to elect director candidates; and
- the exclusive right of our Board to elect a director to fill a vacancy created by the expansion of the Board or the resignation, death or removal of a director, which prevents shareholders from being able to fill vacancies on our Board.

Provisions of the Companies Law and anti-takeover provisions in our Articles could make it difficult for our shareholders to replace or remove our current Board and could have the effect of discouraging, delaying or preventing a merger or acquisition, which could adversely affect the market price of our ordinary shares.

Under the Companies Law, as amended, a merger is generally required to be approved by the shareholders and board of directors of each of the merging companies. Unless an Israeli court determines differently, a merger will not be approved if it is objected to by shareholders holding a majority of the voting rights participating and voting at the meeting, after excluding the shares held by the other party to the merger, by any person who holds 25% or more of the other party to the merger or by anyone on their behalf, including by the relatives of or corporations controlled by these persons. In addition, upon the request of a creditor of either party to the proposed merger, an Israeli 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 any of the parties to the merger. Further, a merger generally may not be completed until the passage of certain time periods. In addition, subject to certain exceptions, an acquisition of shares in a public company must be made by means of a tender offer to the extent that as a result of such acquisition the acquirer will hold 25% or more of the voting rights in the company if there is no other holder of 25% or more of the company's voting rights, or hold 45% or more of the voting rights in the company if there is no other holder of 45% or more of the company's voting rights. In addition, Israeli tax law treats some acquisitions, including stock-for-stock swaps between an Israeli company and a foreign company, less favorably than U.S. tax law. Israeli tax law may, for instance, subject a shareholder who exchanges ordinary shares for shares in a non-Israeli corporation to immediate taxation.

Certain provisions of our Articles may have the effect of rendering more difficult or discouraging an acquisition of the Company deemed undesirable by the Board. Those provisions include:

- limiting the ability of our shareholders to convene general meetings of the Company;
- controlling procedures for the conduct of shareholder and our Board meetings, including quorum and voting requirements; and
- the election and removal of directors.

Moreover, the classification of our Board into three classes with terms of approximately three years each, which was approved by shareholders of the Company, the requirement of affirmative vote of at least 75% of the voting rights represented personally or by proxy and voting thereon at a general meeting in order to amend or replace our Articles and the requirement under the Companies Law to have at least two external directors who cannot readily be removed from office, together with the other provisions of the Articles and Israeli law, could deter or delay potential future merger, acquisition, tender or takeover offers, proxy contests or changes in control or management of the Company, some of which could be deemed by certain shareholders to be in their best interests and which could affect the price some investors are willing to pay for our ordinary shares.

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

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

Your rights, liabilities and responsibilities as a shareholder will be governed by Israeli law and differ in some material respects from those under U.S. law.

Because we are an Israeli company, the rights and responsibilities of our shareholders are governed by the Articles and Israeli law. These rights, liabilities and responsibilities differ in some material respects from the rights, liabilities and responsibilities of shareholders in a U.S. corporation. In particular, a shareholder of an Israeli company has a duty to act in good faith towards the company and other shareholders and to refrain from abusing his, her or its power in the company, including, among other things, in voting at the general meeting of shareholders on certain matters. Israeli law provides that these duties are applicable to shareholder votes on, among other things, amendments to a company's articles of association, increases in a company's authorized share capital, mergers and interested party transactions requiring shareholder approval. In addition, a controlling shareholder, a shareholder who knows that it possesses the power to determine the outcome of a shareholders' vote or a shareholder who has the power to appoint or prevent the appointment of a director or executive officer in the company, has a duty of fairness towards the company. However, Israeli law does not define the substance of this duty of fairness. Because Israeli corporate law has undergone extensive revisions in recent years, there is little case law available to assist in understanding the implications of these provisions that govern shareholder behavior. See Item 10.—B Memorandum and Articles of Association—Shareholder Duties" for additional information. 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.

Any of the risk factors referred to above could significantly and negatively affect our business, results of operations or financial condition, which may reduce our ability to pay dividends and lower the trading price of our ordinary shares. The risks referred to above are not the only ones that may exist. Additional risks not currently known by us or that we deem immaterial may also impair our business operations.

ITEM 4. Information on the Company.

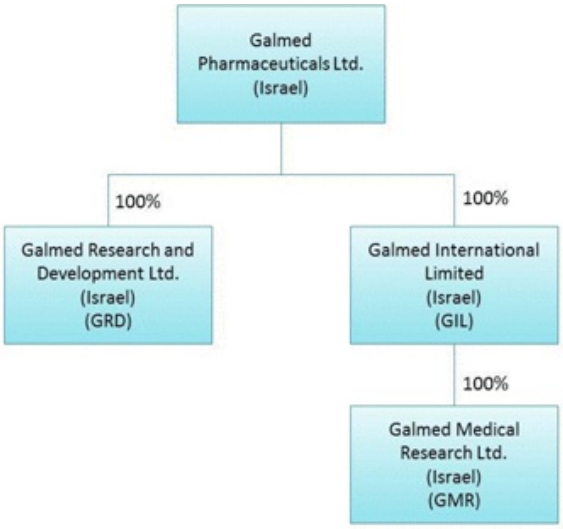
Historical Background and Corporate Structure

Our Company, Galmed Pharmaceuticals Ltd., was incorporated in Israel on July 31, 2013 as a privately held company. However, our business has been operating since 2000 under a different group of companies established in the same year, or the Group. Originally, we operated under the parent company, GHI. GHI held all of the equity rights in and to GTTI. GTTI held all of the equity rights in and to GIL (other than one share held by GRD). GIL held all of the equity rights in and to GMR. Our intellectual property was held by GIL. The research and development was conducted by GMR as a service to GIL on a cost plus basis. GIL was responsible for all product development.

On February 2, 2014, we underwent the Reorganization, pursuant to which all of our current business (including our intellectual property) was transferred to us. The Group was reorganized by share transfers and asset transfers, resulting in the Company as the parent company and 100% equity-owner of the following companies: (1) GRD, which holds all the Group's intellectual property, including the Company's patent portfolio; (2) GIL, which may provide research and development services to GRD on a cost plus basis; and (3) GTTI, which is an inactive company that we expect to liquidate at or following the end of 2015. GIL holds GMR, which became an inactive company in 2014. The Reorganization was conducted in order to simplify our capital structure, reduce our operating cost and to improve our ability to raise funds. Immediately prior to the Reorganization, all our shareholders collectively held 9,739 ordinary shares of GHI. In connection with the Reorganization, and in accordance with the Tax Pre-Ruling, we issued to all such shareholders ordinary shares of the Company, such that upon the Reorganization all our shareholders collectively held 7,099,731 ordinary shares of the Company, in the same proportion among all shareholders, which reflected a ratio of 729 ordinary shares of the Company for each ordinary share of GHI.

In connection with the Reorganization, we obtained the Tax Pre-Ruling, which includes certain restrictions and limitations, including with respect to the transfer of our intellectual property and our ordinary shares and options during a two year period following the completion of our initial public offering, as more fully described in "Item 10. Additional Information—E. Taxation—Certain Israeli Tax Considerations" below. Among other things, the Tax Pre-Ruling required that as of immediately prior to the completion of the Reorganization, the shareholders, option holders and other rights holders of GHI and the Company had to be identical, and that their respective holdings in each of GHI and the Company also had to be identical.

The following is a diagram of our corporate structure following the liquidation of GTTI:



During May 2014, we completed our initial public offering in the United States. In connection with our initial public offering, we listed our ordinary shares on the Nasdaq Capital Market and issued 3,363,010 of our ordinary shares in consideration of approximately $39.7 million, after deducting underwriting discounts, commissions and other estimated offering expenses.

Our principal executive offices and registered office in Israel are located at 8 Shaul Hamelech Blvd., Amot Mishpat Bldg., Tel Aviv, Israel, 6473307 and our telephone number is +972 3-6938448. Our website address is http://www.galmedpharma.com. The information contained on, or that can be accessed through, our website is neither a part of nor incorporated into this report. We have included our website address in this annual report solely as an inactive textual reference. Puglisi & Associates serves as our authorized representative in the United States. Its address is 850 Library Avenue, Newark, Delaware 19711.

Other than as described in "Item 5. Operating and Financial Review and Prospects—Contractual Obligations", we currently do not have and did not have any material commitments for capital expenditures, including any anticipated material acquisition of plant and equipment or interests in other companies, as of December 31, 2014.

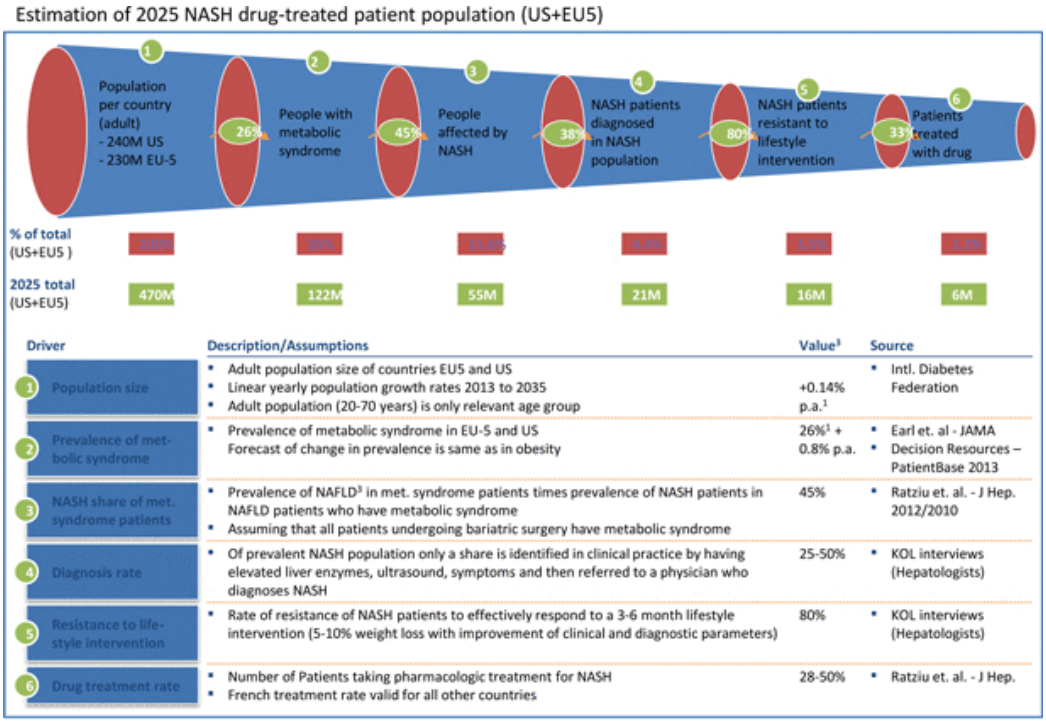
Business Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of a novel, once-daily, oral therapy for the treatment of liver diseases and cholesterol gallstones utilizing our proprietary first-in-class synthetic fatty-acid/bile-acid conjugate, or FABAC, called aramchol. We believe that aramchol has the potential to be a disease modifying treatment for fatty liver disorders, including NASH, which is a chronic disease that we believe constitutes a large unmet medical need.

NASH is a severe form of NAFLD in which patients suffer from inflammation and fat accumulation in the liver. NAFLD, which is the first stage of liver disease, is characterized by an accumulation of more than 6% of fat in the liver of people who drink little or no alcohol, and it is mostly associated with obesity or genetic predisposition, as well as in people with a combination of a high fat, fructose-rich diet and a sedentary lifestyle. Recent studies suggest that whereas NAFLD can be a benign condition, NASH may lead to progressive fibrosis that dramatically increases the risk of late-stage severe liver diseases, such as cirrhosis, carcinoma and end-stage liver disease, each potentially requiring liver transplantation. NASH is also associated with increased risk for metabolic and cardiovascular diseases. Both the medical community's and the public's awareness of NASH and its complications, as well as its economic burden, have increased in recent years. There is currently no approved drug for the treatment of NASH. According to a joint workshop held on September 5 - 6, 2013, sponsored by the FDA and the AASLD to develop guidance on diagnostic and therapeutic modalities for NASH, the FDA is currently working on guidelines for the development of therapies for the treatment of NASH. A recently published manuscript that summarizes the discussion at this joint workshop entitled "CHALLENGES AND OPPORTUNITIES IN DRUG AND BIOMARKER DEVELOPMENT FOR NONALCOHOLIC TEATOHEPATITIS: FINDINGS AND RECOMMENDATIONS FROM AN AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES (AASLD) - FOOD AND DRUG ADMINISTRATION (FDA) JOINT WORKSHOP" clarified, among other things, that the reversal of steatohepatitis with no evidence of progression to advanced fibrosis (stage 3 or 4), may be an acceptable surrogate endpoint suitable both for Phase IIb and Phase III trials that enroll patients with NASH and evidence of early fibrosis.

According to an article in the Journal of Gastroenterology and Hepatology in 2013, NAFLD is believed to affect up to 30% of the population in developed countries and up to 75% of Western populations with diabetes and obesity. Also according to an article in the Journal of Gastroenterology and Hepatology in 2013, approximately 12% of the general population in the United States and in the five most-populated countries in the EU, the United Kingdom, France, Spain, Germany and Italy, has NASH. According to an article in the Journal of Hepatology in 2008, and as summarized in an article in the Journal of Hepatology in 2010, the risk that persons with NASH will suffer a liver disease-related death is ten-times higher than that of the general population, and according to these sources, as well as an article in the Journal of Gastroenterology in 2005, NASH increases overall mortality by between 35% and 85%. NASH patients are also twice as likely to die from cardiovascular disease as the global general population. Publications over the last five years that addressed the connection between NASH and its cardiovascular complications include data from 18 studies with a total of 263,000 patients, with a follow up between 4.6 - 24 years. These studies reveal that the presence of NASH and NAFLD increases the risk of cardiovascular events by between 50% in females and up to 600% in males. An article in the European Scientific Journal in 2013 indicates that the presence of NASH increases the cardiovascular risk by a multiple of 2.4 in addition to the other metabolic risk factors, such as type 2 diabetes, and stresses the importance of treating NASH to prevent cardiovascular disease in addition to the known hepatic complications.

The estimated size of the NASH patient population in the United States and in the five most-populated EU countries is presented in the diagram below.



We are initially developing aramchol for the treatment of NASH in patients who also suffer from obesity and insulin resistance. These patients are at the highest risk of developing both the cardiovascular and hepatic complications associated with NASH. Aramchol is a synthetic conjugate of cholic acid, or a type of bile acid, and arachidic acid, or a type of saturated fatty acid, both of which, in their non-synthetic forms, are naturally occurring. The conjugated molecule acts upon important metabolic pathways, reducing fat accumulation in the liver and regulating the transport of cholesterol, which is essential for maintaining cholesterol balance in the body. The ability of aramchol to decrease liver fat content may also reduce the risk of cardiovascular complications associated with NASH. Independent third-party epidemiologic studies suggest that certain levels of fat reduction may reduce, and ultimately eliminate, liver inflammation in patients who have undergone bariatric surgery or other weight loss programs. We believe that aramchol's ability to reduce liver fat without observable adverse side effects in our studies to date will enable it to be an effective treatment for NASH and prevent the hepatic and cardiovascular complications associated therewith.

On February 1, 2015, we began our ARREST Study, a multi-center, randomized, double-blind, placebo-controlled, dose-ranging Phase IIb clinical trial of aramchol, which we intend to conduct in 240 biopsy-diagnosed NASH patients who also suffer from obesity and insulin resistance. We have initially initiated this study in Israel, and depending on the timing of the respective National Regulatory Authorities' approval, we may also initiate the study in Europe and Latin America. Furthermore, we have also submitted to the FDA an update of our existing IND filing, including the results of chronic toxicology and human PK studies, in order to initiate the study in the United States. Our ARREST Study for aramchol in NASH patients is in accordance with the study design recommended by the Medicines and Healthcare Products Regulatory Agency, or MHRA, and has been deemed acceptable by Bundesinstitut für Arzneimittel und Medizinprodukte, a German medical agency, or BfArM, and deemed satisfactory by Agence nationale de sécurité du médicament, a French medical agency, or ANSM. The study design has been confirmed by the FDA in a written pre-IND advice as acceptable for a Phase IIb study. The BfArM and ANSM also confirmed, in minutes of each of their respective scientific advisory meetings, that if successful, this Phase IIb trial may serve as a basis for Phase III pivotal trials of aramchol. The FDA and MHRA invited us to discuss the next steps in the development of aramchol after we analyze the results of the ARREST Study. If the Phase III trials are successful, we intend to submit an NDA to the FDA and an MAA to the EMA for the approval of aramchol for the treatment of NASH in patients who also suffer from obesity and insulin resistance in the United States and Europe. We currently expect complete results from our ARREST Study to be available at the end of 2016. Once 120 patients in our ARREST Study complete six months of treatment, we intend to conduct an interim analysis for safety and futility of aramchol based on MRS analysis. The interim analysis will provide safety data according to which an independent safety board will decide whether to continue studying both doses or move all patients to one dose, if one is found safer than the other. The MRS, will provide data for a futility decision, namely the decision to stop the study if no trend of reduction in liver fat content is found. We do not anticipate the interim results to lead to the stoppage of the ARREST Study, but no assurance can be given. This highlights the importance of the main secondary endpoint of the resolution of NASH in biopsies, which can be assessed only at the completion of the study and by repeated liver biopsies. We currently expect results from the interim analysis to be available in the first half of 2016. Depending on a number of factors, including, but not limited to, having sufficient resources and the completion of a pre-clinical study in juvenile animals, we may conduct in the future, but give no assurance that we will conduct or when we will conduct, an open-label Phase I clinical trial of aramchol in children.

We are also exploring other indications for the use of aramchol, including the treatment of cholesterol gallstones. On November 13, 2014, we announced the first administration of aramchol in a proof-of-concept Phase IIa clinical trial for the treatment of newly formed cholesterol gallstones following bariatric surgery. The Phase IIa trial is a multi-center, randomized, double blind, placebo controlled study, designed to evaluate the efficacy and safety of a once-daily dose of aramchol for three months in 36 adult patients and is being conducted in four medical centers in Israel. The primary endpoint of the trial is the complete dissolution of newly formed cholesterol gallstones following bariatric surgery. Secondary endpoints include a decrease of more than 50% in the number of newly formed gallstones, prevention of the formation of additional gallstones during the trial period and dissolution of biliary sludge. We currently anticipate reporting top line results in the second half of 2015. Approximately 5% of the general population in most countries develops cholesterol gallstones and the current standard of care is surgery, either laparoscopic or open cholecystectomy.

On April 28, 2014, we commenced PK and food effect studies of aramchol. In written correspondence from December 2013 regarding a requested pre- IND application meeting, the FDA recommended that we conduct such studies prior to commencing our Phase IIb ARREST Study of aramchol for the treatment of NASH. We conducted the PK study at the Sourasky Medical Center in Tel Aviv, Israel. We enrolled 66 healthy male volunteers who received three doses of aramchol: 200mg, 400mg and 600mg. The two higher doses will be used in our ARREST Study. In December 2014, we completed the statistical analysis of the PK study of the three doses of aramchol and observed no serious adverse events. Such PK study provides additional safety data to further support existing safety data from our pre-clinical studies and our Phase I and Phase IIa clinical trials of aramchol.

To date, we have successfully completed four clinical trials of aramchol. The first was a single dose, double-blind, placebo- controlled, Phase Ia study with ascending doses of aramchol in healthy volunteers in one center in Israel. All doses proved to be well-tolerated and no serious adverse side effects were observed. An additional Phase Ib repeated dose trial completed on healthy volunteers in one center in Israel also showed that aramchol has no observable adverse side effects and confirmed the suitability of a once-daily dose of aramchol. A multi-center, randomized, double-blind, placebo-controlled Phase IIa trial of aramchol in 60 NAFLD and NASH patients in 12 centers in Israel, whose study design was deemed acceptable by the FDA in 2007 at a pre-IND scientific advisory meeting, suggested that aramchol reduced liver fat in a dose dependent manner, as evidenced by a statistically significant reduction of liver fat over a three month treatment period of once-daily 300 mg doses of aramchol, and induced positive trends of changes in several metabolic parameters. The fourth was a single-site, randomized, partially double-blind, placebo-controlled PK and food effect study conducted in three parts. The first two parts of the study assessed PK, safety and tolerability of aramchol tablets administered in single doses of 200 mg, 400 mg and 600 mg either following a ten-hour overnight fast or a high-fat, high-calorie meal. The third part of the study assessed PK, safety and tolerability of aramchol tablets administered in the same three doses as the first two parts of the study for ten consecutive days, in each case within one hour after a light breakfast. We did not observe any serious adverse side effects in the PK and food effect study.

Based on our Phase IIa proof-of-concept results, we established a development plan that we believe may confirm that aramchol (i) is safe, (ii) can be administered as a once-daily oral therapy, (iii) targets NASH, (iv) can effectively treat inflammation and thus prevent the progression of NASH and (v) can treat the underlying condition of NASH, metabolic syndrome, by improving insulin resistance and other parameters of metabolic syndrome, such as HOMA levels, or homeostatic model assessment levels, which is a method used to quantify insulin resistance and beta-cell function, which are each biological markers of metabolic syndrome, and adiponectin levels.

Our Development Pipeline

Based on the potential metabolic effects of aramchol, we are considering additional indications with meaningful potential market opportunities, with the view of expanding aramchol's therapeutic applications to cholesterol gallstones and other cholestatic diseases and lipodystrophy, a medical condition characterized by abnormal or degenerative conditions of adipose tissue, or body fat, including the loss of body fat from various regions of the body and its redistribution and accumulation in other areas. The pipeline chart below shows the current stage of development of aramchol for each of these indications and the next planned clinical trial in respect of each such indication, as applicable, as well as the preclinical programs for aramchol.

Indication	Planned Next Clinical Trial	Expected Number of Patients	Anticipated Key Events
Non-Alcoholic Steatohepatis (NASH)	Phase IIb	240 patients	Conduct interim analysis of 120 patients in Phase IIb trial who have completed six months of treatment in the first half of 2016 Release top-line results from Phase IIb trial at the end of 2016
Lipodystrophy (as described below)	Phase IIa, Investigator-Initiated Study	50 patients	Release top-line results in the first half of 2016

Our Competitive Strengths

The pharmaceutical industry is characterized by rapidly evolving technology, intense competition and a highly risky, costly and lengthy research and development process. Adequate protection of intellectual property, successful product development, adequate funding and retention of skilled, experienced and professional personnel are among the many factors critical to success in the pharmaceutical industry. We believe we are strategically positioned to address the unmet medical needs of NASH patients who also suffer from obesity and insulin resistance. Our competitive strengths include:

- **A once-daily oral drug without observable adverse side effects to date in development for the chronic treatment of NASH**. We believe that the characteristics of aramchol, including its ability to reduce liver fat content without observable adverse side effects in our studies to date, which we believe may result in an anti-inflammatory effect, its ability to modulate the transport of cholesterol in the body and simple and convenient delivery through once-daily oral administration, position it well against the competition in the treatment of NASH. We believe that such characteristics may also lead to aramchol's acceptance and adoption by the medical community, including patients, as an alternative to the medical treatments used today, which are not approved by applicable regulatory authorities for NASH as their efficacy has not been proven in well-designed clinical studies. We believe aramchol is well-positioned against drugs in development for NASH, some of which may require intravenous delivery or may cause adverse events, such as itching or an increase in low-density lipoproteins, or LDL (i.e., "bad cholesterol"), which can be highly inconvenient for patients with chronic diseases, such as NASH, and may result in low patient compliance.

- **Extensive knowledge and expertise in the treatment of liver diseases, the development of FABACs and working with lipid molecules**. We believe our management team, scientific advisors and personnel, have extensive knowledge and experience in the treatment of liver diseases and cholesterol gallstones, developing FABACs, such as aramchol, for the treatment of liver diseases and cholesterol gallstones and working with lipid molecules, which due to their special physiochemical characteristics, are difficult to synthesize, develop and work with. We believe that such knowledge and expertise makes us competitive in the NASH and cholesterol gallstones fields.

- **Non-invasive diagnostic tools for the assessment of aramchol's effect**. If we are successful in our clinical trial correlating fat reduction in the liver as measured by MRS, an FDA validated and commonly used test for the measurement of liver fat content, with aramchol's effect on inflammation in the liver, MRS may become a non-invasive biomarker that is able to measure the effect of aramchol in patients following treatment with aramchol. Additionally, we intend to co-develop a non-invasive biomarker, which can identify the metabolomic, or a mapping of lipids and proteins in different body components, such as blood and liver tissue, profile for NASH patients responding to aramchol treatment and thus would be able to predict individual responses to aramchol prior to treatment. We believe that such biomarkers may facilitate aramchol's market penetration and accelerate its acceptance and adoption by the medical community and NASH patients as a treatment option, thereby increasing our competitiveness in the NASH market. On September 29, 2014, we purchased 60 EndoPAT™ devices and accessories from, and entered into a collaboration with, Itamar to include an assessment of endothelial, or arterial, function in our Phase IIb ARREST Study of aramchol in NASH patients. In the completed Phase IIa study we observed a trend of improvement in endothelial function in patients treated with 300mg. of aramchol. The EndoPAT™ device will allow for a validated, consistent measurement of endothelial function in all patients participating in the study. As mentioned, NASH patients develop cardiovascular complications and present with endothelial dysfunction as a marker of their propensity for atherosclerosis, or hardening of the arteries. A significant improvement in endothelial function, if found, will provide an additional advantage for patients treated with aramchol and will be a differentiating factor for aramchol among other NASH drugs in development.

Our Strategy

Our strategy is to build a specialized biopharmaceutical company that discovers, develops and commercializes novel FABAC drugs and potentially other molecules for the treatment of liver diseases and cholesterol gallstones, beginning with the treatment of fatty liver disorders, primarily NASH, and cholesterol gallstones. We focus on drugs and drug conjugates for liver diseases and cholesterol gallstones with global market potential and we seek to create global partnerships with academic institutions and biotechnology or pharmaceutical companies to effectively assist us in developing our portfolio and marketing our products. Using this approach, we have successfully advanced aramchol into various stages of clinical development. Key elements of our strategy include:

- **Continuing to advance our development of aramchol for the treatment of NASH**. Our development of aramchol for treatment of NASH currently includes our Phase IIb ARREST Study of aramchol for the treatment of NASH in patients who also suffer from obesity and insulin resistance. If our ARREST Study is successful, the results will serve as a basis for potential Phase III pivotal trials in Europe and Israel for the same indication and as a basis for discussion for potential Phase III pivotal trials in the United States for the same indication. If the Phase III trials are completed successfully, we intend to seek regulatory approval of aramchol in the United States and Europe for the treatment of NASH in patients who also suffer from obesity and insulin resistance**.**

- **Exploring other indications for the use of aramchol, which currently includes the treatment of cholesterol gallstones**. We have commenced an open-label Phase IIa proof-of-concept clinical trial of aramchol for the treatment of cholesterol gallstones and expect that we will report the top line results in the second half of 2015.

- **Establishing a development and commercialization partnership for aramchol upon completion of our ARREST Study or after the successful completion of the first of the potential Phase III trials of aramchol for the treatment of NASH**. Following applicable regulatory approval, which we provide no assurance we will receive, we intend to commercialize aramchol, and our other future products, through outlicensing agreements with major pharmaceutical or biotechnology companies that possess experience, resources and infrastructure to execute a successful market launch and provide sales support for aramchol. Such companies may perform any or all of the following tasks: Completing development, securing regulatory approvals, manufacturing, marketing and sales. We may ultimately, in the future, consider building an internal commercial infrastructure.

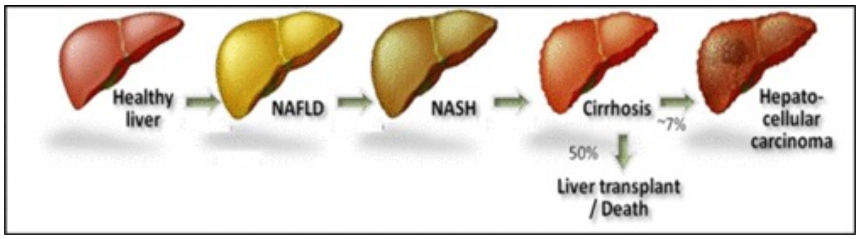
- **Advancing existing collaborations for the discovery and validation of diagnostic tools and biomarkers for the diagnosis of liver disease**. We intend to advance our existing collaborations and strategic arrangements for the discovery and validation of non-invasive diagnostic tools and biomarkers for the diagnosis of liver disease, including NASH. We are currently collaborating with One Way Liver Genomics S.L., or OWL, on the development of a non-invasive biomarker which, if successful, may help to stratify patients for our planned Phase III clinical trial and may help to predict individual responses to aramchol for the treatment of liver diseases. OWL also granted us a right of first refusal, exercisable upon completion of our ARREST Study, to enter into a business transaction with OWL regarding the commercial exploitation of the data generated during the collaboration. Additionally, we purchased 60 EndoPAT™ devices and accessories from and collaborated with Itamar in September 2014 to include an assessment of endothelial, or arterial, function in our ARREST Study of aramchol in NASH patients. Endothelial dysfunction, an early sign of atherosclerosis, is often present in NASH patients. In the Phase IIa study, we observed improvement in endothelial function in patients treated with aramchol. Our ARREST Study is designed to confirm aramchol's positive effect on endothelial function by measuring the endothelial function in all participating patients. In the Phase IIa study, all patients measured their own endothelial function by flow-mediated dilation, or FMD, in one center in Israel. Due to the geographic spread of our ARREST Study, we searched for a validated method to measure endothelial function that would not be dependent upon the test performer. We determined that the EndoPAT™ device is best-suited, easy to operate device for measuring endothelial function and perhaps the only method to measure endothelial function consistently across a number of patients.

- **In-license, develop or acquire additional drug candidates for the treatment of liver diseases**. Aramchol is directed at the treatment of liver diseases, particularly NASH, that have major global markets and cholesterol gallstones. Our intent is to explore opportunities to in-license, develop or acquire other molecules and/or conjugates for the treatment of liver diseases.

We believe that our strategy will increase the likelihood of advancing clinical development and potential commercialization of aramchol, as well as increase awareness of liver disease and cholesterol gallstones, our brand and our potential market share.

Overview of NAFLD and NASH

NAFLD. NAFLD is a spectrum of conditions characterized by the accumulation of fat in the liver, encompassing fatty liver, a relatively benign increase in liver fat content, NASH, or fat infiltration and inflammation of the liver, and liver cirrhosis, or scarring of the liver tissue. Although some fat in the liver is normal, if fat comprises more than 6% of the liver, it may lead to inflammation and subsequent liver disease. In some cases, over time, liver cells may be replaced by scar tissue, which causes cirrhosis. When this happens, the liver is unable to function properly, necessitating a liver transplant or leading to liver cancer, and potentially liver-related death. The following diagram demonstrates the progression of liver disease.



According to the Journal of Gastroenterology and Hepatology in 2013, NAFLD is believed to affect up to 30% of the population in developed countries, and up to 75% of Western populations with diabetes and obesity. According to the World Gastroenterology Organization, in 2012, 30%, 25%, 25% and 15%, respectively, of the general population in each of the United States, Europe, the Middle East and Asia, respectively, had NASH.

Associated with the Western diet, which is rich in processed foods with high fat and sugar content, and a sedentary lifestyle, NAFLD's prevalence is rapidly growing in parallel with metabolic syndrome, obesity and diabetes, each of which are on the rise in Western countries. Metabolic syndrome is a serious health condition caused by obesity, physical inactivity and genetic factors that results in a higher risk of cardiovascular disease, diabetes, stroke and NAFLD. According to the Journal of Gastroenterology and Hepatology in 2013, NAFLD is associated with insulin resistance and its physical and biochemical manifestations, such as obesity, visceral adiposity, type 2 diabetes, hypertriglyceridemia and arterial hypertension. Recently, the medical community has widely come to consider NAFLD as the liver disease of metabolic syndrome, which is the cause of atherosclerosis and its associated complications. Concordant studies over the last five years in Europe and Japan have indicated that over a follow-up period of five to six years, individuals with NAFLD also develop major cardiovascular complications, such as myocardial infarction, more frequently than those without NAFLD. Further, an article in the Journal of Gastroenterology and Hepatology in 2013 acknowledges a causal relationship between the progression of metabolic syndrome and the occurrence of NAFLD. The 2013 handbook, Non-Alcoholic Fatty Liver Disease: A Practical Guide, notes that the amount of liver fat influences the severity of insulin resistance, such that patients with fat accumulation in the liver have substantially more insulin resistance than those without such accumulation. Moreover, according to an article in the Journal of Hepatology in **2014**, patients with NAFLD develop atherosclerosis earlier than those without NAFLD. It is therefore considered by the medical community that NAFLD is not only a manifestation of metabolic syndrome, but may also be involved in its development and severity. The current management of NAFLD demands lifestyle changes such as weight reduction and physical activity, which are hard to achieve and long-term compliance is difficult.

NASH. NASH is a severe form of NAFLD characterized by inflammation in the liver in addition to the presence of excess fat. A subset of approximately 30% to 50% of individuals with NAFLD in all age groups, including children, develop NASH, although this more often occurs in obese individuals. Independent third-party studies suggest that whereas simple fatty liver can be a benign condition, in NASH patients, for reasons that are still not completely understood, the fat build-up in the liver induces chronic inflammation which leads to progressive fibrosis that can lead to cirrhosis with a high risk of carcinoma and to end-stage liver disease. According to an article in the Journal of Gastroenterology, NASH is currently the third leading indication for liver transplantation in the United States, and according to articles in the Journal of Digestive Diseases in 2011 and the Journal of Hepatology in 2010, NASH will become the leading cause for liver transplantation in the United States by 2020.

Based on research and discussions, we believe that the size of the NASH market is somewhere between $10 billion and $40 billion, although there can be no assurance of the market size.

NASH is often discovered incidentally, frequently by observation of elevated liver enzyme levels in blood tests. NASH patients may be asymptomatic or suffer from fatigue, with other symptoms occurring as the liver disease advances. Diagnosis of NASH is based on the exclusion of other reasons for liver disease, such as the use of medications, viral hepatitis or excessive use of alcohol; followed by non-invasive imaging tests, such as ultrasound, Computed Tomography scan, or CT scan, and magnetic resonance imaging, or MRI. Liver biopsy is currently the standard procedure for the diagnosis of NASH.

The underlying pathophysiology, or the explanation of the physiological processes or mechanisms whereby abnormal or undesired conditions develop and progress, of NASH is not well understood. The disease is multifactorial, involving both genetic and environmental factors that regulate lipid metabolism and the transportation of fat to, within and from the liver cells. Insulin resistance and subsequent hyperinsulinemia, or increased blood insulin levels as compared to blood glucose levels, lead to alterations in the hepatic metabolism of free fatty acids and ultimately to an accumulation of lipids in the liver cells. As the disease progresses, persistent fatty infiltration and inflammation cause liver damage marked by fibrosis and gradual loss of normal liver cells, which in turn could lead to cirrhosis with a high risk of carcinoma and end-stage liver disease.

Beside its hepatic complications, NASH is also associated with increased risk for the cardiovascular complications associated with metabolic syndrome. A position statement on NAFLD and NASH from the European Association for the Study of the Liver's, or the EASL, 2009 Special Conference found extra-hepatic complications of NAFLD and NASH. The EASL position statement noted that "[b]eyond damage to the liver, steatosis can also worsen and/or induce insulin resistance, worsen glycemic control in patients with type 2 diabetes, and predict subsequent development of metabolic syndrome; it is also associated with increased cardiovascular risk and events and with essential arterial hypertension." The American Journal of Gastroenterology noted in 2012 that "[t]he long-term outcomes of patients with NASH have been reported in several studies… [whose] findings can be summarized as follows: (a) patients with NAFLD have increased overall mortality compared to matched control populations; (b) the most common cause of death in patients with NASH is cardiovascular disease; and (c) patients with NASH (but not NAFL) have an increased liver-related mortality rate.

Currently Available Treatment Options for NASH

Modification of risk factors, such as obesity and hyperlipidemia, and proper diabetic control is generally recommended for the treatment of NASH, and the standard of care includes lifestyle changes to promote weight loss, including low-calorie, low-fat diets and physical activity. Although weight loss can be potentially significant in delaying the progression of NASH, we believe that for most individuals, it is generally very difficult to maintain over the long-term, even following bariatric surgery.

There are currently no drugs approved by regulatory authorities for the treatment of NASH. Even though certain drugs, such as insulin sensitizers and antihyperlipidemic agents, are prescribed for some NASH patients, they are not approved for the treatment of NASH and their efficacy has not been proven in well-designed clinical studies. Such prescription or use of unapproved drugs is typically known as "off-label" prescription or use. According to press releases issued in mid-2011 by the FDA and EMA, the use of other drugs that have historically also been used off-label to treat NASH has been restricted due to their severe side effects, including adverse cardiovascular effects and liver toxicity, or suspected carcinogenicity. Bariatric surgery can be performed in obese patients with NASH, but is not an established procedure to treat NASH. Lastly, vitamin E was found to be beneficial for non- diabetic patients with biopsy proven NASH, but not for diabetics with NASH, NAFLD or liver cirrhosis. As such, the use of vitamin E is fairly limited.

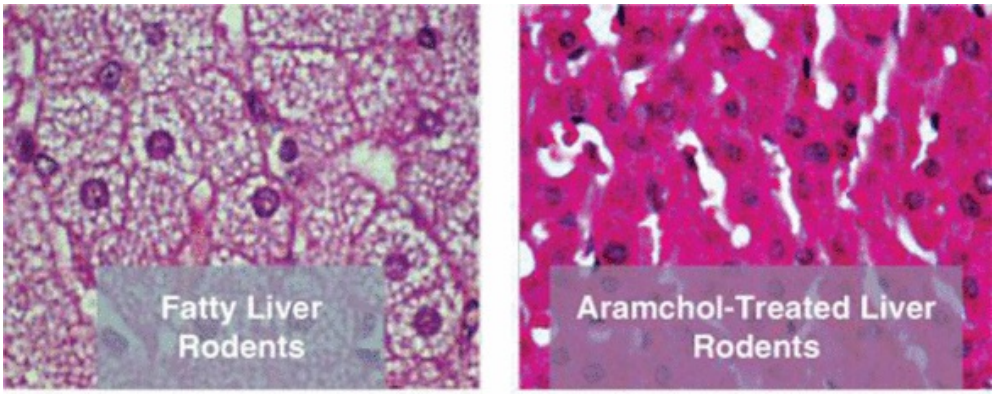
Based on the foregoing, we believe that there is a significant unmet need for a NASH-specific therapy. We believe that aramchol has the potential to provide significant benefits in the treatment of this liver disease due to its ability to reduce liver fat in a dose dependent manner, lack of observable adverse side effects in our studies to date and ease of use through once-daily oral administration. Moreover, based in part on the Journal of Gastroenterology and Hepatology, we believe the increasing rates of diabetes and obesity worldwide likely means that a significant number of patients will be eligible for, and will be interested in, receiving a new therapy for the treatment of NASH if it becomes available on the market. We believe that aramchol's observed positive metabolic effects, if confirmed in future studies, will position it as a valuable tool in the treatment of NASH in early stages of the disease, for helping to prevent both hepatic and cardiovascular complications.

Aramchol for NASH

Overview

Our product candidate, aramchol, is a first-in-class synthetic FABAC which we are initially developing for the once-daily oral treatment of NASH in patients who also suffer from obesity and insulin resistance.

Early in its development, aramchol's ability to modulate hepatic lipid metabolism was observed and validated in numerous preclinical trials with different animal species. Mice fed a high fat diet and treated with aramchol did not develop fatty liver, as opposed to the control mice that were fed a high fat diet, but were not treated with aramchol, in which fatty liver was observed. In such early studies, we also observed that the mechanism of this effect was not a result of malabsorption of fat in the intestines because the FABAC-treated mice gained weight throughout the test periods to a similar degree as the control mice. This led us to conclude that FABAC therapy triggers a beneficial modulation of intra-hepatic lipid metabolism and thus reduces liver fat content. The images below show the reduction of liver fat content in rodents after treatment with aramchol.



Gilat et. al., HEPATOLOGY, Vol. 38, No. 2, 2003

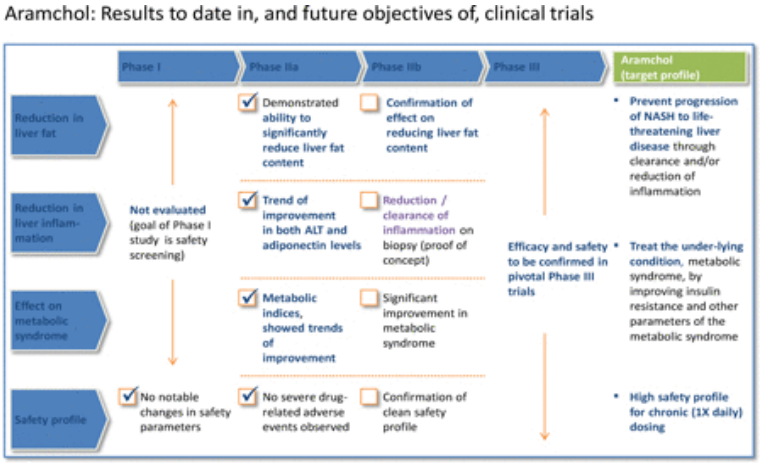
In in-vitro studies, aramchol partially inhibited the Stearoyl-Coenzyme A Desaturase1, or the SCD1 enzyme, an enzyme recognized as playing an important role in the metabolism of fatty acids. The SCD1 enzyme is essentially the gateway that regulates the use and storage of fat in the body by converting saturated fatty acids to monounsaturated fatty acids. Experimental animal studies showed that inhibition of the SCD1 enzyme protects against diet-induced obesity, hepatic steatosis, or fatty liver, and insulin resistance by instructing the body to use, rather than store, all fatty acids. However, various animal studies have indicated that complete SCD1 enzyme inhibition has dangerous side effects, such as inflammation, atherosclerosis and pancreatic beta cell dysfunction. As observed by us in our studies and subsequently published in the European Journal of Gastroenterology and Hepatology and Archives of Medical Research in 2008 and 2010 respectively, one of aramchol's unique characteristics is that it triggers a partial SCD1 enzyme inhibition without any significant adverse events.

Aramchol also has the ability to up-regulate ABCA1, an enzyme that induces "reverse cholesterol transport." Each cell in the body has a specific receptor for cholesterol entry, the LDL receptor, and a transporter, the ABCA1 transporter that pumps cholesterol out of the cell towards the high-density lipoprotein, or HDL, which transports it towards the liver to be excreted into the intestine. This pathway from the cell to the liver is called the "reverse cholesterol transport" and is essential for maintaining cholesterol balance in the body. Excess levels of "bad" cholesterol are deposited mainly in vascular walls, causing atherosclerosis, or a vascular disease in which an artery wall thickens as a result of the accumulation of calcium and fatty materials, such as cholesterol. Activation of the reverse cholesterol transport reduces the bad cholesterol deposited in vascular walls and is therefore beneficial. As published in the Biochemical Journal, the Archives of Medical Research and the Current Opinion in Lipidology in 2006, 2010 and 2014, respectively, in several experimental models in animals, aramchol has been shown in independent studies to increase ABCA1 activity by between 300% and 400%, thereby stimulating reverse cholesterol transport, reducing cholesterol levels and preventing atherosclerosis. An article in the April 2014 issue of Biochimie further supports the importance of the regulation of ABCA1-induced reverse cholesterol transport on the pathogenesis of NASH.

The Company expects aramchol to reduce and eventually eliminate liver inflammation by the mechanism of action described above, while also mitigating cardiovascular comorbidities.

We commenced our Phase IIb ARREST Study on February 1, 2015, to evaluate the efficacy and determine the safest and most efficient dose of aramchol as a novel treatment for NASH patients with obesity and insulin resistance. We filed an IND application with the FDA in order to use the results of our previously conducted, and to be conducted clinical studies in Europe, Latin America and Israel, as a basis for the FDA's future approval to conduct our ARREST Study and the pivotal Phase III clinical trials for NASH and other clinical trials in the United States. On July 22, 2014, the FDA cleared this IND application, permitting us to conduct clinical trials of aramchol in the United States for the treatment of fatty liver disorders, and in September 2014, the FDA granted Fast Track designation status to aramchol for the treatment of NASH. Fast Track designation may accelerate the development process and may expedite the review of INDs that show promise in treating serious, life-threatening medical conditions for which no other drug either exists or is as effective. In March 2015 we submitted to the FDA an updated IND request, which, if cleared, will allow us to conduct the Phase IIb ARREST Study in the United States.

Summary of Aramchol Clinical Trials



Our Phase IIb ARREST Study for Aramchol

We are currently conducting our Phase IIb ARREST Study to determine the safest and most effective dose of aramchol for the treatment of NASH. In order to be eligible to participate in our ARREST Study, patients must be affected by NASH, as diagnosed by a biopsy, and also suffer from overweight or obesity, measured by a Body Mass Index between 26 and 29 and 30 or greater, respectively and insulin resistance, measured by fasting plasma glucose levels of 100 mg/dl or greater. We target this specific population as it is at the greatest risk of developing the complications that are associated with NASH. Although we do not expect aramchol to reduce the fibrosis levels of such patients, we include both fibrotic and non-fibrotic patients in the trial. Patients are randomized into one of three trial groups taking either one of two different once-daily oral doses of aramchol or a placebo. The treatment part of the trial is designed to be 12 months in duration and patients completing this phase will be observed for a three month follow-up period. This trial is designed to enroll 240 patients (89 patients in the 400 mg aramchol group, 89 patients in the 600 mg aramchol group and 62 patients in the placebo group) across approximately 60 clinical sites in the United States, Israel, Europe and Latin America, and we currently expect results from the trial to be available at the end of 2016.

The primary endpoint of the 12-month double-blind portion of the trial is a statistically significant reduction in liver fat concentration, which according to the trial design, would be a reduction in liver fat of 10% more than the placebo group, as measured by MRS, which is a surrogate endpoint that is generally accepted by the FDA with respect to Phase I and Phase II NASH studies.

Secondary endpoints of the trial are changes in diagnosis as measured by a biopsy, such as the resolution of NASH, and/or a two point reduction in the NAFLD activity score, or NAS (a measurement of the disease severity that measures the parameters of fat, ballooning and inflammation), which reduction is caused by more than one parameter, with no worsening of fibrosis. Other secondary endpoints are improved liver and metabolic biomarker levels and exploratory endpoints, such as FibroMax, which is a non-invasive comprehensive biomarker for the diagnosis of the most common liver diseases, including NASH, and metabolomics. The Company believes that finding a non-invasive test which correlates well with biopsy findings would significantly increase the likelihood of the future use of aramchol in an outpatient setting, where biopsies, which are expensive and painful, are not the standard diagnostic procedures.

During the trial, we plan to conduct an interim analysis for safety and futility with respect to 120 participants who have completed six months of treatment. An independent expert committee, the DSMB, will review the interim safety data to determine whether emergent safety issues are present, and if so, whether they are dose-related. Depending on its severity, any emergent safety issues may warrant a suspension of the higher dose used in the trial or of the entire trial itself. Our pre-specified interim criterion for futility is a trend of reduction in liver fat content measured by MRS in treated patients compared to placebo-treated patients. If this interim criterion is met, the trial will continue for the full period and number of patients, as planned. If this result is not reached, however, the trial will be suspended.

With respect to conducting trials in the United States, on December 13, 2013, in connection with a pre-IND meeting that we requested with the FDA for aramchol for the treatment of NASH in obese patients with insulin resistance, the FDA provided a written response, or the FDA Response, regarding our planned ARREST Study design, including its primary and secondary endpoints and inclusion and exclusion criteria. The FDA Response and prior correspondence confirmed that we may conduct our planned ARREST Study in the United States, but recommended that we perform a PK and a food effect study prior to doing so. We have since completed the PK study and the statistical analysis showed no observable serious adverse events. The FDA also indicated that it will require data from nine-month toxicology studies in animals prior to the initiation of any year-long clinical trial conducted within the United States; the EU, Israel and Latin America only require six-month toxicology data. In September 2014, we successfully completed two six-month chronic toxicology studies of aramchol with no observed significant adverse events and continued these studies into December 2014 to satisfy the above initial requirement of the FDA to complete nine-month pre-clinical toxicology studies of aramchol prior to conducting clinical trials in the United States. In February 2015, we successfully completed the nine-month pre-clinical toxicology studies of aramchol with no observed significant adverse events. As such, we intend to include U.S.-based sites in our ARREST Study of aramchol.

The FDA also recommended that future clinical studies should be discussed at an end-of-Phase II meeting with the FDA to take place within three months from the date we complete the analysis of the results of our ARREST Study, where the data captured in such trial will be taken into consideration. The FDA Response further noted that we must discuss with the FDA a methodology for our drug development processes as our development of aramchol progresses to determine which surrogate endpoints, if any, the FDA will allow us to use to predict the clinical benefit of aramchol. In light of the publication of the FDA and AASLD joint workshop minutes, we speculate that the discussion will focus on the appropriateness of the resolution of NASH, as measured by biopsies.

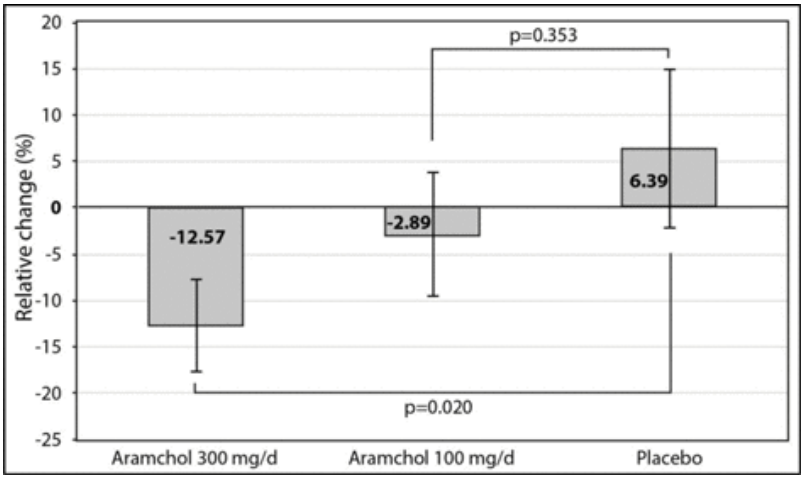
Potential Phase III Program for Aramchol

The development work we have completed to date with regard to aramchol was deemed appropriate for the initiation of a phase IIb study by the FDA, MHRA, BfArM and ANSM, and our ARREST Study design is in accordance with the study design recommended by the MHRA, deemed acceptable by BfArM and deemed satisfactory by ANSM. In, addition, the FDA recently confirmed in a written pre-IND advisory letter that such study design was acceptable for our ARREST Study. BfArM and ANSM also confirmed, in minutes of each of their respective scientific advisory meetings, that, if our ARREST Study is successful in reaching its primary endpoint, we may proceed to pivotal randomized, double-blind, placebo-controlled, Phase III trials. We expect the primary end-points of such trials to be the resolution of inflammation in the liver. The FDA, in the FDA Response, and the MHRA invited us to discuss the next steps in the development of aramchol after we complete the analysis of the results of our ARREST Study, where the data captured in such trial will be taken into consideration. In July 2014, the FDA granted Fast Track designation to aramchol, which designation may accelerate the development process and may expedite the review of INDs that show promise in treating serious, life-threatening medical conditions for which no other drug either exists or is as effective.

Phase IIa Trial: Aramchol Treatment in NAFLD or NASH Patients

In January 2012, we completed a 60 patient multi-center, randomized, double-blind, placebo-controlled Phase IIa clinical trial of aramchol in patients with NAFLD or NASH between the ages of 18 and 75 in 12 centers in Israel. The Phase IIa study results were published in July 2014 in the peer-reviewed medical journal, Clinical Gastroenterology and Hepatology Journal. In accordance with the AASLD's guidelines for Phase IIa studies in NAFLD or NASH, the trial was performed in patients with either NAFLD or NASH, rather than only in NASH patients. The trial's primary efficacy endpoint was a reduction in liver fat content, and did not consider inflammation or fibrosis, which can only be diagnosed by liver biopsy. We believe that the short study duration of three months of treatment followed by a one-month follow-up period did not warrant repeated biopsies. The trial evaluated the effects on liver fat content of 100 mg and 300 mg once-daily doses of aramchol compared to a placebo. At the end of the three month treatment period, statistically significant reductions in liver fat concentration as measured by MRS, a noninvasive and sensitive method for quantification of the amount of fat in the liver, were observed in the 300 mg patient group. Specifically, a 12.57% mean liver fat content reduction was observed in the 300 mg group, as compared to a mean reduction of 2.89% in the 100 mg group and a mean increase of 6.39% in the placebo-treated patients, indicating that the effects of aramchol are dose-dependent, as demonstrated in the graph below, which presents the results with respect to the 57 patients who completed the entire treatment period and experienced no protocol violations.

Relative Change in MRS from Baseline After Three Months of Treatment



The difference between baseline and liver fat concentration at the end-of-treatment, as measured by MRS, for patients diagnosed with NASH and with NAFLD is presented in the following table, which also presents the results with respect to the 57 patients who completed the entire treatment period and experienced no protocol violations.

Relative Change in Liver Fat Concentrations in the NASH and NAFLD Groups

Liver MRS	Aramchol 300 mg/d Mean ± SD	Aramchol 100 mg/d Mean ± SD	Placebo Mean ± SD
NASH	-35.42 ± 50.09 (N=2)	-9.82 ± 4.57 (N=2)	19.24 ± 29.69 (N+2)
NAFLD	-10.03 ± 18.22 (N+18)	-6.05 ± 26.10 (N=16)	4.88 ± 37.44 (N+17)

N = number of patients

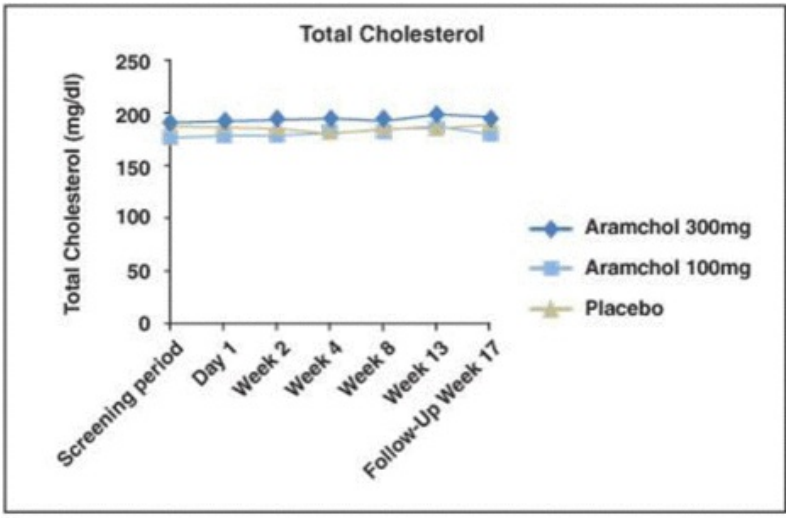
SD = standard deviation

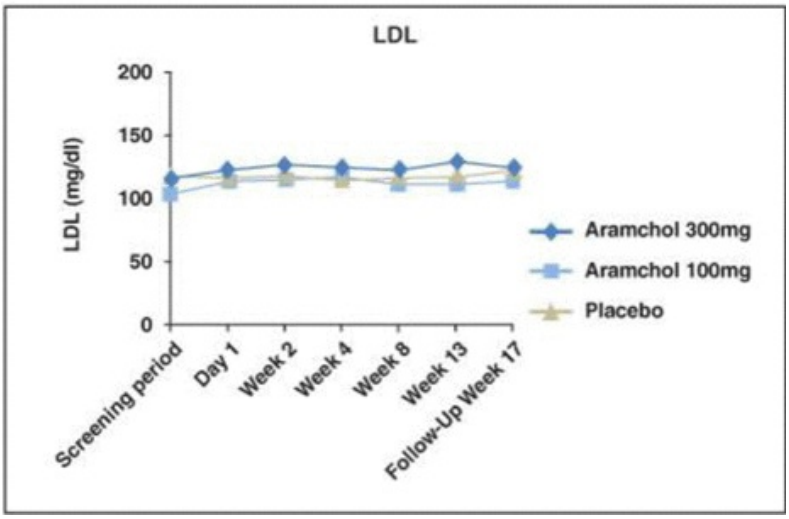
The graph and table above show that the primary endpoint of the study was attained. The study demonstrated a statistically significant, dose dependent reduction in fat content in the livers of patients treated with aramchol, with a 19% difference between the 300 mg dose group and the placebo group, while the difference between the 100 mg dose group and the placebo group was not statistically significant.

No statistically significant changes in body weight were observed between the three groups, suggesting that weight-loss did not influence the observed reduction in liver fat content experienced in the aramchol treated groups.

In addition, both treated patients and the placebo group showed a trend of reduction in alanine aminotransferase, or ALT, levels, which is a marker of hepatocellular injury and an indicator of liver disease. We believe that the reason the treated and placebo groups showed such a trend may be a result of the fact that the individuals in the placebo may have changed their lifestyle based on the guidance they received from the Company on adopting a healthy lifestyle. The aramchol treated groups' ALT values relapsed 30 days post-treatment, indicating that after the cessation of aramchol treatment, the patients experienced recurring liver inflammation. The placebo group did not demonstrate a relapse in ALT levels. This supports the supposition that aramchol has a real biological effect.

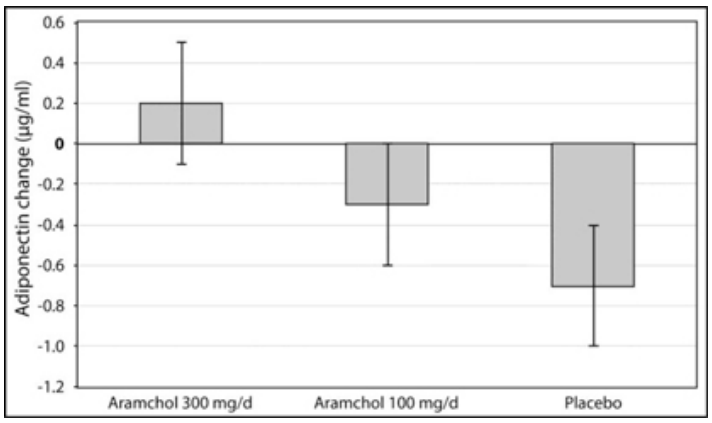
Total cholesterol and LDL cholesterol levels were determined as safety parameters in our Phase IIa study. Differences between low-dose aramchol (100 mg/d), high-dose aramchol (300 mg/d) and the placebo were also analyzed for secondary efficiency endpoints. The graphs below show no statistically significant differences among the three treatment groups for cholesterol and LDL.





Adiponectin is a protein that modulates metabolic processes, including the regulation of glucose levels and fatty acid breakdown in the body. Adiponectin has an anti-inflammatory and antifibrotic effect on the liver. Adiponectin deficiency, or low amounts of adiponectin, results in insulin resistance, glucose intolerance, abnormal levels of fat in the blood and vascular injury, all of which are characteristic of metabolic syndrome. The graph below shows the change in serum adiponectin levels from baseline during treatment. At the end of the three month treatment period, increased serum adiponectin levels were observed in the aramchol treated patient groups, indicating that aramchol increases serum adiponectin levels in a dose dependent manner, suggesting that aramchol may act as a protective factor for the prevention of metabolic syndrome, as increased serum adiponectin is itself such an independent protective factor.

Change in Serum Adiponectin Levels from Baseline During Three Months of Treatment



The arterial endothelium is a target for the atherosclerotic process. Atherosclerosis is associated with endothelial dysfunction in the very early stages of the disease process. Several studies have shown that metabolic syndrome is associated with endothelial dysfunction as an early pathogenic event. Thus, assessing endothelial function serves as an early marker for both metabolic syndrome and atherosclerosis. In the present study, endothelial function was assessed using flow-mediated dilation, a noninvasive ultrasound-based method that measures the ability of a large conduit artery to dilate in response to a shear stress stimulus, or an external force acting on the blood vessel. At the end of the three month treatment period, improved endothelial function was observed in the 300 mg aramchol treated patient group. The table and graph below present the change in endothelial function, as measured by flow mediated dilation observed between baseline and the end-of-treatment for the 48 patients who performed two flow mediated dilation examinations.

Change in Endothelial Function between Baseline and the End-of-Treatment

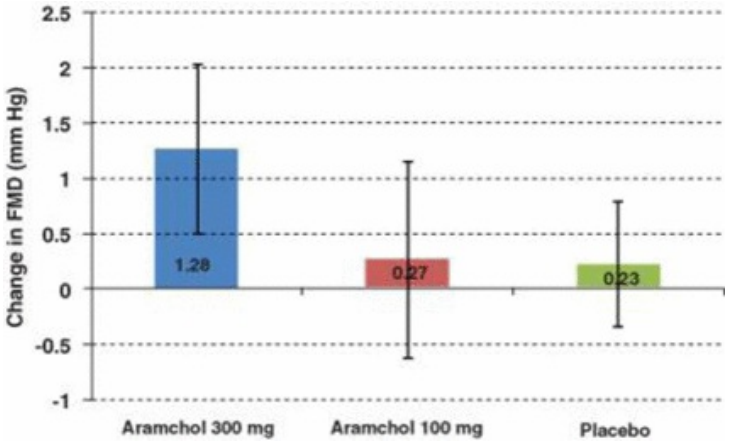
FMD (mm Hg)	**Aramchol 300 mg/d Mean ± SD N=20**	**Aramchol 100 mg/d Mean ± SD N=18**	**Placebo Mean ± SD N=19**
Pre-treatment	4.6 ± 2.5	5.4 ±2.8*	6.4 ±2.9
Post-treatment	5.9±2.1	5.7±3.9	6.6±2.3
Change	1.28±2.92	0.27±3.42	0.23±2.42
P value**	0.453	0.8979	

N = number of patients

SD = standard deviation

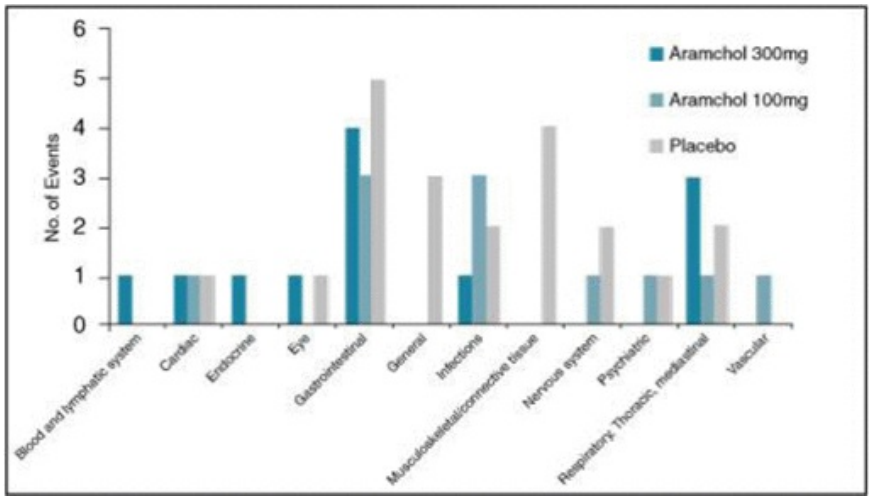
* N = 16 for this data point.

** P value is determined according to an analysis of covariance using the Dunnett method, or a multiple comparison method, for the difference between treatment group and placebo, adjusted for age, gender, diagnosis, baseline HbA1c and baseline weight.



The improvement in endothelial function suggests a positive effect on metabolic syndrome, specifically on vascular function.

Furthermore, treatment with aramchol was well-tolerated. There were no notable changes in biochemical, hematological, cardiovascular or other safety parameters, and there were no serious drug related adverse events during the three month treatment period or the subsequent recovery period. Aramchol's adverse event profile was comparable to that of the placebo, as portrayed in the chart below.



The results of our Phase IIa clinical trial of aramchol in the peer-reviewed Clinical Gastroenterology and Hepatology Journal were published in December 2014. The trial manuscript, entitled "The Fatty Acid-Bile Acid Conjudgate Aramchol Reduced Liver Fat Content in Patients with Nonalcoholic Fatty Liver Disease," provides the full report of the Phase IIa trial, which was completed in January 2012 and presented at the 47th Annual Meeting of the European Association for the Study of the Liver in 2012.

Phase I Trials

Aramchol was evaluated in two Phase I clinical trials to study its safety, tolerability and PK profile in healthy volunteers, in both single and multiple dose administrations. The first Phase I clinical trial was an escalating single-dose trial conducted in 16 subjects testing single aramchol doses in the range of 30 mg to 900 mg. The subsequent Phase I clinical trial was a repeated-dose trial conducted over four days in 25 subjects testing repeated daily doses of aramchol of 30 mg and 300 mg. The profiles for the groups were similar and the maximal plasma concentration of aramchol increased with the higher doses. The PK profile demonstrated that aramchol is suitable at each dose for once-daily administration and there were neither significant adverse events observed in either Phase I trial nor any notable changes in biochemical, hematologic, cardiovascular or other safety parameters.

Additional Preclinical and Clinical Studies Required for Regulatory Submissions

The tolerability of aramchol has been demonstrated in toxicity studies performed in rats (up to six months) and dogs (up to nine months), as well as reproductive studies in rats and rabbits. More recently, we conducted a food effect and PK study in 66 healthy volunteers to evaluate the PK of aramchol following single and multiple escalating doses (200mg, 400mg and 600mg), as well as to evaluate the effect of a high-fat, high-calorie meal on the PK of aramchol following a single dose (600mg) in healthy volunteers. The safety and tolerability of aramchol was assessed during the study period.

The results showed dose-related, but less than dose-proportional, increases in the mean aramchol plasma concentrations, or Cmax, area under the curve, or AUC (0-t), and AUC (inf) of 200 mg, 400 mg and 600 mg doses administered under fasting conditions or following a light meal, both at single and repeated dose administration. Cmax and AUC are metrics used to indicate the significance of a drug's exposure. Steady-state was achieved by 144 hours (day seven). Administration of aramchol after a high-fat, high-calorie meal afforded a 2.6 fold increase in exposure, as measured by Cmax, AUC(0-t), and AUC(inf) compared to the fasting group.

The clinical exposure level observed after daily repeat dosing at 600 mg for ten days was used to determine a safety margin of greater than 50 times when compared to the maximum exposure levels detected in the nine month dog toxicology study (after allometric scaling).

The safety assessment demonstrated that all doses of aramchol administered during the study were safe and well-tolerated. No serious adverse events or deaths occurred during the study and only one patient withdrew due to an adverse event, which was categorized as unrelated to aramchol. Of the 27 adverse events reported in the study, 24 were considered to be unrelated to aramchol and three were considered to be possibly related (all three of which were mild). No clinically significant abnormalities related to any aramchol dose were noted in ECGs, laboratory results, vital signs or physical examinations.

Chronic Toxicology studies

Since the completion of the Phase IIa study, additional non-clinical chronic toxicology studies have been conducted in pharmacologically-relevant species to support the initiation of our ARREST Study and Phase III clinical studies. These studies were performed in compliance with the EMA's ICH M3 (R2) guidelines by WIL Research, a global contract research organization, at its facility in Holland. The studies are required in advance of the commencement of human clinical trials and marketing authorization for pharmaceuticals in Europe and the United States. The toxicity program for aramchol included repeat dose studies of up to six months in rats and up to nine months in dogs by oral administration, the intended clinical dose route. These studies demonstrated that aramchol was well-tolerated at the dose levels investigated with no-observed-adverse-effect-level, values of 1000 mg/kg/day in rats and 1500 mg/kg/day in dogs, the maximum feasible dose in both species. There were no observations noted in the rat study. The findings in the dog study were limited to changes in plasma lipids, including decreases in total blood cholesterol levels, LDL, HDL and phospholipids, and a slight increase in the size of the adrenal glands, which were considered to be an extension of the primary pharmacology of aramchol and non-toxic effects, and skin scales from week 13 onwards in all aramchol-treated groups, with a dose-related incidence. The decrease in total blood cholesterol levels in the dog study further supports our understanding of the positive effect of aramchol on lipids as we previously observed in our preclinical studies in other animals. After six months this was not accompanied by any microscopic alteration of the skin and therefore considered not toxicologically relevant. Preliminary results from the study show that after nine months the presence of scales in all aramchol-treated groups was accompanied by minor test item-related microscopic findings in the skin: Hyperkeratosis of the epidermis, correlating to the scales, and keratin plugs in the hair follicles (in males at 750/500 and 1500 mg/kg). After a 12-week treatment-free recovery period, fewer scales were noted and microscopically there was partial recovery. As these findings were minor and no clinical symptoms like scratching were noted, these findings were considered not adverse.

Aramchol was non-mutagenic in vitro in the Ames test and chromosomal aberrations test, each of which is a test to determine whether the subject chemical can cause mutations in the DNA of an organism. In addition, aramchol was not clastogenic, or a mutagenic agent giving rise to or inducing disruption or breakages of chromosomes, nor aneugenic, or a chemical agent that promotes the number of chromosomes in the nucleus of a cell to not be an exact multiple of the monoploid number of a particular species, in bone marrow micronucleus test in male rats at a 2000 mg/kg oral dose (the maximum recommended dose in accordance with ICH S2 (R1)).

Embryo-fetal development toxicity was assessed in rats and rabbits. No maternal or fetal development toxicity was observed in either species. The NOAEL for maternal and development toxicity was at least 1000 mg/kg in rats and 750 mg/kg in rabbits (the maximum feasible dose in both species).

No maximum tolerated doses were reached in the studies. A 50 fold safety margin exposure multiple was achieved in dogs but not in rats. However, for rats, at least three of the four ICH M3(R2) safety margin criteria were met, and for dogs all four criteria were met. Blood tests revealed a decrease in total blood cholesterol levels, including LDL, HDL and phospholipids, and there was a slight increase in the size of the adrenal glands of the dogs, which WIL Research assessed as a physiologic compensatory response to the decrease in blood cholesterol levels. WIL Research did not consider the decrease in blood cholesterol levels or the physiologic response of the adrenal glands as a toxic effect, but rather as a pharmacodynamic effect, which is a biochemical and physiological effect of the drug on the body. Based on the above, WIL Research concluded that the overall safety data for aramchol is sufficient to support the proposed Phase IIb clinical trial.

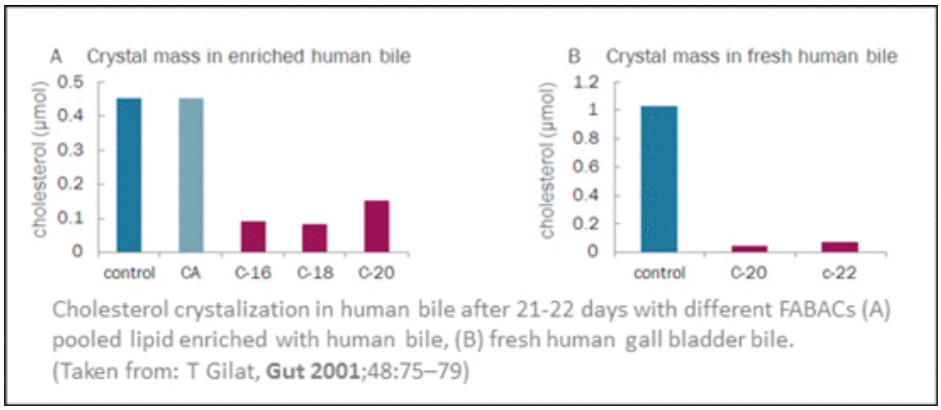
Aramchol Formulation Development

There has been a progression of the formulations of aramchol used so far in the preclinical and clinical studies. In the Phase IIa study, we administered a simple compressed tablet form that was developed directly from the suspension used in the Phase Ia and Ib studies and the preclinical studies in animals. Upon completion of our Phase IIa study, drug product formulation options were reviewed comprehensively, leading to the development of an immediate release tablet formulation for aramchol. Based on this formulation, aramchol tablets with matching placebos at 400 mg and 200 mg strengths have been developed to enable the convenient administration of 400 mg and 600 mg doses (for a 600 mg dose, patients will administer one 400 mg tablet and one 200 mg tablet). At the end of our Phase IIb study, we expect to determine the efficacious dose (400 mg or 600 mg). In case we select 600 mg, there may be an additional development of a single dose tablet of 600 mg.

Notwithstanding the foregoing, the optimized conventional tablet for the aramchol free acid form may be suitable for Phase III clinical trial and commercial use, subject to minor alterations for dosage strength after confirmation of the efficacious dose. If we decide to develop the formulations of aramchol salts due to the improvement in solubility and bioavailability and longer patent protection, we may conduct an appropriate bioequivalence studiy, or studies of the biological equivalence of two proprietary preparations of a drug, prior to administering an aramchol salt formulation to patients in our clinical studies.

Potential Use of Aramchol to Treat Cholesterol Gallstones

Cholesterol gallbladder stones, or cholesterol gallstones, are mostly composed of cholesterol, for which bile is the only significant pathway for excretion from the body. Given that phospholipids have been recognized as the major natural cholesterol solubilizers in bile, and which also possess anti-crystallizing activity, we hypothesize that aramchol, which increases the proportion of phospholipids in bile, will be able to prevent or reduce the precipitation of cholesterol gallstones and also clear existing stones. Preliminary in-vivo and in-vitro studies conducted by the Company have shown that aramchol prevents the formation of cholesterol crystals in the gallbladders of hamsters and mice and is able to dissolve existing cholesterol crystals. The chart below shows that the levels of cholesterol crystallization in human bile is lower after the addition of FABACs to the bile, including aramchol (C-20).



Cholesterol crystalization in human bile after 21-22 days with different FABACs (A) pooled lipid enriched with human bile, (B) fresh human gall bladder bile. (Taken from: T Gilat, **Gut 2001**;48:75–79)

Cholesterol gallstones is a common disorder in the Western world, largely due to dietary and life style factors. According to Schiff's Diseases of the Liver in 2006, gallstones are present in about 10% of the general population, and cholesterol gallstones comprise approximately 80% of such gallstones. In addition, patients who undergo bariatric surgery commonly develop gallstones as a result of such surgery. Almost a quarter of all cholesterol gallstone carriers develop pain as a result of their cholesterol gallstones, as well as complications, and up to half of these carriers eventually undergo surgery to have their cholesterol gallstones removed. Currently, laparoscopic cholecystectomy is the main treatment option for cholesterol gallstones. Surgery is, however, expensive and may cause morbidity and even mortality in high-risk populations, such as the elderly and those with co-morbidities. We expect that the dissolution of cholesterol gallstones using aramchol will only cost a fraction of the price of surgery and will eliminate the mortality and morbidity associated with laparoscopic and open surgery. We also expect aramchol to become an alternative treatment for patients for whom surgery carries a high risk, such as the elderly population, patients with suspected abdominal adhesions and patients with heart, lung or renal problems. Further studies are required to determine whether intermittent maintenance therapy will be required following dissolution of the cholesterol gallstones.

On November 13, 2014, we commenced an open-label Phase IIa proof-of-concept clinical trial of aramchol for the treatment of cholesterol gallstones. The Phase IIa trial is being conducted at the Assuta Medical Center in Tel Aviv, Israel and is a single center, randomized, double blind, placebo controlled study, designed to evaluate the efficacy and safety of a once-daily dose of aramchol for three months in 36 adult patients. The primary endpoint of the trial is a complete dissolution of newly formed cholesterol gallstones following bariatric surgery. Secondary endpoints include a decrease of more than 50% in the number of newly formed gallstones, prevention of the formation of additional gallstones during the trial period and dissolution of biliary sludge. We anticipate reporting top line results in the second half of 2015.

We are party to an agreement with Aventis Pharma Deutschland GmbH, or Aventis, which merged with Sanofi S.A. and the company is now called Sanofi S.A., pursuant to which we are obligated to pay Aventis a 10% royalty on sales of aramchol that are indicated for the treatment and prevention of cholesterol gallstones. See "Item 4.B. Information on the Company—Business Overview—Strategic Collaborations, Research Arrangements and other Material Agreements—Aventis Pharma Deutschland GmbH."

Potential Use of Aramchol to Treat Lipodystrophy

Lipodystrophy is a medical condition characterized by abnormal or degenerative conditions of adipose tissue, or body fat, including the loss of body fat from various regions of the body and its redistribution and accumulation in other areas. Lipodystrophy may be hereditary, but is commonly associated with HIV and AIDS patients who develop lipodystrophy from treatment with highly active antiretroviral therapies, or HAARTs, or other protease inhibitors. There is currently no approved medical treatment for lipodystrophy or its associated conditions. According to AIDS Reviews, 2005, approximately 40% of HIV patients treated for over one year with a protease inhibitor will develop induced lipodystrophy. Patients with HAART-induced lipodystrophy may also develop NAFLD with some of such patients progressing to cirrhosis, hypertriglyceridemia, or high triglyceride blood levels, or diabetes. In our Phase IIa clinical trial of aramchol in 60 NAFLD patients, we observed a significant reduction in liver fat and improvement of certain metabolic parameters. In February 2015, we entered into an Investigator Initiated Trial Agreement with the University of California, San Diego to conduct a proof-of-concept phase IIa study in 50 HIV-positive patients with lipodystrophy and nonalcoholic fatty liver disease, or the LD Study. The LD Study principal investigator is Dr. Rohit Loomba, a member of our scientific advisory board. The LD Study will be a single center, randomized, double blinded, placebo-controlled study. The LD Study is designed to evaluate the efficacy of a 600 mg oral, daily dosing of aramchol in HIV-positive patients with lipodystrophy and nonalcoholic fatty liver disease over 16 weeks of treatment. The primary endpoint of the trial is the improvement in hepatic steatosis assessed by MRS. The secondary endpoint includes the improvement of total body fat content and serum alanine aminotransferase, an enzyme found mainly in the liver that is present in higher than normal levels in the blood when the liver is damaged or diseased, and aspartate aminotransferase, an additional enzyme found in red blood cells and liver tissue, among other places, that is present in higher than normal levels in the blood when the liver is diseased or damaged.

On June 9, 2014, we filed a provisional patent application in the United States for the use of aramchol for the treatment of lipodystrophy.

Other Indications

After conducting market research, at this point in time we have decided not to pursue the indications of feline fatty liver or chemotherapy-associated steatohepatitis for aramchol due to what we believe is limited commercial potential for aramchol for such indications.

Potential Future Biomarkers for Non-Invasive Diagnosis of NAFLD and NASH

Currently, the initial diagnosis of NAFLD and/or NASH is based on elevated levels of liver enzymes, such as serum ALT levels, in blood tests. Once further evaluation excludes other reasons for liver disease, such as medications, viral hepatitis or excessive alcohol use, non-invasive imaging tests such as ultrasound, CT scans and MRS are good indicators of the presence of NAFLD and/or NASH. However, such tests are not reliable in assessing the degree of inflammation and fibrosis which would distinguish between the diseases. Moreover, some of these tests suffer from high rates of false negatives; up to 20% in ultrasound and CT scans. Necro inflammation, or premature cell death coupled with inflammation, hepatocellular ballooning, or a form of liver cell death, and the degree of fibrosis strongly predict the risk of disease progression, all are based on histology. Therefore, the liver biopsy is the standard approach for the diagnosis of inflammation and fibrosis associated with NASH and NAFLD, and the differentiation between them. However, the procedure-related morbidity, pain, sample errors and costs limit its use.

The current lack of specific, non-invasive diagnostic tools for patient monitoring and clinical drug development for NAFLD and NASH presents a major challenge to the scientific and medical communities. Initiation of treatment depends on an accurate diagnosis of NASH, which for now can only be arrived at by biopsy, thus limiting patient care and prognosis. We believe that a non-invasive, reliable diagnostic tool is also needed for the assessment of the efficacy of treatment in a particular patient with NAFLD or NASH, once treatment is initiated.

In light of this unmet need, new non-invasive methods for the diagnosis of NASH have been developed or are currently under development. Among those, MRS is a validated, commonly used and non-invasive technique for in-vivo fat quantification. According to an article in the Journal of Hepatology in 2004, MRS is routinely used for measuring triglycerides and potentially other liver fat components and is increasingly being used as an endpoint in clinical trials and observational studies, as is the case in our ARREST Study of aramchol. If we are successful in our clinical trials in correlating fat reduction in the liver as measured by MRS with aramchol's effect on inflammation in the liver, MRS may become a non-invasive biomarker with the ability to measure the effect of aramchol in patients following treatment with the drug.

However, MRS does not measure inflammation, and thus the need for additional markers must still be addressed. As such, there is currently a growing interest in clinical prediction algorithms and biomarkers, such as the NAFLD fibrosis score, Enhanced Liver Fibrosis panel score and circulating biomarkers, such as CK-18, which is a marker of inflammation.

Recognizing this unmet need, we are collaborating with OWL, which developed the proprietary OWL LIVERTest®, a test seeking to stratify patients according to their metabolites profile. By correlating the findings of OWL LIVERTest® with liver biopsies in the patients enrolled in our studies, we are working towards finding a specific non-invasive test which would predict individual responses to aramchol, which we believe could increase the likelihood of success of our Phase III trials and facilitate the market adoption of aramchol, although there is no assurance. On February 6, 2015, we entered into a term sheet with OWL with respect to the foregoing. See "Item 4.B. Information on the Company—Business Overview—Strategic Collaborations, Research Arrangements and other Material Agreements—OWL."

We hope that our efforts will lead to the identification of specific biomarkers, which will differentiate NASH from NAFLD patients without the need for liver biopsy, and serve as a tool for the prediction and assessment of aramchol's efficacy. The identification of such specific biomarkers would greatly improve aramchol's chances of qualifying for reimbursement from third-party payors, by providing an indication of the patients who are most likely to benefit from treatment with aramchol. We do not expect to generate any revenue directly from such biomarkers.

Strategic Collaborations, Research Arrangements and other Material Agreements

OWL

On February 6, 2015, we entered into a non-binding term sheet with OWL, or the OWL Term Sheet, with respect to developing a companion diagnostic tool that would predict individual responses to aramchol, which we believe could increase the likelihood of success of our Phase III trials and facilitate the market adoption of aramchol. Pursuant to the OWL Term Sheet, we or GRD have an option, which is exercisable at any time until December 31, 2016, to obtain a worldwide, exclusive license for all indications for a companion diagnostic based on OWL liver technologies, or OWLiverGAL. OWLiverGAL is intended to be a set of biomarkers detectable in the plasma or serum of patients suffering from NAFLD/NASH that will allow physicians and other authorities to treat and follow-up with the patients without the need for a liver biopsy. The OWL Term Sheet provides that we and OWL will use our best efforts to enter into definitive agreements within four months following a two month due diligence period. We may terminate the OWL Term Sheet upon thirty days' prior written notice to OWL.

Upon execution of the OWL Term Sheet, we advanced to OWL €50,000, which is to be applied by OWL to research and development as set forth in the work plan included in the OWL Term Sheet. If we enter into a definitive agreement with OWL, then at such time we will fund the first year of the work plan, less a credit for the €50,000 that we already advanced to OWL. Additionally, we will fund the second year of the work plan on a quarterly basis in advance of each applicable quarter. We have also agreed to make certain milestone payments to OWL in the amounts of €75,000 and €100,000 upon obtaining successful interim results of the ARREST Study and the successful completion of the ARREST Study, respectively, and in return for such milestone payments, OWL will issue us a corresponding number of OWL's shares of common stock. Furthermore, we will have the option to purchase additional shares of OWL's common stock during any of OWL's subsequent financing rounds on the same terms and conditions as the most senior class of shareholders participating in such financing round. If aramchol becomes commercially available, we will pay OWL 10% of the cash payments we receive for the sale of the OWLiverGAL kit. We will own any new intellectual property associated with the companion diagnostic for aramchol that results from our collaboration with OWL.

Itamar Medical Ltd.

On September 29, 2014, we purchased 60 EndoPAT™ devices and accessories from, and entered into a collaboration with, Itamar to include an assessment of endothelial, or arterial, function in our ARREST Study of aramchol in NASH patients suffering from obesity and insulin resistance. The purchase price for the EndoPAT™ devices and accessories was approximately $750,000.

Aventis Pharma Deutschland GmbH

In September 2002, we entered into an agreement, which we refer to as the Aventis Agreement, with Aventis, which merged with Sanofi S.A. and the company is now called Sanofi S.A., in connection with the settlement of court proceedings regarding an invention covered by Israeli patent application 123998 and PCT/IL99/00173. The invention relates to certain FABACs, pharmaceutical compositions containing FABACs and the use of FABACs for dissolving cholesterol gallstones in bile and preventing the formation thereof, as well as for the prevention and reduction of atherosclerosis, or the hardening of the arteries. Such court proceedings resulted from a claim filed by us and Prof. Tuvia Gilat, our founder, in the Tel- Aviv District Court seeking a declaratory judgment that Prof. Gilat was the sole inventor of the invention and the owner of all rights in and to the invention and the patent application with respect thereto, and that neither Aventis nor anyone on its behalf has any rights in or to the invention or such patent application. We filed the claim with Prof. Gilat based on assertions by Aventis that it had certain rights to the invention as a result of the participation of one of its employees in the discovery of the same. Under the Aventis Agreement, Aventis agreed that we had the exclusive worldwide right to commercialize the invention and we agreed to pay Aventis a royalty of 10% in respect of all income that we or our affiliates may receive from the commercialization of such invention for the prevention and treatment of cholesterol gallstones (less certain standard deductions, including taxes, credits, allowances, rebates, freight and insurance costs), for as long as there is a valid patent or pending patent application covering such invention. Once all valid patents covering the invention expire, which will occur in 2018, and provided that one of Aventis' other patents that covers an aspect of the invention is still valid and has received marketing approval prior to the expiration of all the patents covering the invention, the royalty will be reduced to 5%.

The Aventis Agreement does not contain any diligence obligations that require us to exert any special efforts to develop a product for the prevention and treatment of cholesterol gallstones, nor are we contractually required to meet any milestones in respect of the development or commercialization of the invention. We have not yet paid, nor do we currently owe, any amounts to Aventis under the Aventis Agreement.

Perrigo API Ltd.

On January 28, 2015, the Company entered into a Manufacturing Services Agreement, or the Perrigo Agreement, with Perrigo API Ltd., or Perrigo, a subsidiary of Perrigo Company plc, for, among other things, the large-scale production of aramchol's API and the scale-up and manufacturing process optimization for large-scale production of the aramchol API. As such, the Company is currently in the process of transferring the development and scale-up process of the manufacturing process from Cambridge Major Laboratories to Perrigo. Pursuant to the Perrigo Agreement, Perrigo will provide manufacturing process optimization services for large-scale production of the aramchol API, manufacture the aramchol API pursuant to current good manufacturing practices, or cGMP, and perform additional development services regarding scale-up and manufacturing optimization for the aramchol API. In consideration for the services to be provided by Perrigo, the Company agreed to pay in accordance with the Perrigo Agreement a maximum aggregate amount of approximately $3.6 million U.S. dollars to Perrigo. The Perrigo Agreement also provides Perrigo, under certain circumstances, with the option to manufacture commercial supplies of the aramchol API in the future.

University of California, San Diego

On February 2015, we entered into an Investigator Initiated Trial Agreement with the University of California, San Diego to conduct the LD Study. The LD Study principle investigator is Dr. Rohit Loomba, a member of our scientific advisory board. The LD Study will be a single center, randomized, double blinded, placebo-controlled study. The LD Study is designed to evaluate the efficacy of a 600 mg oral, daily dosing of aramchol in HIV-positive patients with lipodystrophy and nonalcoholic fatty liver disease over 16 weeks of treatment. The primary endpoint of the trial is the improvement of hepatic steatosis assessed by MRS. The secondary endpoint includes the improvement of total body fat content and serum alanine aminotransferase and aspartate aminotransferase.

Competition

The pharmaceutical industry is characterized by rapidly evolving technology, intense competition and a highly risky, costly and lengthy research and development process. Adequate protection of intellectual property, successful product development, adequate funding and retention of skilled, experienced and professional personnel are among the many factors critical to success in the pharmaceutical industry.

We believe that aramchol offers key potential advantages over other drugs in development that could enable aramchol, if approved for these indications, to capture meaningful market share. We believe that aramchol's ability, as observed in our studies to date, to reduce liver fat content without adverse side effects, which we believe may prove to have an anti-inflammatory effect, and convenient once-daily oral administration make aramchol a potentially valuable drug for the treatment of liver disease.

Other companies, including Intercept Pharmaceuticals, Inc., Genfit S.A. and Gilead Sciences, Inc. have agonists and antibodies in Phase II or earlier stages of clinical development for the treatment of NASH and the fibrosis associated therewith. Antibodies cannot be delivered orally. Some of these companies are focusing their trials on NASH patients with advanced fibrosis, whereas our studies relate to NASH, or the onset of fat accumulation in and inflammation of the liver, in which we expect that aramchol will reduce and eventually eliminate liver inflammation by reducing the fat content of the liver.

We believe that the characteristics of aramchol, as exhibited in our clinical studies to date, including its convenient once-daily oral administration and lack of observable adverse side effects, position it well against the potential competition in the NASH market. Currently used treatments are not approved by applicable regulatory authorities for the indication they are prescribed or used for as they have not proven efficacious in well-designed clinical studies. In addition, drugs in development for the treatment of NASH may, according to published data, be injectable or require intravenous delivery and may cause side effects, such as dyslipidemia, or an abnormal amount of lipids in the blood, severe itching, which can be highly inconvenient for patients with chronic diseases, such as NASH, and which may result in low patient compliance.

Aside from laparoscopic cholecystectomy surgery, the only therapeutic product available for the treatment of cholesterol gallstones and for the prevention of cholesterol gallstones in selected cases, is the bile acid known as ursodeoxycholic acid, both of which have been shown in clinical studies to have low efficacy, slow action and are characterized by cholesterol gallstone recurrence. We are not aware of any other company that has a new product candidate in development for the treatment of cholesterol gallstones. Our preclinical studies demonstrated that aramchol prevents and treats cholesterol gallstones without adverse effects, and we currently have an ongoing proof-of-concept Phase IIa clinical trial for the treatment of patients with cholesterol gallstones.

Notwithstanding the foregoing, see "Item 3. Key Information—Risk Factors—Risks Related to Our Business, Industry and Regulatory Requirements—Our market is subject to intense competition. If we are unable to compete effectively, aramchol or any other product candidate that we develop may be rendered noncompetitive or obsolete."

Intellectual Property and Patent Strategy

The proprietary nature of, and protection for, our product candidates and our discovery programs, processes and know-how are important to our business. We own patent rights to aramchol in various jurisdictions worldwide, including within and outside of Israel. We have sought patent protection in the United States and internationally for aramchol and our discovery programs, and any other inventions to which we have rights, where available and when appropriate. We expect that patent protection covering the use of aramchol for the treatment of fatty liver will not expire until 2022 (2021 in Israel), subject to any applicable extensions then-available. Within Israel, we agreed to negotiate the grant of an exclusive license to Unipharm Ltd., or Unipharm, with respect to the use of patents within our first patent family covering the composition of matter of aramchol on to-be-agreed upon terms and conditions. We are not in negotiations with Unipharm and no definitive agreement has been executed as of the date hereof. Should we decide to commercialize aramchol for the treatment and prevention of cholesterol gallstones in any country of the world, we will be obligated to pay Aventis a 10% royalty on related sales. See "Item 4. Information on the Company—Business Overview—Potential Use of Aramchol to Treat Cholesterol Gallstones", "Item 4.B. Information on the Company—Business Overview—Strategic Collaborations, Research Arrangements and other Material Agreements." and "Item 10. Additional Information—Material Contracts."

Our policy is to pursue, maintain and defend patent rights, whether developed internally or licensed from third parties, and to protect the technology, inventions and improvements that are commercially important to the development of our business. We also rely on trade secrets that may be important to the development of our business.

Patent Portfolio for Aramchol (First-in-Class Synthetic FABAC)

The patent portfolio for aramchol contains patents and pending patent applications directed to composition of matter, manufacturing methods and methods of use. As of February 5, 2015, we own five U.S. patents, one pending U.S. patent application and corresponding foreign patents and pending patent applications, as detailed below. We have also recently filed a PCT patent application for second generation FABAC compounds.

The first patent family discloses and claims FABACs, including aramchol, as well as methods for preventing or dissolving cholesterol gallstones in bile and reducing or preventing arteriosclerosis using FABACs. This patent family includes three issued U.S. patents and an issued European patent that was validated in Austria, Belgium, Cyprus, Denmark, Finland, France, Germany Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, Monaco, Netherlands, Portugal, Romania, Slovenia, Spain, Sweden, Switzerland and the United Kingdom. Corresponding patents have been granted in Australia, Brazil, Canada, China, Czech Republic, Eurasia, Hungary, Indonesia, Israel, Japan, Korea, Mexico, New Zealand, Norway, Poland, Turkey and the Ukraine. Foreign patent applications are pending in the Czech Republic and Norway, and patent applications in Brazil and Hungary have been allowed. If the appropriate maintenance, renewal, annuity or other governmental fees are paid, the non-extended patent term for this patent family is due to expire on March 25, 2019, with the exception of the Israeli patent, which is due to expire on April 8, 2018.

The second patent family discloses and claims additional FABACs with different conjugation moieties, as well as the use of these and the compounds disclosed in the first patent family above, including aramchol, in the treatment of fatty liver, reduction of serum cholesterol and treatment of hyperglycemia and diabetes. This patent family includes a U.S. patent directed to the treatment of fatty liver and a U.S. patent directed to reduction of serum cholesterol by administering additional forms of FABACs. A Continuation-in-Part application is directed to the treatment of a disease or disorder associated with an altered glucose metabolism or insulin action, such as hyperglycemia, diabetes, insulin resistance and obesity. The application has been allowed with claims directed to the treatment of hyperglycemia and diabetes. This patent family also includes two European patents that were validated in Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Monaco, Netherlands, Portugal, Spain, Sweden, Switzerland, Turkey and the United Kingdom, as well as patents in Australia, Canada, China, Czech Republic, Eurasia, Indonesia, Japan, Korea, Israel, Mexico, New Zealand, Norway, Poland and the Ukraine. Foreign patent applications are pending in Hungary and the Czech Republic. If the appropriate maintenance, renewal, annuity or other governmental fees are paid, the non-extended patent term for this patent family is due to expire on April 15, 2022, with the exception of the Israeli patent, which is due to expire on April 17, 2021. The terms of the U.S. patents in this family have been extended due to patent term adjustments of 567 days for U.S. Patent 7,501,403, which is directed to the treatment of fatty liver, and 24 days for U.S. Patent 8,110,564, which is directed to reduction of serum cholesterol.

A third patent family that is due to expire on February 1, 2030, discloses the use of FABACs in the treatment, prevention and inhibition of progression of Alzheimer's Disease, cerebral amyloid angiopathy and other brain diseases characterized by amyloid plaque deposits. This patent family includes pending patent applications in the United States, Europe (decision to grant issued) and Israel.

A fourth patent family, including one PCT patent application, discloses and claims second generation FABAC compounds.

A fifth patent family, including one provisional patent application, covers the use of aramchol for the treatment of lipodystophy.

It is possible that the term of the patents issued in the United States within our first patent family, which includes the composition of matter patents, may be extended up to five additional years under the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act. Patent term extension or supplementary protection certificates may be available in certain foreign countries upon regulatory approval. Independent of patent term extensions, five years of data exclusivity may be provided for this patent in the United States automatically from the day of receiving FDA approval of an NCE in the United States. If the Company pursues commercialization of aramchol in other jurisdictions, longer periods of data exclusivity may pertain.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of our current and future product candidates and the methods used to develop and manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products depends on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. We believe that our patents provide broad and comprehensive coverage for the use of aramchol for the treatment of certain liver diseases. However, the patent positions of biopharmaceutical companies, such as ourselves, are generally uncertain and involve complex legal and factual questions. Our ability to maintain and solidify our proprietary position for the technology will depend on our success in obtaining effective claims and enforcing those claims once granted. There is no certainty that any of the Company's pending patent applications will result in the issuance of any patents. The issued patents and those that may be issued in the future, may be challenged, narrowed, circumvented or found to be invalid or unenforceable, which could limit our ability to stop competitors from marketing related products or the length of term of patent protection that we may have for our products. In addition, our competitors may independently develop similar technologies or duplicate any technology developed by us, and the rights granted under any issued or future patents may not provide us with any meaningful competitive advantages against these competitors. Furthermore, because of the extensive time required for development, testing and regulatory review of a potential product, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of such patent. For more risks associated with the protection of our licensed intellectual property, see "Item 3. Key Information—Risk Factors—Risks Related to Our Intellectual Property."

Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. Trade secrets and know-how can be difficult to protect. We seek to protect our proprietary processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. These agreements are designed to protect our proprietary information. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, such agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors or others.

Seasonality

Our business and operations are generally not affected by seasonal fluctuations or factors.

Raw Materials and Suppliers

We believe that the raw materials that we require to manufacture aramchol are readily available commodities commonly used in the pharmaceutical industry. Demand for certain of the required raw materials, such as cholic acid, has recently increased, resulting in a price increase. Although there is no assurance, we anticipate that the price levels of cholic acid will revert back to prior levels and will not experience continued volatility as a result of the entrance of additional manufacturers into the cholic acid market.

Manufacturing

We do not own or operate manufacturing facilities for the production of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on third-party contract manufacturers for all of our required raw materials, API and finished product for our preclinical research and clinical trials, including our ARREST Study for aramchol for the treatment of NASH. We do not have long-term agreements with any of these third parties. We also do not have any current contractual relationships for the manufacture of commercial supplies of our product candidate if it is approved; however, the Perrigo Agreement (as described below) provides Perrigo with the option to negotiate an exclusive commercial contract for the manufacture of commercial supplies of the aramchol API in the future for a minimum term of five years. If our product candidate or future product candidates are approved by any regulatory agency, we intend to enter into agreements with a third-party contract manufacturer and one or more back-up manufacturers for the commercial production of those products. Development and commercial quantities of any products that we develop will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA and the regulatory agencies of other jurisdictions in which we are seeking approval. We currently employ internal resources to manage our manufacturing contractors. The relevant manufacturers of our drug products for our current preclinical and clinical trials have advised us that they are compliant with both cGMP and current Good Laboratory Practices, or cGLP.

There can be no assurance that our product candidate, if approved, can be manufactured in sufficient commercial quantities, in compliance with regulatory requirements and at an acceptable cost. We and our contract manufacturers are, and will be, subject to extensive governmental regulation in connection with the manufacture of any pharmaceutical products or medical devices. We and our contract manufacturers must ensure that all of the processes, methods and equipment are compliant with cGMP and cGLP for drugs on an ongoing basis, as mandated by the FDA and other regulatory authorities, and conduct extensive audits of vendors, contract laboratories and suppliers.

We currently use Cambridge Major Laboratories, a leading provider of chemistry services to the global pharmaceutical industry, to develop and manufacture aramchol clinical API. However, on January 28, 2015, we entered into the Perrigo Agreement with Perrigo, a subsidiary of Perrigo Company plc, for, among other things, the large-scale production of aramchol's API and the scale-up and manufacturing process optimization for large-scale production of the aramchol API. As such, the Company is currently in the process of transferring the development and scale-up of the manufacturing process from Cambridge Major Laboratories to Perrigo. See "Item 4.B. Information on the Company—Business Overview—Strategic Collaborations, Research Arrangements and other Material Agreements—Perrigo API Ltd." for a more information regarding the Perrigo Agreement.

Contract Research Organizations

We outsource certain clinical trial activities to CROs. Our clinical CROs comply with guidelines from the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, which attempt to harmonize the FDA, the EMA, and the Pharmaceuticals and Medical Devices Agency of Japan regulations and guidelines. We create and implement the drug development plans and manage the CROs according to the specific requirements of the drug candidate under development. To the extent clinical research is overseen by the CROs (or us in the future), compliance with certain federal regulations, including but not limited to 21 C.F.R. parts 50, 54, 56, 58 and 312, which pertain to, among other things, IRBs, informed consent, financial conflicts of interest by investigators, correct administration of treatment, follow up of adverse events, good laboratory practices and submitting IND applications, may be required.

Marketing, Sales and Commercialization

Given our stage of development, we do not have any internal sales, marketing or distribution infrastructure or capabilities. In the event we receive regulatory approval for aramchol, we intend, where appropriate, to pursue commercialization relationships, including strategic alliances and licensing, with pharmaceutical companies and other strategic partners, which are equipped to market and/or sell our products, if any, through their well-developed sales, marketing and distribution organizations in order to gain access to global markets. In addition, we may out-license some or all of our worldwide patent rights to more than one party to achieve the fullest development, marketing and distribution of any products we develop. Over the longer term, we may consider ultimately building an internal marketing, sales and commercial infrastructure.

Environmental Matters

We, our agents and our service providers, including our manufacturers, may be subject to various environmental, health and safety laws and regulations, including those governing air emissions, water and wastewater discharges, noise emissions, the use, management and disposal of hazardous, radioactive and biological materials and wastes and the cleanup of contaminated sites. We believe that our business, operations and facilities, including, to our knowledge, those of our agents and service providers, are being operated in compliance in all material respects with applicable environmental and health and safety laws and regulations. All information with respect to any chemical substance is filed and stored as a Material Safety Data Sheet, as required by applicable environmental regulations. Based on information currently available to us, we do not expect environmental costs and contingencies to have a material adverse effect on us. However, significant expenditures could be required in the future if we, our agents or our service providers are required to comply with new or more stringent environmental or health and safety laws, regulations or requirements.

Government Regulation and Product Approval

Governmental authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, packaging, promotion, storage, advertising, distribution, marketing and export and import of products such as those we are developing. Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States and by the Committee on Human Medicinal Products, or CHMP, via the EMA and European Commission through the MAA process before they may be legally marketed in Europe. Our product candidate and future product candidates will be subject to similar requirements in other countries prior to marketing in those countries. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

We are conducting a global development program for aramchol for the treatment of NASH in patients who also suffer from obesity and insulin resistance, and we may make our submissions for regulatory approval in parallel; initially in Europe and in the United States. Typically, approval time in the United States with the FDA for an NDA is faster than that within Europe with the EMA and the European Commission for an MMA, especially when the novelty of the submission is considered. First in class, high medical need and rare disease drugs can experience faster review. Nevertheless, marketing and pricing approval presents a further delay in many countries that should be considered in addition to the regulatory approvals noted above.

United States Government Regulation

NDA Approval Processes

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and implementing regulations. Failure to comply with the applicable U.S. requirements at any time during the product development process or approval process, or after approval, may subject an applicant to administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, warning letters, product seizures, total or partial suspension of production or distribution, or injunctions, fines, disgorgement, and civil or criminal penalties.

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

- completion of nonclinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices, or GLPs, or other applicable regulations;
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCPs, to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current Good Manufacturing Practices, or cGMPs, to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of FDA inspections of clinical sites and GLP toxicology studies; and
- FDA review and approval of the NDA.

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

Once a product candidate is identified for development, it enters the preclinical or nonclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some preclinical testing may continue after the IND is submitted. In addition to including the results of the nonclinical studies, the IND will also include a clinical trial protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. A clinical hold may occur at any time during the life of an IND, due to safety concerns or non-compliance, and may affect one or more specific studies or all studies conducted under the IND.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCPs and relevant FDA regulations. These regulations include the requirement that all research subjects provide informed consent. Further, an IRB must review and approve the plan for any clinical trial before it commences at any institution. An IRB considers, among other things, whether the risks to individuals participating in the trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative and must monitor the study until completed. All clinical trials must be conducted under protocols detailing the objectives of the trial, dosing procedures, research subject inclusion and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors must also report within set timeframes to FDA serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigation brochure, or any findings from other studies or animal or in-vitro testing that suggest a significant risk in humans exposed to the drug.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

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

- *Phase II.* Clinical trials are performed on a limited patient population intended to identify possible adverse effects and risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- *Phase III.* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. Phase III clinical trials are conducted to provide sufficient data for the statistically valid evidence of safety and efficacy.

Human clinical trials are inherently uncertain and Phase I, Phase II and Phase III testing may not be successfully completed. The FDA or the sponsor may suspend a clinical trial at any time for a variety of reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to the submission of an IND, at the end of Phase II and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice on the next phase of development. Sponsors typically use the meeting at the end of Phase II to discuss their Phase II clinical results and present their plans for the pivotal Phase III clinical trial that they believe will support the approval of the NDA. If a Phase II clinical trial is the subject of discussion at the end of Phase II meeting with the FDA, a sponsor may be able to request a Special Protocol Assessment, or SPA, the purpose of which is to reach agreement with the FDA on the Phase III clinical trial protocol design and analysis that will form the primary basis of an efficacy claim.

According to published guidance on the SPA process, a sponsor which meets the prerequisites may make a specific request for an SPA and provide information regarding the design and size of the proposed clinical trial. The FDA is supposed to evaluate the protocol within 45 days of the request to assess whether the proposed trial is adequate, and that evaluation may result in discussions and a request for additional information. An SPA request must be made before the proposed trial begins, and all open issues must be resolved before the trial begins. If a written agreement is reached, it will be documented and made part of the record. The agreement will be binding on the FDA and may not be changed by the sponsor or the FDA after the trial begins except with the written agreement of the sponsor and the FDA or if the FDA determines that a substantial scientific issue essential to determining the safety or efficacy of the drug was identified after the testing began. There is no indication that we will be able to meet the requirements necessary for an SPA.

Concurrent with clinical trials, sponsors usually complete any remaining animal safety studies and also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing commercial quantities of the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug and the manufacturer must develop methods for testing the quality, purity and potency of the drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its proposed shelf-life.

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests and other control mechanisms, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of user fees, but a waiver of such fees may be obtained under specified circumstances. We will seek a waiver of these fees as a small company submitting its first marketing application. If the waiver is granted it would not extend to establishment or product fees. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Submission of a pediatric assessment is not required for an application to market a product for an orphan-designated indication, and waivers are not needed at this time. However, if only one indication for a product has orphan designation, a pediatric assessment may still be required for any applications to market that same product for the non- orphan indication(s).

Once the submission is accepted for filing, the FDA begins an in-depth review. NDAs receive either standard or priority review. A drug representing a significant improvement in treatment, prevention or diagnosis of disease may receive priority review. The FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured and tested. The FDA will also inspect selected clinical sites that participated in the clinical studies and may inspect the testing facilities that performed the GLP toxicology studies cited in the NDA.

Expedited Review and Approval

NDAs receive either standard or priority review. A drug representing a significant improvement in treatment, prevention or diagnosis of disease may receive priority review. The FDA has various specific programs, including Fast Track, Breakthrough Therapy, Accelerated Approval and Priority Review, which are each intended to expedite the process for reviewing drugs, and in certain cases involving Accelerated Review, permit approval of a drug on the basis of a surrogate endpoint. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will be shortened. Generally, drugs that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development and expedite the review of drugs to treat serious or life-threatening diseases or conditions and fill unmet medical needs, and Breakthrough Therapy designation is designed to expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s). Priority review is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months as compared to a standard review time of ten months. Although Fast Track, Breakthrough Therapy designation and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track or Breakthrough Therapy designated drug and expedite review of the application for a drug designated for priority review. The FDA will also provide Breakthrough Therapy designated drugs intensive guidance on an efficient drug development program and provide these drug developers with an organizational commitment from the FDA involving senior managers. Since sponsors can design clinical trials in a number of ways, in providing its guidance for drugs designated as breakthrough therapies, the FDA will seek to ensure that the sponsor of the product designated as a breakthrough therapy receives timely advice and interactive communications in order to help the sponsor design and conduct a development program as efficiently as possible. During these interactions, the FDA may suggest, or a sponsor can propose, alternative clinical trial designs (e.g., adaptive designs, an enrichment strategy, use of historical controls) that may result in smaller trials or more efficient trials that require less time to complete. Such trial designs could also help minimize the number of patients exposed to a potentially less efficacious treatment (i.e., the control group treated with available therapy). Accelerated Approval, which is described in 21 C.F.R. § 314.500 *et seq*., provides for an earlier approval for a new drug that is intended to treat a serious or life-threatening disease or condition and that fills an unmet medical need based on a surrogate endpoint. A surrogate endpoint is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post- marketing clinical trials. Priority Review and Accelerated Approval do not change the standards for approval, but may expedite the approval process.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases, subpopulations, and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require us to conduct Phase IV testing, which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized.

Food and Drug Administration (FDA) Regulatory Pathways

The FDA has two main pathways for drug development. The first pathway is the "regular" or "traditional" pathway for drug approval, in which a drug is approved based on either a clinical benefit endpoint or a surrogate endpoint that is known to predict clinical benefit on irreversible morbidity or mortality. A clinical endpoint is one that affects how a patient feels, functions or survives.

The second option is the Accelerated Approval Pathway (21 CFR 314.510 and 601.41, Subpart H and E). Accelerated approval applies to drugs and biologics that are intended to treat serious and life threatening illness AND that provide meaningful therapeutic benefit over existing treatments.

Accelerated approval is based on effects of a surrogate endpoint that is "reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence to predict benefit" on irreversible morbidity or mortality. The Agency may grant accelerated approval to a product for a serious or life-threatening condition upon a determination that the product 1) has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or, 2) an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality and is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. The term "reasonable likely" implies that some uncertainty remains about the relationship of the surrogate to the clinical benefit to the patient. Therefore, accelerated approval is usually contingent on a sponsor's agreement to conduct additional post-approval studies to verify and describe the drug's clinical benefit. This regulatory pathway requires that when marketing approval is granted based on the surrogate, or a clinical endpoint other than survival or irreversible morbidity, clinical trials must be carried out after marketing approval to verify and describe the drug's clinical benefit. The preamble to the Accelerated Approval Rule, (Federal Register/Vol.57, No.239/Friday. December 11, 1992/Rules and Regulations), acknowledged that surrogate endpoints can be used for regular or traditional approval when these surrogates are validated by definitive studies. It states that "Ordinarily, products used to treat serious or life-threatening illness, for which approval is based on a surrogate endpoint that is recognized as validated by definitive studies, will be considered for approval under the traditional process rather that under accelerated approval." The Agency's draft Guidance for Industry - Expedited Programs for Serious Conditions—Drugs and Biologics (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf) states: "For purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Depending on the strength of the evidence supporting the ability of a marker to predict clinical benefit, the marker may be a surrogate endpoint that is known to predict clinical benefit (a validated surrogate endpoint, which could be used for traditional approval), a surrogate endpoint that is reasonably likely to predict a drug's intended clinical benefit (which could be used for accelerated approval), or a marker for which there is insufficient evidence to support reliance on the marker as either kind of surrogate endpoint (and thus cannot be used to support traditional or accelerated approval of a marketing application). Change in the rate of decline in renal function as measured by creatinine clearance, and changes in blood pressure and Hg A1C have been accepted as validated surrogates to support traditional drug approvals. However, the preamble does not specifically define the criteria for "validated by definitive studies" that allows a surrogate to be used for traditional approval. Therefore the level of evidence necessary to determine if a surrogate is validated (i.e., acceptable for traditional or regular approval pathways), or if a surrogate is reasonably likely to predict clinical benefit is made on a case-by-case basis by the Agency. Whether an endpoint is reasonably likely to predict clinical benefit is a function of the biological plausibility of the relationship between the disease, endpoint, and the desired effect, and the empirical evidence to support that relationship. The empirical evidence may include "epidemiological, pathophysiological, therapeutic, pharmacologic, or other evidence developed using biomarkers, for example, or other scientific methods or tools." Clinical data should be provided to support the assertion that a relationship of the surrogate or intermediate clinical endpoint to the outcome is reasonably likely, and should be relevant to the relationship between the specific endpoint to be used and the specific intended clinical benefit of the drug. What is clear is that there are pitfalls with using surrogates, i.e., examples of where a plausible surrogate that showed improvement with treatment resulted in an overall poor outcome for the patient. Some of these unexpected outcomes may be from off-target effects of a drug. Several things should be taken into consideration when evaluating a surrogate for use in the regular approval pathway. A surrogate that directly measures tissue loss or organ function e.g. liver failure is particularly plausible for use as an endpoint. Also helpful are the results of controlled trials that show the relationship of the effect on outcomes in trials of other drugs, especially trials involving drugs with different mechanisms, as is the case for example with antihypertensives. See Guidance "Expedited Programs for Serious Conditions—Drugs and Biologics": http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf for further details. As noted above, surrogate endpoints can be used as part of the regular approval pathway if these endpoints have been validated by definitive trials to predict outcomes on clinically meaningful endpoints. Surrogates may be used to support accelerated approval when there is not an established link of the surrogate to the clinical outcome. The long duration over which NASH evolves before patients develop clinical outcomes, and the inability to identify the population that will progress, creates a major challenge in designing and conducting clinical trials for those with early stage NASH. This challenge, however, does not diminish the need to develop therapeutics in these patients, and identify who is at risk of progression, given the growing contribution of progressive NASH to the burden of chronic liver disease. It is also important to identify endpoints that can be achieved within a reasonable time interval and that are reliable surrogates for meaningful outcomes. Moreover, these endpoints should both reflect changes in the disease process and be 'biologically plausible', in other words, linked mechanistically to the disease's pathogenesis.

Liver histology currently offers the best short-term method for tracking the progression of NASH. Certain features on histopathology provide some prognostic information regarding risk for progression. Steatohepatitis, not isolated fatty liver, is associated with a substantial increase in the long-term risk of developing cirrhosis and liver-related outcomes (15, 35). This is believed to be related to the underlying inflammation and activation of pro-fibrogenic pathways in NASH. Based on this current understanding of the pathogenesis of NASH, one would expect that reversal of steatohepatitis would reduce the risk of developing cirrhosis. However, steatosis and inflammation can decrease as fibrosis advances (37). Therefore, the reversal of steatohepatitis with no evidence of progression to advanced fibrosis (stage 3 or 4), may be an acceptable surrogate endpoint suitable both for phase 2b and 3 trials that enroll patients with NASH and evidence of early fibrosis.

On September 23, 2014, the FDA granted Fast Track designation status to aramchol for the treatment of NASH.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our product candidates, U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND, and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for extension must be made prior to expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five year and three year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Post-approval Requirements

Once an approval is granted, the FDA, European authorities and other regulatory authorities may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further regulatory authority review and approval. Some of these modifications, especially adding indications, would likely require additional clinical studies. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Any drug product manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things record-keeping requirements; reporting of adverse experiences with the drug; providing the FDA with updated safety and efficacy information; drug sampling and distribution requirements; notifying the FDA and gaining its approval of specified manufacturing or labeling changes; and complying with FDA promotion and advertising requirements.

Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP and other laws.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Reimbursement

Sales of our products will depend, in part, on the extent to which the costs of our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly challenging the prices charged for medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products after approved as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Modernization Act imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries under Part B. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Parts A and B, Part D reimbursement is not set by the government, but rather by private insurers. Moreover, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Recently, the Centers for Medicare & Medicaid Services proposed a rule that would enable Part D plans to offer fewer drugs than would otherwise be the case. The impact of this proposed rule on a product such as ours cannot be predicted at this time, but it could have a material adverse impact on our product were it being marketed at this time. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the Modernization Act may result in a similar reduction in payments from non-governmental payors.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Affordable Care Act, enacted in March 2010, is expected to have a significant impact on the health care industry. The Affordable Care Act is expected to expand coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, the Affordable Care Act is expected to expand and increase industry rebates for drugs covered under Medicaid programs and make changes to the coverage requirements under the Medicare Part D program. We cannot predict the impact of the Affordable Care Act on pharmaceutical companies. See "Item 3. Key Information—Risk Factors—Risks Related to Our Business, Industry and Regulatory Requirements—We expect the healthcare industry to face increased limitations on reimbursement, rebates and other payments as a result of healthcare reform, which could adversely affect third-party coverage of our products and how much or under what circumstances healthcare providers will prescribe or administer our products."

In addition, in some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States and generally tend to be significantly lower.

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 Medicare-Medicaid Anti-Fraud and Abuse Act, as amended (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 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 federal authorities.

European Economic Area

In addition to approval in the United States, we currently intend to seek regulatory approval of aramchol in the EU. As such, a summary of the EU regulatory processes follows below.

A medicinal product may only be placed on the market in the European Economic Area, or EEA, composed of the 28 EU member states, plus Norway, Iceland and Lichtenstein, when a marketing authorization has been issued by the competent authority of a member state pursuant to Directive 2001/83/EC (as recently amended by Directive 2004/27/EC), or an authorization has been granted under the centralized procedure in accordance with Regulation (EC) No. 726/2004 or its predecessor, Regulation 2309/93. There are essentially three community procedures created under prevailing European pharmaceutical legislation that, if successfully completed, allow an applicant to place a medicinal product on the market in the EEA.

Centralized Procedure

Regulation 726/2004/EC now governs the centralized procedure when a marketing authorization is granted by the European Commission, acting in its capacity as the European Licensing Authority on the advice of the EMA. That authorization is valid throughout the entire community and directly or (as to Norway, Iceland and Liechtenstein) indirectly allows the applicant to place the product on the market in all member states of the EEA. The EMA is the administrative body responsible for coordinating the existing scientific resources available in the member states for evaluation, supervision and pharmacovigilance of medicinal products. Certain medicinal products, as described in the Annex to Regulation 726/2004, must be authorized centrally. These are products that are developed by means of a biotechnological process in accordance with Paragraph 1 to the Annex to the Regulation. Medicinal products for human use containing a new active substance for which the therapeutic indication is the treatment of acquired immune deficiency syndrome, or AIDS, cancer, neurodegenerative disorder or diabetes must also be authorized centrally. Starting on May 20, 2008, the mandatory centralized procedure was extended to autoimmune diseases and other immune dysfunctions and viral diseases. Finally, all medicinal products that are designated as orphan medicinal products pursuant to Regulation 141/2000 must be authorized under the centralized procedure. An applicant may also opt for assessment through the centralized procedure if it can show that the medicinal product constitutes a significant therapeutic, scientific or technical innovation or that the granting of authorization centrally is in the interests of patients at the community level. For each application submitted to the EMA for scientific assessment, the EMA is required to ensure that the opinion of the Committee for Medicinal Products for Human Use, or CHMP, is given within 210 days after receipt of a valid application. This 210 days period does not include the time that the applicant to answer any questions raised during the application procedure, the so-called 'clock stop' period. If the opinion is positive, the EMA is required to send the opinion to the European Commission, which is responsible for preparing the draft decision granting a marketing authorization. This draft decision may differ from the CHMP opinion, stating reasons for diverging for the CHMP opinion. The draft decision is sent to the applicant and the member states, after which the European Commission takes a final decision. If the initial opinion of the CHMP is negative, the applicant is afforded an opportunity to seek a re-examination of the opinion. The CHMP is required to re-examine its opinion within 60 days following receipt of the request by the applicant. All CHMP refusals and the reasons for refusal are made public on the EMA website. Without a centralized marketing authorization it is prohibited to place a medicinal product that must be authorized centrally on the market in the EU.

Mutual Recognition and Decentralized Procedures

With the exception of products that are authorized centrally, the competent authorities of the member states are responsible for granting marketing authorizations for medicinal products placed on their national markets. If the applicant for a marketing authorization intends to market the same medicinal product in more than one member state, the applicant may seek an authorization progressively in the community under the mutual recognition or decentralized procedure. Mutual recognition is used if the medicinal product has already been authorized in a member state. In this case, the holder of this marketing authorization requests the member state where the authorization has been granted to act as reference member state by preparing an updated assessment report that is then used to facilitate mutual recognition of the existing authorization in the other member states in which approval is sought (the so-called concerned member state(s)). The reference member state must prepare an updated assessment report within 90 days of receipt of a valid application. This report together with the approved Summary of Product Characteristics, or SmPC (which sets out the conditions of use of the product), and a labeling and package leaflet are sent to the concerned member states for their consideration. The concerned member states are required to approve the assessment report, the SmPC and the labeling and package leaflet within 90 days of receipt of these documents. The total procedural time is 180 days.

The decentralized procedure is used in cases where the medicinal product has not received a marketing authorization in the EU at the time of application. The applicant requests a member state of its choice to act as reference member state to prepare an assessment report that is then used to facilitate agreement with the concerned member states and the grant of a national marketing authorization in all of these member states. In this procedure, the reference member state must prepare, for consideration by the concerned member states, the draft assessment report, a draft SmPC and a draft of the labeling and package leaflet within 120 days after receipt of a valid application. As in the case of mutual recognition, the concerned member states are required to approve these documents within 90 days of their receipt.

For both mutual recognition and decentralized procedures, if a concerned member state objects to the grant of a marketing authorization on the grounds of a potential serious risk to public health, it may raise a reasoned objection with the reference member state. The points of disagreement are in the first instance referred to the Co-ordination Group on Mutual Recognition and Decentralized Procedures, or CMD, to reach an agreement within 60 days of the communication of the points of disagreement. If member states fail to reach an agreement, then the matter is referred to the EMA and CHMP for arbitration. The CHMP is required to deliver a reasoned opinion within 60 days of the date on which the matter is referred. The scientific opinion adopted by the CHMP forms the basis for a binding European Commission decision.

Irrespective of whether the medicinal product is assessed centrally, de-centrally or through a process of mutual recognition, the medicinal product must be manufactured in accordance with the principles of good manufacturing practice as set out in Directive

2003/94/EC and Volume 4 of the rules governing medicinal products in the European community. Moreover, community law requires the clinical results in support of clinical safety and efficacy based upon clinical trials conducted in the European community to be in compliance with the requirements of Directive 2001/20/EC, which implements good clinical practice in the conduct of clinical trials on medicinal products for human use. Clinical trials conducted outside the European community and used to support applications for marketing within the EU must have been conducted in a way consistent with the principles set out in Directive 2001/20/EC. The conduct of a clinical trial in the EU requires, pursuant to Directive 2001/20/EC, authorization by the relevant national competent authority where a trial takes place, and an ethics committee to have issued a favorable opinion in relation to the arrangements for the trial. It also requires that the sponsor of the trial, or a person authorized to act on his behalf in relation to the trial, be established in the community.

National Procedure

This procedure is available for medicinal products that do not fall within the scope of mandatory centralized authorization. Specific procedures and timelines differ between member states, but the duration of the procedure is generally 210 days and based on a risk/efficacy assessment by the competent authority of the member state concerned, followed by determination of SmPC, package leaflet and label text/layout and subsequently grant of the marketing authorization. Marketing authorizations granted on this basis are not mutually recognized by other member states.

There are various types of applications for marketing authorizations:

- *Full Applications*. A full application is one that is made under any of the community procedures described above "stands alone" in the sense that it contains all of the particulars and information required by Article 8(3) of Directive 2001/83 (as amended) to allow the competent authority to assess the quality, safety and efficacy of the product and in particular the balance between benefit and risk. Article 8(3)(l) in particular refers to the need to present the results of the applicant's research on (i) pharmaceutical (physical-chemical, biological or microbiological) tests, (ii) preclinical (toxicological and pharmacological) studies and (iii) clinical trials in humans. The nature of these tests, studies and trials is explained in more detail in Annex I to Directive 2001/83/EC. Full applications would be required for products containing new active substances not previously approved by the competent authority, but may also be made for other products.

- *Abridged Applications*. Article 10 of Directive 2001/83/EC contains exemptions from the requirement that the applicant provide the results of its own preclinical and clinical research. There are three regulatory routes for an applicant to seek an exemption from providing such results, namely (i) cross-referral to an innovator's results without consent of the innovator, (ii) well established use according to published literature and (iii) consent to refer to an existing dossier of research results filed by a previous applicant.

Cross-referral to Innovator's Data

Articles 10(1) and 10(2)(b) of Directive 2001/83/EC provide the legal basis for an applicant to seek a marketing authorization on the basis that its product is a generic medicinal product (a copy) of a reference medicinal product that has already been authorized, in accordance with community provisions. A reference product is, in principle, an original product granted an authorization on the basis of a full dossier of particulars and information. This is the main exemption used by generic manufacturers for obtaining a marketing authorization for a copy product. The generic applicant is not required to provide the results of preclinical studies and of clinical trials if its product meets the definition of a generic medicinal product and the applicable regulatory results protection period for the results submitted by the innovator has expired. A generic medicinal product is defined as a medicinal product:

- having the same qualitative and quantitative composition in active substance as the reference medicinal product;

- having the same pharmaceutical form as the reference medicinal product; and

- whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies.

Applications in respect of a generic medicinal product cannot be made before the expiry of the protection period. Where the reference product was granted a national marketing authorization pursuant to an application made before October 30, 2005, the protection period is either six years or 10 years, depending upon the election of the particular member state concerned. Where the reference product was granted a marketing authorization centrally, pursuant to an application made before November 20, 2005, the protection period is 10 years. For applications made after these dates, Regulation 726/2004 and amendments to Directive 2001/83/EC provide for a harmonized protection period regardless of the approval route utilized. The harmonized protection period is in total 10 years, including eight years of research data protection and two years of marketing protection. The effect is that the originator's results can be the subject of a cross-referral application after eight years, but any resulting authorization cannot be exploited for a further two years. The rationale of this procedure is not that the competent authority does not have before it relevant tests and trials upon which to assess the efficacy and safety of the generic product, but that the relevant particulars can, if the research data protection period has expired, be found on the originator's file and used for assessment of the generic medicinal product. The 10 year protection period can be extended to 11 years where, in the first eight years post-authorization, the holder of the authorization obtains approval for a new indication assessed as offering a significant clinical benefit in comparison with existing products.

If the copy product does not meet the definition of a generic medicinal product or if certain types of changes occur in the active substance(s) or in the therapeutic indications, strength, pharmaceutical form or route of administration in relation to the reference medicinal product, Article 10(3) of Directive 2001/83/EC provides that the results of the appropriate preclinical studies or clinical trials must be provided by the applicant.

Well-established Medicinal Use

Under Article 10a of Directive 2001/83/EC, an applicant may, in substitution for the results of its own preclinical and clinical research, present detailed references to published literature demonstrating that the active substance(s) of a product have a well- established medicinal use within the community with recognized efficacy and an acceptable level of safety. The applicant is entitled to refer to a variety of different types of literature, including reports of clinical trials with the same active substance(s) and epidemiological studies that indicate that the constituent or constituents of the product have an acceptable safety/efficacy profile for a particular indication. However, use of the published literature exemption is restricted by stating that in no circumstances will constituents be treated as having a well- established use if they have been used for less than 10 years from the first systematic and documented use of the substance as a medicinal product in the EU. Even after 10 years' systematic use, the threshold for well-established medicinal use might not be met. European pharmaceutical law requires the competent authorities to consider among other factors the period over which a substance has been used, the amount of patient use of the substance, the degree of scientific interest in the use of the substance (as reflected in the scientific literature) and the coherence (consistency) of all the scientific assessments made in the literature. For this reason, different substances may reach the threshold for well-established use after different periods, but the minimum period is 10 years. If the applicant seeks approval of an entirely new therapeutic use compared with that to which the published literature refers, additional preclinical and/or clinical results would have to be provided.

Informed Consent

Under Article 10c of Directive 2001/83/EC, following the grant of a marketing authorization the holder of such authorization may consent to a competent authority utilizing the pharmaceutical, preclinical and clinical documentation that it submitted to obtain approval for a medicinal product to assess a subsequent application relating to a medicinal product possessing the same qualitative and quantitative composition with respect to the active substances and the same pharmaceutical form.

Law Relating to Pediatric Research

Regulation (EC) 1901/2006 (as amended by Regulation (EC) 1902/2006) was adopted on December 12, 2006. This Regulation governs the development of medicinal products for human use in order to meet the specific therapeutic needs of the pediatric population. It requires any application for marketing authorization made after July 26, 2008 in respect of a product not authorized in the European Community on January 26, 2007 (the time the Regulation entered into force), to include the results of all studies performed and details of all information collected in compliance with a pediatric investigation plan agreed by the Pediatric Committee of the EMA, unless the product is subject to an agreed waiver or deferral or unless the product is excluded from the scope of Regulation 1902/2006 (generics, hybrid medicinal products, biosimilars, homeopathic and traditional (herbal) medicinal products and medicinal products containing one or more active substances of well-established medicinal use). Waivers can be granted in certain circumstances where pediatric studies are not required or desirable. Deferrals can be granted in certain circumstances where the initiation or completion of pediatric studies should be deferred until appropriate studies in adults have been performed. The EMA does not evaluate an application for market authorization if there is no agreed PIP, deferral or waiver. Moreover, this regulation imposes the same obligation from January 26, 2009 on an applicant seeking approval of a new indication, pharmaceutical form or route of administration for a product already authorized and still protected by a supplementary protection certificate granted under Regulation EC 469/2009 and its precursor (EEC) 1768/92 or by a patent that qualifies for the granting of such a supplementary protection certificate. The pediatric Regulation 1901/2006 also provides, subject to certain conditions, a reward for performing such pediatric studies, regardless of whether the pediatric results provided resulted in the grant of a pediatric indication. This reward comes in the form of an extension of six months to the supplementary protection certificate granted in respect of the product, unless the product is subject to orphan drug designation, in which case the 10 year market exclusivity period for such orphan products is extended to 12 years. If any of the non-centralized procedures for marketing authorization have been used, the six month extension of the supplementary protection certificate is only granted if the medicinal product is authorized in all member states.

Post-authorization Obligations

In the pre-authorization phase the applicant must provide a detailed pharmacovigilance plan that it intends to implement post- authorization. An authorization to market a medicinal product in the EU carries with it an obligation to comply with many post- authorization organizational and behavioral regulations relating to the marketing and other activities of authorization holders. These include requirements relating to post-authorization efficacy studies, post-authorization safety studies, adverse event reporting and other pharmacovigilance requirements, advertising, packaging and labeling, patient package leaflets, distribution and wholesale dealing. The regulations frequently operate within a criminal law framework and failure to comply with the requirements may not only affect the authorization, but also can lead to financial and other sanctions levied on the company in question and responsible officers. As a result of the currently on-going overhaul of EU pharmacovigilance legislation the financial and organizational burden on market authorization holders will increase significantly, such as the obligation to maintain a pharmacovigilance system master file that applies to all holders of marketing authorizations granted in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004. Marketing authorization holders must furthermore collect data on adverse events associated with use of the authorized product outside the scope of the authorization. Pharmacovigilance for biological products and medicines with a new active substance will be strengthened by subjecting their authorization to additional monitoring activities. The EU is currently in the process of issuing implementing regulations for the new pharmacovigilance framework.

Any authorization granted by member state authorities, which within three years of its granting is not followed by the actual placing on the market of the authorized product in the authorizing member state ceases to be valid. When an authorized product previously placed on the market in the authorizing member state is no longer actually present on the market for a period of three consecutive years, the authorization for that product shall cease to be valid. The same two three year periods apply to authorizations granted by the European Commission based on the centralized procedure.

Israel

Clinical Testing in Israel

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

Israeli Ministry of Health

Israel's Ministry of Health, which regulates medical testing, has adopted guidelines that correspond, generally, to those of the FDA and the EMA, making it comparatively straightforward for studies conducted in Israel to satisfy FDA and the EMA requirements, thereby enabling medical technologies subjected to clinical trials in Israel to reach U.S. and EU commercial markets in an expedited fashion. Many members of Israel's medical community have earned international prestige in their chosen fields of expertise and routinely collaborate, teach and lecture at leading medical centers throughout the world.

Other Countries

In addition to regulations in the United States, the EU and Israel, we are subject to a variety of other regulations governing clinical trials and commercial sales and distribution of drugs in other countries. Whether or not our product candidate or future product candidates receive approval from the FDA, approval of such product candidates must be obtained by the comparable regulatory authorities of countries other than the United States before we can commence clinical trials or marketing of the product in those countries. The approval process varies from jurisdiction to jurisdiction, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials and product licensing vary greatly from country to country.

The requirements that we and our collaborators must satisfy to obtain regulatory approval by government agencies in other countries prior to commercialization of our products in such countries can be rigorous, costly and uncertain. In the European countries, Canada and Australia, regulatory requirements and approval processes are similar in principle to those in the United States. Additionally, depending on the type of drug for which approval is sought, there are currently two potential tracks for marketing approval in the European countries: Mutual recognition and the centralized procedure. These review mechanisms may ultimately lead to approval in all EU countries, but each method grants all participating countries some decision-making authority in product approval. Foreign governments also have stringent post-approval requirements including those relating to manufacture, labeling, reporting, record keeping and marketing. Failure to substantially comply with these on-going requirements could lead to government action against the product, us and/or our representatives.

Related Matters

From time to time, legislation is drafted, introduced and passed in governmental bodies that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA or EMA and other applicable regulatory bodies to which we are subject. The estimated size of the NASH patient population in the United States and in the five most-populated EU countries is presented in the diagram below. In addition, regulations and guidance are often revised or reinterpreted by the national agency in ways that may significantly affect our business and our therapeutic candidates. It is impossible to predict whether such legislative changes will be enacted, whether FDA or EMA regulations, guidance or interpretations will change, or what the impact of such changes, if any, may be. We may need to adapt our business and therapeutic candidates and products to changes that occur in the future. For information regarding the Company's corporate structure and its subsidiaries, see also "Item 4. Information on the Company—Historical Background and Corporate Structure" below.

Description of Property and Facilities

Our corporate headquarters are located at 8 Shaul Hamelech Blvd., Amot Mishpat Bldg., Tel Aviv, Israel, 6473307, where we lease and occupy approximately 78 square meters of space. The lease for our office expires in April 2016. The aggregate monthly rental payment, together with the maintenance fees, is approximately $2,542. Our headquarters do not include laboratory or product manufacturing facilities. Due to an increase in the number of employees, we have entered into a sublease agreement with GEMS Investment Research Ltd., for approximately 250 square meters of additional space in the same building, which expires on March 31, 2015. The aggregate monthly rental payment for the additional space is approximately $4,615, including maintenance fees and taxes. On March 22, 2015, we entered into a lease agreement with Mintz K. Construction Company Ltd., for approximately 356 square meters of space, which we refer to as the New Lease. The initial term of the New Lease expires on March 21, 2019, but we have an option to extend the term of the New Lease for two additional years after the expiration of the initial term. The aggregate monthly rental payment under the New Lease for the initial term, together with adjustments and the maintenance fees, is approximately $8,159.

In addition, in April 2014, we entered into a sublease agreement with Radix Organization Inc. for one office, which expires in May 2015. The aggregate monthly rental payment is approximately $1,980.

ITEM 4A. Unresolved Staff Comments.

Not applicable.

ITEM 5. Operating and Financial Review and Prospects.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with "Item 3. Key Information—Selected Financial Data" above and our financial statements and related notes that appear elsewhere in this annual report. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates and beliefs. Our actual results could differ materially from those discussed in the forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this prospectus, particularly in the sections titled "Risk Factors" and "Cautionary Note Regarding Forward-Looking Statements."

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of a novel, once-daily, oral therapy for the treatment of liver diseases and cholesterol gallstones utilizing our proprietary first-in-class synthetic FABAC called aramchol. We believe that aramchol has the potential to be a disease modifying treatment for fatty liver disorders, including NASH, which is a chronic disease that we believe constitutes a large unmet medical need.

On February 1, 2015, we began our ARREST Study, a multi-center, randomized, double-blind, placebo-controlled, dose-ranging Phase IIb clinical trial of aramchol in 240 biopsy-diagnosed NASH patients who also suffer from obesity and insulin resistance. Our ARREST Study for aramchol in NASH patients is in accordance with the study design recommended by the MHRA and has been deemed acceptable by the BfArM and deemed satisfactory by the ANSM. The study design has been confirmed by the FDA in a written pre-IND advice as acceptable for a Phase IIb study. The BfArM and ANSM also confirmed, in minutes of each of their respective scientific advisory meetings, that if successful, this ARREST Study may serve as a basis for Phase III pivotal trials of aramchol. The FDA and MHRA invited us to discuss the next steps in the development of aramchol after we analyze the results of the ARREST Study. If the Phase III trials are successful, we intend to submit an NDA to the FDA and an MAA to the EMA for the approval of aramchol for the treatment of NASH in patients who also suffer from obesity and insulin resistance in the United States and Europe. We currently expect complete results from the ARREST Study to be available at the end of 2016. Once 120 patients in the ARREST Study complete six months of treatment, we intend to conduct an interim analysis of the efficacy and safety of aramchol based on MRS analysis. The interim analysis will provide safety data according to which an independent safety board will decide whether to continue studying both doses or move all patients to one dose, if one is found to be safer than the other. The MRS will provide data for a futility decision, namely the decision to stop the study if no trend of reduction in liver fat content is found. We do not anticipate the interim results to lead to the stoppage of our ARREST Study, but no assurance can be given. This reflects the importance of the main secondary endpoint of the resolution of NASH in biopsies, which can be assessed only at the completion of the study and by repeated liver biopsies. We currently expect results from the interim analysis to be available in the first half of 2016.

We are also exploring other indications for the use of aramchol, including the treatment of cholesterol gallstones. On November 13, 2014, we announced the first administration of aramchol in a proof-of-concept Phase IIa clinical trial for the treatment of newly formed cholesterol gallstones following bariatric surgery. The Phase IIa trial is a multi-center, randomized, double blind, placebo controlled study, designed to evaluate the efficacy and safety of a once-daily dose of aramchol for three months in 36 adult patients and is being conducted in four medical centers in Israel. The primary endpoint of the trial is a complete dissolution of newly formed cholesterol gallstones following bariatric surgery. Secondary endpoints include a decrease of more than 50% in the number of newly formed gallstones, prevention of the formation of additional gallstones during the trial period and dissolution of biliary sludge. We currently anticipate reporting top line results in the second half of 2015. Approximately 5% of the general population in most countries develops cholesterol gallstones and the current standard of care is surgery, either laparoscopic or open cholecystectomy.

On April 28, 2014, we commenced PK and food effect studies of aramchol. In written correspondence from December 2013 regarding a requested pre- IND, application meeting, the FDA recommended that we conduct such studies prior to commencing our ARREST Study of aramchol for the treatment of NASH. We conducted the PK study at the Sourasky Medical Center in Tel Aviv, Israel. We enrolled 66 healthy male volunteers who received three doses of aramchol: 200 mg, 400 mg and 600 mg. The two higher doses will be used in our ARREST Study. In December 2014, we completed the statistical analysis of the PK study of the three doses of aramchol and observed no serious adverse events. Such PK study provides additional safety data to further support existing safety data from our pre-clinical studies and our Phase I and Phase IIa clinical trials of aramchol.

To date, we have successfully completed four clinical trials of aramchol, one of which, the PK study, was conducted pursuant to an FDA-cleared IND. The first was a single dose, double-blind, placebo- controlled, Phase Ia study with ascending doses of aramchol in healthy volunteers in one center in Israel. All doses proved to be well-tolerated and no serious adverse side effects were observed in our studies to date. An additional Phase Ib repeated dose trial completed on healthy volunteers in one center in Israel also showed that aramchol has no observable adverse side effects and confirmed the suitability of a once-daily dose of aramchol. A multi-center, randomized, double-blind, placebo-controlled Phase IIa trial of aramchol in 60 NAFLD and NASH patients in 12 centers in Israel, whose study design was deemed acceptable by the FDA in 2007 at a pre-IND scientific advisory meeting, suggested that aramchol reduced liver fat in a dose dependent manner, as evidenced by a statistically significant reduction of liver fat over a three month treatment period of once-daily 300 mg doses of aramchol, and induces positive trends of changes in several metabolic parameters. The fourth was a single-site, randomized, partially double-blind, placebo-controlled PK and food effect study conducted in three parts. The first part of the study assessed the PK, safety and tolerability of aramchol tablets at single doses of either 200 mg or 400 mg under fasting conditions. The second part of the study evaluated the effect of a high-calorie, high-fat meal on the bioavailability of a single 600 mg dose of aramchol and assessed the safety and tolerability. The third part of the study assessed the PK and comparative bioavailability, safety and tolerability of aramchol tablets after repeated administrations of three different doses (200 mg, 400 mg and 600 mg) for ten consecutive days, with dosing occurring following the consumption of a light meal. No serious adverse events have been observed in any study. All observed adverse events were generally minimal to mild and transient. Furthermore, no clinically significant abnormalities related to aramchol were noted in the ECG or laboratory data.

To date, we have not generated revenue from the sale of any product, and we do not expect to generate any significant revenue unless and until we commercialize aramchol. As of December 31, 2014, the Company had an accumulated deficit of approximately $36.7 million.

Our financing activities are described below under “Liquidity and Capital Resources.” Obtaining approval of an NDA, MMA, or other similar application is an extensive, lengthy, expensive and uncertain process, and the FDA, EMA and other regulatory agencies may delay, limit or deny approval of our product.

Financial Overview

Since inception, we have incurred significant losses in connection with our research and development and have not generated any revenue. At December 31, 2013, we had an accumulated deficit of $27.6 million and at December 31, 2014, we had an accumulated deficit of $36.7 million.

We have funded our operations primarily through the sale of equity and debt securities in private equity offerings and debt financings in Israel to our affiliates, shareholders and third-party investors. As of December 31, 2014, we had $23.7 in cash and cash equivalents and $8.2 million in short-term deposit and marketable securities, and an accumulated deficit of approximately $36.7 million. Although we provide no assurance, we believe that such existing funds and the proceeds from our initial public offering will be sufficient to continue our business and operations as currently conducted into 2017, although there is no assurance of this. However, we will continue to incur operating losses, which may be substantial over the next several years, and we may need to obtain additional funds to further develop our research and development programs.

Costs and Operating Expenses

Our current costs and operating expenses consist of two components: (i) research and development expenses; and (ii) general and administrative expenses.

Research and Development Expenses

Our research and development expenses consist primarily of outsourced development expenses, salaries and related personnel expenses and fees paid to external service providers, patent-related legal fees, costs of preclinical studies and clinical trials, drug and laboratory supplies and costs for facilities and equipment. We charge all research and development expenses to operations as they are incurred. We expect our research and development expense to remain our primary expense in the near future as we continue to develop our products. Increases or decreases in research and development expenditures are attributable to the number and/or duration of the preclinical and clinical studies that we conduct.

We expect that a large percentage of our research and development expense in the future will be incurred in support of our current and future preclinical and clinical development projects. Due to the inherently unpredictable nature of preclinical and clinical development processes, we are unable to estimate with any certainty the costs we will incur in the continued development of aramchol for NASH and other indications in our pipeline for potential commercialization. Clinical development timelines, the probability of success and development costs can differ materially from expectations. We expect to continue to test our product candidate in preclinical studies for toxicology, safety and efficacy, and to conduct additional clinical trials for our product candidate.

While we are currently focused on advancing our product development, our future research and development expenses will depend on the clinical success of our product candidate, as well as ongoing assessments of the candidate's commercial potential. As we obtain results from clinical trials, we may elect to discontinue or delay clinical trials for our product candidate in certain indications in order to focus our resources on more promising indications for such product candidate. Completion of clinical trials may take several years or more, but the length of time generally varies according to the type, complexity, novelty and intended use of a product candidate.

We expect our research and development expenses to increase in the future from current levels as we continue the advancement of our clinical product development and to the extent we in-license new product candidates. The lengthy process of completing clinical trials and seeking regulatory approval for our product candidate requires the expenditure of substantial resources. Any failure or delay in completing clinical trials, or in obtaining regulatory approvals, could cause a delay in generating product revenue and cause our research and development expenses to increase and, in turn, have a material adverse effect on our operations. Because of the factors set forth above, we are not able to estimate with any certainty when we would recognize any net cash inflows from our projects.

General and Administrative Expenses

General and administrative expenses consist primarily of compensation for employees in executive and operational roles, including accounting, finance, legal and investor relations. Our other significant general and administrative expenses include non-cash stock-based compensation costs and facilities costs (including, the rental expense for our offices in Tel Aviv, Israel), professional fees for outside accounting and legal services, travel costs, investors relations, insurance premiums and depreciation.

We expect our general and administrative expenses, such as accounting and legal fees, to increase as we grow and operate as a public company, and we expect an increase in our salary and benefits expense as a result of the additional management and operational personnel that we hired since our initial public offering to address the anticipated growth of our company.

Financial Expenses, Net

Our financial expense consists of bank fees and loan interest. Our financial income consists of income from short term bank deposits.

Critical Accounting Policies and Estimates

We prepare our financial statements in accordance with accounting principles generally accepted in the United States, or GAAP. In doing so, we must make estimates and assumptions that affect our reported amounts of assets, liabilities and expenses, as well as related disclosure of contingent assets and liabilities. In some cases, we could reasonably have used different accounting policies and estimates. Changes in the accounting estimates are reasonably likely to occur from period to period. Accordingly, actual results could differ materially from our estimates. To the extent that there are material differences between these estimates and actual results, our financial condition or results of operations will be affected. For further significant accounting policies please see Note 2 to our audited consolidated financial statements of this annual report. We believe that our accounting policies contained therein are critical in fully understanding and evaluating our financial condition and operating results.

Jumpstart Our Business Startups Act of 2012

We are an emerging growth company within the meaning of the rules under the Securities Act of 1933, as amended, or the Securities Act, and we will utilize certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies. We could remain an "emerging growth company" for up to five years from the date of our first sale of common equity securities pursuant to an effective registration statement under the Securities Act, or until the earliest of (a) the last day of the first fiscal year in which our annual gross revenue exceeds $1 billion (as such amount is indexed for inflation every five years by the SEC to reflect the change in the Consumer Price Index for All Urban Consumers published by the Bureau of Labor Statistics, setting the threshold to the nearest $1.0 million) or more, (b) the date that we become a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our ordinary shares that is held by non-affiliates exceeds $700.0 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.

The JOBS Act also permits us, as an "emerging growth company," to take advantage of an extended transition period to comply with certain new or revised accounting standards if such standards apply to companies that are not issuers. We are choosing to "opt out" of this provision and, as a result, we will comply with new or revised accounting standards when they are required to be adopted by issuers. This decision to opt out of the extended transition period under the JOBS Act is irrevocable.

Stock-Based Compensation and Fair Value of Ordinary Shares

We apply ASC 718-10, "Share-Based Payment," which requires the measurement and recognition of compensation expense for all share-based payment awards made to employees and directors, including employee stock options under the Company's stock plans, based on estimated fair values. ASC 718-10 requires companies to estimate the fair value of equity-based payment awards on the date of the grant using an option-pricing model. The value of the portion of the award that is ultimately expected to vest is recognized as an expense over the requisite service periods in the Company's consolidated statement of operations. The foregoing estimates of fair value that the Company has made are highly complex and subjective. The estimates of the fair value of the Company's ordinary shares will not be necessary to estimate the fair value of new awards as the shares started trading on the Nasdaq Capital Market as of March 2014.

We recognize compensation expense for the value of non-employee awards, which have graded vesting, based on the accelerated attribution method over the requisite service period of each award, net of estimated forfeitures. We recognize compensation expense for the value of employee awards that have graded vesting, based on the straight-line method over the requisite service period of each of the awards, net of estimated forfeitures.

In determining the fair value of our ordinary shares that was used to value previous equity issuances, we relied upon previous offering valuations while taking into account the clinical development of the Company's product candidate. We believe that the fair value of our ordinary shares has continuously increased since inception as the development of our product candidate has continuously progressed.

The valuations were performed contemporaneously with the offerings of ordinary shares to which such valuations relate. Such valuations were conducted by us and were directly observable in the marketplace. Such valuations were in accordance with the provisions of ASC 820-35 and based on the purchase price paid by new external and independent investors with pharmaceutical or financial expertise, who purchased our convertible notes contemporaneously with or around the time of our equity issuances. Increases in the Company's valuations were based upon the progress in the clinical development of our product candidate, submissions of new families of patent applications for new potential indications and new formulations of our product candidate, an investment round and our initial public offering in March 2014.

Information regarding each such issuance, on a post-Reorganization[(1)] basis, is included in the following table:

Year of issuance of equity	Instrument issued	Number of shares derived from the instrument issued	Number of options/warrants	Consideration ($)	Exercise price ($)
2000	Ordinary shares	3,754,350	—	650,000	—
2002	Options	—	38,637	—	1.47
2005 – 2008	Ordinary shares upon conversion of convertible notes	1,241,487	—	3,596,778	—
2012	Warrants (2)	—	241,299	—	3.57
2012	Options	—	241,299	—	3.57
2013	Ordinary shares upon conversion of the Convertible Loan Agreement (3)	1,043,928	—	3,724,462	—
2013	Ordinary shares upon conversion of the Bridge Loans	511,029	—	1,824,300	—
2013	Ordinary shares upon conversion of the Convertible Security Notes (4)	515,403	—	4,717,641	—
2013	Options	—	1,219,617	—	0.01 – 3.57
2013	Ordinary Shares	33,534		120,000	
2014	Ordinary shares	560,224	—	2,000,000	—
2014	Option	—	25,749	—	3.57
2014	Ordinary shares upon initial public offering (5)	3,263,010	—	39,856	—
2014	Cashless exercise of options	177,488	(241,299)	—	—
2014	Options (6)	—	330,000	—	5.49

(1) Retroactively adjusted to reflect the 729:1 share split, which occurred upon the consummation of the Reorganization.

(2) The warrant was issued with several performance conditions to its exercise. The Company estimated that the conditional performances set forth in the warrant would not be met and accordingly did not record expenses due to such warrant, which expired in May 2013.

(3) The convertible loan agreement, dated December 21, 2011, by and among GHI, its shareholders and Shirat HaChaim Ltd., or the Convertible Loan Agreement, was entered into in 2011, but for accounting purposes it was deemed issued in January 2012 and was classified as an equity instrument. In 2013, the Convertible Loan Agreement was converted into ordinary shares.

(4) In August and September 2013, GHI issued to its shareholders convertible security notes, or the Convertible Security Notes, convertible into ordinary shares of GHI, or any of its successors, with an aggregate face value of $1.84 million. The Company revalued the Convertible Security Notes based on their fair value as a result of a modification of their conversion price in December 2013. For further elaboration see the notes to our financial statements contained elsewhere herein.

(5) Net of offering expenses in the amount of $ 4,204.

(6) Excluding the grant of 330,000 options to purchase our ordinary shares to certain Office Holders (as such term is defined below and includes executive officers and directors), of which (i) 310,000 are subject to shareholder approval and certain of which are also subject to obtaining a tax pre-ruling from the Israeli Tax Authority; and (ii) 20,000 are subject to obtaining a tax pre-ruling from the Israeli Tax Authority only. For further details, see below under "Item 6. Directors, Senior Management and Employees—E. Share Ownership—Certain Information Concerning Equity Awards to Office Holders."

The intrinsic value of the Company's vested and unvested options outstanding as of March 15, 2015 and 2014, based on the market price per share, was $12.2 million and $17.7 million, respectively.

Results of Operations

The table below provides our results of operations (which reflect the results of operations of GHI, our predecessor, prior to the Reorganization, as well as the financial data of the Company (the successor) post Reorganization) for the year ended December 31, 2014 as compared to the year ended December 31, 2013 and for the year ended December 31, 2013 as compared to the year ended December 31, 2012.

	Year Ended December 31,			
	2011	2012	2013	2014
	(in thousands)			
Research and development expenses	$ 1,326	$ 2,443	$ 7,207	$ 6,664
General and administrative expenses	151	694	7,355	2,478
Capital Loss	—	—	10	-
Operating loss	1,477	3,137	14,572	9,142
Financial income (expenses), net	(3)	(6)	(2,912)	40
Operating loss post-finance expense & other income, net	1,480	3,143	17,484	9,102
Taxes on income	2	6	1	1
Net loss	$ 1,482	$ 3,149	$ 17,485	$ 9,103
Other comprehensive income:				
Net unrealized gain on available for sale securities	—	—	—	4
Comprehensive loss	$ 1,482	$ 3,149	$ 17,485	$ 9,099
Loss per share (*)	$ 0.30	$ 0.63	$ 3.45	$ 0.88

(*) Retroactively adjusted to reflect the 729:1 share split, which occurred upon the consummation of the Reorganization.

Research and Development Expenses

Our research and development expenses amounted to $6.7 million during the year ended December 31, 2014, representing a decrease of $0.5 million, or 8%, as compared to such expenses for the year ended December 31, 2013. The decrease primarily resulted from a decrease in non-cash-stock-based compensation of $4.3 million offset by an increase in research and development subcontractor expenses in connection with aramchol for the treatment of NASH in obese patients with insulin resistance of $3.2 million and an increase of $573,000 in salaries and benefits paid to five new employees hired since the comparable prior year period, including Chief Medical Officer, Director of Clinical Operations, Director of Drug Development, Clinical Project Manager and Clinical Research Associate.

Our research and development expenses amounted to $7.2 million for the year ended December 31, 2013, representing an increase of $4.8 million, or 195%, as compared to such expenses for the year ended December 31, 2012. This increase primarily resulted from stock-based compensation of $4.3 million and increased studies in connection with aramchol for the treatment of NASH in obese patients with insulin resistance.

General and Administrative Expenses

Our general and administrative expenses amounted to $2.5 million for the year ended December 31, 2014, representing a decrease of $4.9 million, or 66%, as compared to such expenses for the year ended December 31, 2013. This decrease primarily resulted from a decrease in non-cash stock-based compensation of $6.0 million offset by an increase in salaries and benefits paid to employees of $443,000 and an increase in professional services expenses of $516,000, which primarily includes legal, accounting and consulting services.

Our general and administrative expenses amounted to $7.4 million during the year ended December 31, 2013, representing an increase of $6.7 million, or 960%, as compared to such expenses for the comparable prior year period. This increase primarily resulted from an increase in salaries and benefits as a result of greater non-cash stock-based compensation to employees of $6.4 million and greater professional fees of $496,000.

Operating Loss

As a result of the foregoing research and development and general and administrative expenses, as well as our failure to generate operating revenues since our inception, our operating loss for the year ended December 31, 2014 was $9.1 million, representing a decrease in our operating loss of $5.4 million, or 37%, as compared to our operating loss for the year ended December 31, 2013. This decrease primarily resulted from a decrease in non-cash stock-based compensation of $10.3 million offset by an increase in our research and development subcontractor expenses of $3.2 million and an increase in our salaries and benefits expenses of $1.0 million.

Our operating loss for the year ended December 31, 2013 was $14.6 million, representing an increase of $11.4 million, or 364%, as compared to our operating loss for the comparable prior year period. This increase primarily resulted from an increase in non-cash stock-based compensation to employees of $10.8 million as compared to $208,000 for the comparable prior year period.

Financial Income (Expense), Net

Our financial income (expense), net, for the year ended December 31, 2014 was $40,000, representing a decrease of $2.9 million of financial expense, or 100%, as compared to such expenses for the comparable prior year period. This decrease resulted from recording the difference between the fair value of new convertible notes and the net carrying amount of the extinguished notes, in the amount of approximately $2.9 million, in the statement of operations report for the year ended December 31, 2013.

Our financial income (expense), net, for the year ended December 31, 2013 was $(2.9) million, representing an increase of $2.9 million, or 484%, as compared to such expense for the comparable prior year period. This increase resulted from recording the difference between the fair value of new convertible notes and the net carrying amount of the extinguished notes, in the amount of approximately $2.9 million, in the statement of operations report for the year ended December 31, 2013.

Net Loss

As a result of the foregoing research and development and general administrative expenses as well as our failure to generate revenue since our inception, our net loss for the year ended December 31, 2014 was $9.1 million, representing a decrease of $8.4 million, or 48%, as compared to our net loss for the year ended December 31, 2013. This decrease primarily resulted from a decrease in non-cash stock-based compensation of $10.3 million offset by an increase in our research and development subcontractor expenses of $3.2 million, an increase in our salaries and expenses of $1.0 million and a decrease in our financial income (expense), net, of $2.9 million.

For the year ended December 31, 2013 our net loss was $17.5 million, representing an increase of $14.3 million, or 455%, as compared to our net loss for the comparable prior year period. The increase was primarily due to an increase in non-cash stock-based compensation of $10.8 million and finance income (expense), net, of $(2.9) million.

Liquidity and Capital Resources

Overview

We have incurred substantial losses since our inception. As of December 31, 2014, we had an accumulated deficit of approximately $36.7 million and working capital (current assets less current liabilities) of $31.0 million. We expect that losses will continue for the foreseeable future.

As of December 31, 2014, we had cash and cash equivalents of $23.7 million and short—term deposits and marketable securities of $8.3 million invested in accordance with our investment policy, primarily with a view towards liquidity and capital preservation with an average maturity of 1.5 years, as compared to $137,000 and $0 as of December 31, 2013, respectively. This increase was primarily due to net proceeds from our initial public offering of approximately $39.9 million offset by our negative cash flow from operating activity in the amount of $9.2 million.

As of December 31, 2013, we had cash and cash equivalents of $137,000 as compared to $718,000 as of December 31, 2012. This decrease of $581,000 was primarily due to our net loss of $17.5 million during the year ended December 31, 2013, an increase in trade payables in the amount of $954,000, an increase in accounts receivable in the amount of $228,000, the issuance of a convertible note in the amount of $1.8 million, a non-cash financial expense due to convertible note modification in the amount of $2.9 million and a stock based compensation expense in the amount of $10.8 million.

Cash Flow from Operating Activities

We had negative cash flow from operating activities of $9.2 million for the year ended December 31, 2014 as compared to a negative cash flow from operating activities of $2.5 million for the year ended December 31, 2013. The negative cash flow from operating activities for the year ended December 31, 2014 was mainly attributable to our net loss of $9.1 million

We had negative cash flow from operating activities of $2.5 million for the year ended December 31, 2013 as compared to a negative cash flow from operating activities of $3.1 million for the year ended December 31, 2012. The negative cash flow from operating activities for the year ended December 31, 2013 was mainly attributable to our net loss of $17.5 million, a non cash financial expense due to convertible note modification in the amount of $2.9 million and a stock based compensation expense in the amount of $10.9 million.

Cash Flow from Investing Activities

We had negative cash flow from investing activities of $9.0 million for the year ended December 31, 2014 as compared to a positive cash flow from investing activities of $3,000 for the year ended December 31, 2013. The negative cash flow from investing activities for the year ended December 31, 2014 was due to an investment in short-term deposits and marketable securities in the amount of $8.3 million and the purchase of medical equipment in the amount of $750,000.

We had positive cash flow from investing activities of $3,000 for the year ended December 31, 2013 as compared to a negative cash flow from investing activities of $32,000 for the year ended December 31, 2012. The positive cash flow from investing activities for the year ended December 31, 2013 was due to the sale of equipment in the amount of $16,000 less the investment in such equipment in the amount of $13,000, while the negative cash flow from investing activities for the year ended December 31, 2012 was due to the investment in such equipment.

Cash Flow from Financing Activities

We had positive cash flow from financing activities of $41.9 million for the year ended December 31, 2014 as compared to a positive cash flow from financing activities of $1.9 million for the year ended December 31, 2013. The positive cash flow from financing activities for the year ended December 31, 2014 was primarily due to the issuance of our ordinary shares in our initial public offering for net proceeds of approximately $39.9 million and the issuance of our ordinary shares in the amount of $2.0 million in a private placement financing completed in February 2014, prior to the consummation of our initial public offering.

We had positive cash flow from financing activities of $1.9 million for the year ended December 31, 2013 as compared to a positive cash flow from financing activities of $3.7 million for the year ended December 31, 2012. The positive cash flow from financing activities for the year ended December 31, 2013 was primarily due to the issuance of a convertible note in the amount of $1.8 million, while the positive cash flow from financing activities for the year ended December 31, 2012 was primarily due to the issuance of a capital note in the amount of $3.7 million.

We believe that our existing cash resources and the net proceeds from our initial public offering will be sufficient to fund our projected cash requirements approximately into 2017, although there is no assurance of this. Nevertheless, we will require significant additional financing in the future to fund our operations if and when we progress into Phase III trials of aramchol and clinical trials for other indications, obtain regulatory approval of aramchol and commercialize the drug.

Current Outlook

According to our estimates and based on our budget, if we are not successful in obtaining additional capital resources, there is substantial doubt that we will be able to continue our activities beyond 2017. Even with the funds raised in our initial public offering, we believe that we will need to raise significant additional funds before we have any cash flow from operations, if at all.

Developing drugs, conducting clinical and preclinical trials and commercializing products is expensive and we will need to raise substantial additional funds to achieve our strategic objectives. We believe that our existing cash resources and the net proceeds from our initial public offering will be sufficient to fund our projected cash requirements approximately into 2017, although there is no assurance of this. Nevertheless, we will require significant additional financing in the future to fund our operations, including if and when we progress into Phase III trials of aramchol for the treatment of NASH in patients who also suffer from obesity and insulin resistance and clinical trials for other indications, obtain regulatory approval for aramchol and commercialize the drug. We currently anticipate that we will utilize approximately $12.0 million for clinical trial activities over the course of the next 12 months. Our future capital requirements will depend on many factors, including:

- the progress and costs of our preclinical studies, clinical trials and other research and development activities;
- the scope, prioritization and number of our clinical trials and other research and development programs;
- the amount of revenues and contributions we receive under future licensing, development and commercialization arrangements with respect to our product candidate;
- the costs of the development and expansion of our operational infrastructure;
- the costs and timing of obtaining regulatory approval for our product candidate;
- the ability of us, or our collaborators, to achieve development milestones, marketing approval and other events or developments under our potential future licensing agreements;
- the costs of filing, prosecuting, enforcing and defending patent claims and other intellectual property rights;

- the costs and timing of securing manufacturing arrangements for clinical or commercial production;
- the costs of contracting with third parties to provide sales and marketing capabilities for us;
- the costs of acquiring or undertaking development and commercialization efforts for any future products, product candidates or platforms;
- the magnitude of our general and administrative expenses; and
- any cost that we may incur under future in- and out-licensing arrangements relating to our product candidate.

Until we can generate significant recurring revenues, we expect to satisfy our future cash needs through the net proceeds from our initial public offering, debt or equity financings or by out-licensing applications of our product 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 product candidate. This may raise substantial doubts about the Company's ability to continue as a going concern.

Contractual Obligations

The following table summarizes our significant contractual obligations (which reflect the significant contractual obligations of GHI, our predecessor, prior to the Reorganization) at December 31, 2014.

	Total	Less than 1 year	1 – 3 years	More than 3 years
		(in thousands)		
Facility leases (1)	$ 30	$ 30	$ -	$ -
Termination payment (2)	426	280	-	146
Total	$ 456	$ 310	$ -	$ 146

(1) For a more detailed description of the facility leases, see "Description of Property and Facilities" above.

(2) Consists of remuneration for our CEO's non-competition undertakings, in the event of termination of his employment, other than for cause, and the settlement with the beneficiaries of the late Professor Tuvia Gilat, which was paid during the first quarter of 2015.

We enter into contracts in the ordinary course of business with CROs for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes, which generally provide for termination within 30 days of notice, and therefore are cancelable contracts and not included in the Contractual Obligations table above.

Other than as described below, we did not have any material commitments for capital expenditures, including any anticipated material acquisition of plant and equipment or interests in other companies, as of December 31, 2014.

Trend Information

We are a development stage company and it is not possible for us to predict with any degree of accuracy the outcome of our research, development or commercialization efforts. As such, it is not possible for us to predict with any degree of accuracy any significant trends, uncertainties, demands, commitments or events that are reasonably likely to have a material effect on our net sales or revenues, income from continuing operations, profitability, liquidity or capital resources, or that would cause financial information to not necessarily be indicative of future operating results or financial condition. However, to the extent possible, certain trends, uncertainties, demands, commitments and events are in this "Operating and Financial Review and Prospects."

Off-Balance Sheet Arrangements

The Company currently does not have any off-balance sheet arrangements that have had, or are reasonably likely to have, a current or future effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources that are material to investors.

ITEM 6. Directors, Senior Management and Employees.

A. Directors and Senior Management.

Set forth below is information concerning the directors, senior management and executive officers of the Company as of March 15, 2015. The business address for each of our directors, senior management and corporate officers is c/o Galmed Pharmaceuticals Ltd., 8 Shaul Hamelech Blvd., Amot Mishpat Bldg., Tel Aviv, Israel 6473307.

Name	Age	Position
Chaim Hurvitz(1)	54	Chairman of the Board, Class III Director; Chairperson of the R&D Committee
Allen Baharaff	50	President and Chief Executive Officer, Class II Director
Dr. Maya Halpern	62	Chief Medical Officer, Class I Director
Josh Blacher(2)	42	Chief Financial Officer
George Tonelli(3)	55	Vice President of Clinical Operations
Dr. Maureen Graham	58	Vice President – Regulatory Affairs & Project Management
Dr. Antony Appleyard	40	Vice President – Drug Development
William Marth(1)(4)	60	Class III Director
Shmuel Nir(4)(5)(6)	53	Class II Director
Tali Yaron-Eldar(4)(5)(6)(7)	51	Director; External Director
David Sidransky, M.D. (1)(4)(5)(6)(7)	54	Director; External Director

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(1) A member of our research & development committee, or our R&D Committee.

(2) On October 7, 2014, the Company and Mr. Ray Morris, the Company's former Chief Financial Officer, mutually agreed to terminate the consulting agreement dated March 4, 2014, pursuant to which Mr. Morris served as the Company's Chief Financial Officer. The termination was effective as of December 31, 2014. On December 30, 2014, the Company approved the appointment of Josh Blacher, effective as of January 1, 2015, to replace Mr. Morris and serve as Chief Financial Officer. Mr. Blacher's employment with the Company was consummated on October 19, 2014, where he previously served as Senior Director, Corporate Development.

(3) On March 6, 2015, the Company entered into a Consulting Agreement to engage Mr. Tonelli to provide consulting services in connection with the Company's clinical trials, subject to the Company's remuneration committee and Board approval. Such approvals were granted on March 30, 2015. In providing such services Mr. Tonelli, shall act as the Company's Vice President of Clinical Operations.

(4) Independent director under applicable Nasdaq Capital Market and SEC rules, as affirmatively determined by our Board.

(5) A member of our audit committee, or our Audit Committee.

(6) A member of our remuneration committee, or our Remuneration Committee.

(7) An external director under the Companies Law, approved by our shareholders.

Chaim Hurvitz, our chairman of the Board and a member of our R&D committee, joined our Board in 2011. Mr. Hurvitz currently serves as the CEO of CH Health, a private venture capital firm, a position he has held since May 2011. Mr. Hurvitz served as a member of the board of directors of Teva Pharmaceuticals Industries Ltd. from 2010 to 2014. Previously, he was a member of the senior management of Teva Pharmaceuticals Industries Ltd., serving as the President of Teva International Group from 2002 until 2010, as President and CEO of Teva Pharmaceuticals Europe from 1992 to 1999 and as Vice President - Israeli Pharmaceutical Sales from 1999 until 2002. Mr. Hurvitz presently serves as a member of the management of the Manufacturers Association of Israel and head of its pharmaceutical branch. Mr. Hurvitz holds a Bachelor of Arts degree in political science and economics from Tel Aviv University, which was awarded in 1985.

Allen Baharaff, our controlling shareholder, President and Chief Executive Officer and a member of our Board, who co-founded the Group in 2000 and served as the Chief Financial Officer of GHI since 2000, as our Chief Executive Officer since January 2012 and as our President since March 2015. Prior to which, he held a number of senior executive positions, including a Senior Vice President position at Isramex Projects Ltd., an energy project financing company, and Managing Director of T+M Trusteeship & Management Services (Israel) Ltd., a subsidiary of a Swiss company providing trust and similar services. Since 2001, Mr. Baharaff also serves as a member of the board of directors of the Tel-Aviv Museum of Arts, chairing its educational activities and, since 2005, Mr. Baharaff serves as a Director of the Rubin Museum. Mr. Baharaff holds a Bachelor of Science degree in economics from the London School of Economics, University of London and LLB and MA degrees from Cambridge University. Since 1993, Mr. Baharaff has been a member of the Israel Bar Association.

Dr. Maya Halpern, our Chief Medical Officer and a member of our Board since 2011, is a Medical Advisor at CH Health, an Israeli private venture capital company controlled by our Chairman since 2011, prior to which, from 2000 to 2010, Dr. Halpern worked in the pharmaceutical industry as a medical director of Teva Pharmaceutical Industries Ltd. in Israel and in Teva's international group of subsidiaries. Dr. Halpern's experience covers managing clinical trials, as well as medical and ethical aspects of drug marketing. Dr. Halpern holds a Medical Degree from Hadassah Medical School, the Hebrew University, Jerusalem and an M.A. in philosophy from the Tel Aviv University.

Josh Blacher, our Chief Financial Officer, has served in such capacity since January 2015. Prior to that, Mr. Blacher joined the Company in October 2014 as Senior Director, Corporate Development. Mr. Blacher has six years of experience in biotech-related business development, operations and investing, as well as 14 years in capital markets. Prior to joining the Company, among other things, Mr. Blacher served as Director of Business Development at Teva Innovative Ventures, Teva Pharmaceuticals' early- and mid-stage investment and in-licensing arm from 2008 to 2011. In that capacity, Mr. Blacher helped build and manage Teva's portfolio of approximately 20 equity investments in biotech companies, spanning a wide range of development stage companies from pre-clinical through Phase III projects, as well as various therapeutic areas. Previously, from 1995 to 2005. Mr. Blacher also held positions in portfolio management at Deutsche Asset Management and equity research at Morgan Stanley, as well as in mergers & acquisitions at Lehman Brothers. Mr. Blacher holds an MBA in Finance from Columbia Business School and a BA in Economics from Yeshiva University, which he was awarded in 2001 and 1995, respectively.

George Tonelli, our Vice President of Clinical Operations, has served in such capacity since March 2015. Mr. Tonelli has 20+ years of progressive experience in clinical development operations and regulatory affairs. Prior to joining the Company, Mr. Tonelli planned and executed multiple clinical trials in the therapeutic area of Diabetes Mellitus at MannKind Corporation from 2005 to 2014, culminating in the FDA approval of Afrezza®. Prior to that, Mr. Tonelli held several leadership positions in clinical development and project management at Innapharma. He began his career in regulatory affairs in the Medical Research Division of American Cyanamid (Lederle Labs). He holds a Bachelor of Science degree from Rutgers University.

Dr. Maureen Graham, our Vice President - Regulatory Affairs and Project Management, has served in such capacity since 2012. Dr. Graham has over 25 years of experience within the pharmaceutical industry and has worked for several different companies, including GlaxoSmithKline from 1982 to 1985, Merck & Co from 1985 to 1994, IVAX Pharmaceuticals, Inc. from 1994 to 1998 and Amgen Inc. from 1998 to 2004. She has held a number of directorships, including within Niche Generics Limited, where she served from 2004 to 2005, and has served as the European Director of Regulatory Affairs at Amgen. Dr. Graham founded, and is the managing director of, Diamond BioPharm Limited in 2005, which is a leading technical and scientific consulting group of companies serving the biotechnology and pharmaceutical industry. Dr. Graham has direct experience with many types of products, including biotechnology, gene-therapy, new chemical entities and generics as well as experience and expertise in regulatory and product development issues associated with medicinal products for rare indications. Her extensive experience covers products at all stages of development ranging from preclinical to registration. Dr. Graham is a pharmacist by trade with a Ph.D. in Pharmaceutical Sciences from De Montfort University, Leicester, United Kingdom, which was awarded in 1983, and a Diploma in Regulatory Affairs from Cardiff University, Cardiff, Wales, United Kingdom, which was awarded in 2001.

Dr. Antony Appleyard, our Vice President - Drug Development and head of chemistry manufacturing and controls, or CMC, has served in such capacity since 2013. Dr. Appleyard is also Head of Development Projects at Diamond BioPharm Ltd., providing product development, regulatory and project management services with over 15 years of experience in research and development, drug discovery, drug delivery, new chemical entities, biologics, formulation, manufacturing and technology transfer. Prior to joining the Company, Dr. Appleyard was an Associate Director of Natural Products Chemistry at Novacta Biosystems Ltd, or Novacta, from 2009 to 2011 and at Cantab Biopharmaceuticals Ltd from 2012 to 2013, where he also held the development positions of CMC Lead and Head of Analysis for development programs. Prior to Novacta, from 2003 to 2004, Dr. Appleyard was engaged in international technology transfer activities for MAb processes at Abbott Laboratories in Dartford, England. He was awarded a degree in chemistry with honors in 1995 and a Ph.D. in biochemistry in 2001, both from the University of Leeds. From 2001 to 2003, Dr. Appleyard carried out post- doctoral research in the Departments of Chemistry and Biochemistry at the University of Cambridge. He is a Fellow of The Royal Society of Chemistry and a Chartered Chemist.

William Marth, a director of the Company since March 2014, serves as president and chief executive officer elect of Albany Molecular Research Inc. since January 2014 and serves as the chairman of the board of directors of Sorrento Therapeutics since January 2014. Previously, Mr. Marth has served as chairman of the Board of Albany Molecular Research Inc. from May 2012 to December 2013, prior to which he served as President and Chief Executive Officer of Teva Pharmaceutical Industries Ltd. in the Americas from June 2010 to November 2012. From January 2008 to June 2010, he served as President and Chief Executive Officer of Teva North America and as President and Chief Executive Officer of Teva USA from January 2005 to January 2008. From July 1999 to January 2002, he was the Executive Vice President and Vice President of Sales and Marketing for Teva USA. Prior to joining Teva USA, he held various positions with the Apothecon division of Bristol-Myers Squibb. In February 2008, Mr. Marth was elected Chairman of the Generic Pharmaceutical Association where he is also a member of the executive committee. He is a licensed pharmacist and serves on various boards and committees, including The University of the Sciences in Philadelphia, the American Society for Health-System Pharmacists and the Board of Ambassadors for John Hopkins' Project RESTORE. Mr. Marth earned his B.Sc. in pharmacy from the University of Illinois in 1977 and his M.B.A. in 1989 from the Keller Graduate School of Management, DeVry University.

Shmuel Nir, a director since 2007, serves as President and Chief Executive Officer of Tushia Consulting Engineers Ltd., an investment and management services company, and Chairman of the board of directors of Matan Digital Printers Ltd. From March 1998 to January 2008, he served as President and Chief Executive Officer of Macpell Industries Ltd., a leading industrial group. Between January 1991 and March 1998, Mr. Nir was an Executive Vice President of Operations at Macpell Industries Ltd. and President and Chief Executive Officer of two of its subsidiaries, New Net Industries Ltd. and New Net Assets Ltd. Prior to January 1991, Mr. Nir had held various positions with Intel Corporation in Jerusalem, Israel and Tefen Management Consulting. Between 1999 and 2006, Mr. Nir served as managing partner at Spring Venture Capital Fund. Mr. Nir holds a B.Sc. in Industrial Engineering and Management from the Technion - Israel Institute of Technology in Haifa, which was awarded in 1989.

Tali Yaron-Eldar, a director of the Company since March 2014 and an external director since June 2014, is an Israeli attorney specializing in taxation. Ms. Yaron-Eldar co-founded Yaron-Eldar, Paller, Schwartz & Co., Law Offices, in January 2013. Prior to January 2013, she was a partner at the law firm of Tadmor & Co. from March 2007 until December 2012 and a partner at the law firm of Cohen, Yaron-Eldar & Co. from 2004 until March 2007. From January 2004 until January 2008, Ms. Yaron-Eldar served as the Chief Executive Officer of Arazim Investment Company and she has also served in a variety of public positions, including as the Chief Legal Advisor of the Customs and V.A.T department of the Finance Ministry of the State of Israel from 1998 to 2001 and as the Commissioner of Income Tax and Real Property Tax Authority of the State of Israel from 2002 to 2004. Ms. Yaron-Eldar also serves as a director of a number of public companies, including Alliance Tire Company Ltd., Rossetta Genomics Ltd., Medtechnica Ltd., Magicjack Vocaltec Ltd., Lodgia Rotex Investments Ltd. and Tadea Technological Development and Automation Ltd. Ms. Yaron- Eldar holds an M.B.A. specializing in finance from Tel Aviv University which was awarded in 1995 and an LL.B. from Tel Aviv University which was awarded in 1987. Ms. Yaron-Eldar is also a member of the Israeli Bar Association.

David Sidransky, M.D., has been an external director of the Company since June 2014. Dr. Sidransky is a renowned oncologist and research scientist named and profiled by TIME magazine in 2001 as one of the top physicians and scientists in America, recognized for his work with early detection of cancer. He serves as the Director of the Head and Neck Cancer Research Program at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University. He is a Professor of Oncology, Otolaryngology, Cellular & Molecular Medicine, Urology, Genetics, and Pathology at John Hopkins University and Hospital. Dr. Sidransky has written over 450 peer-reviewed publications, and has contributed to more than 60 cancer reviews and chapters. Dr. Sidransky is a founder of a number of biotechnology companies and holds numerous biotechnology patents. He has been the recipient of many awards and honors, including the 1997 Sarstedt International prize from the German Society of Clinical Chemistry, 1998 Alton Ochsner Award Relating Smoking and Health by the American College of Chest Physicians and the 2004 Hinda Rosenthal Award presented by the American Association of Cancer Research. Dr. Sidransky has served as Vice Chairman of the Board of Directors of ImClone. He is Chairman of the Board of Champions Oncology and Tamir Biotechnology and is on the board of directors of Rosetta Genomics Ltd., Celsus Therapeutics Plc and Advaxis, Inc. He is serving and has served on scientific advisory boards of corporations and institutions, including Amgen, MedImmune, Roche and Veridex, LLC (a Johnson & Johnson diagnostic company), among others. In addition, Dr. Sidransky served as Director of American Association for Cancer Research from 2005 to 2008. Dr. Sidransky received his B.A. from Brandeis University and his M.D. from the Baylor College of Medicine. There are no family relationships between any director or executive officer. There are no arrangements or understandings with major shareholders, customers, suppliers or others, pursuant to which any director or executive officer was selected as a director or member of senior management, as the case may be.

Basic Research Scientific Advisory Board and Clinical Advisory Board

We seek advice from our Basic Research Scientific Advisory Board and our Clinical Advisory Board generally on scientific and medical matters. Our Basic Research Scientific Advisory Board includes: Prof. Jose Mato, from CIC bioGUNE and CIC biomaGUNE, Spain, Prof. Zamir Halpern, from the Gastroenterology Institute of the Tel Aviv Sourasky Medical Center (Ichilov) in Tel Aviv, Israel; Prof. Fred Konikoff, Head of the Department of Gastroenterology and Hepatology at Meir Medical Center in Kfar Saba, Israel; Professor Kenichi Ikejima from Juntendo University in Tokyo, Japan; Dr. P. Jane Armstrong from the College of Veterinary Medicine at the University of Minnesota in Minneapolis, Minnesota, and who is also a member of the WSAVA Liver Study Group; Prof. Albert K. Groen from the University of Groningen in Groningen, Netherlands; and Prof. Paolo Parini from the department of Laboratory Medicine at the Karolinska Institute in Stockholm, Sweden. Our Clinical Advisory Board includes Professor Vlad Ratziu, from the University Pierre et Marie Curie in Paris, France and coordinator of the EU FP7 FLIP consortium; Professor Arun Sanyal, from the Virginia Commonwealth University in Richmond, Virginia; Dr. Rohit Loomba, from the University of California San Diego School of Medicine in San Diego, California; Professor Ran Oren from Hadassah University Hospital in Ein Kerem, Jerusalem, Israel and Prof. Eric Gershwin, Chief, Division of Rheumatology Allergy and Clinical Immunology of University of California at Davis, in Davis, California.

B. Compensation.

Certain Approvals Required for Office Holders' Compensation of the Companies Law

Pursuant to the Companies Law, the Company was required to adopt a compensation policy regarding the Terms of Office and Employment of its Office Holders (as such terms are defined below), including exemption and release of the Office Holders from liability for breach of his or her duty of care to the Company, an undertaking to indemnify the Office Holder, post factum indemnification or insurance; any grant, payment, remuneration, compensation, or other benefit provided in connection with termination of service; and any benefit, other payment or undertaking to provide any payment as aforesaid, or the Terms of Office and Employment. The Company's compensation policy with respect to the Terms of Office and Employment of the Company's Office Holders, or the Compensation Policy, was approved by the Board in November 2014 after considering the recommendations of the Remuneration Committee and was adopted by the Company's shareholders in December 2014.

The term 'Office Holder' as defined in the Companies Law includes a general manager, chief executive officer, executive vice president, vice president, any other person fulfilling or assuming any of the foregoing positions without regard to such person's title, as well as a director, or a manager directly subordinate to the general manager or the chief executive officer. As of March 2015, in addition to the seven members of the Board, the Company considers four other individuals, including its Chief Financial Officer, its Vice President of Clinical Operations, its Vice President – Drug Development and its Vice President – Regulatory Affairs & Project Management to be Office Holders.

Pursuant to the Companies Law, arrangements between the Company and its office holders must generally be approved by the Remuneration Committee and the Board, and be consistent with the Compensation Policy. However, under certain circumstances, the Company may approve an arrangement that is not consistent with the Compensation Policy, if such arrangement is approved by a majority of the Company's shareholders, provided that (i) such majority includes a majority of the votes cast by 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 votes cast by shareholders who are not controlling shareholders and who do not have a personal interest in the matter who were present and voted against the arrangement constitute two percent or less of the voting power of the company, or the Special Majority.

The Terms of Office and Employment of directors (including an officer who is a director but is not a controlling shareholder) further require the approval of the shareholders by a simple majority; with respect to a chief executive officer or an officer who is a controlling shareholder, the approval of the shareholders must be made by the Special Majority. In addition, under certain circumstances, a company may be exempt from receiving the shareholders' approval with respect to the Terms of Office and Employment of a non-affiliated candidate for chief executive officer.

Under certain circumstances, if the Terms of Office and Employment of Office Holders (who are not directors or controlling shareholders) are not approved by the shareholders, where such approval is required, the Remuneration Committee and the Board may subsequently override the resolution of the shareholders following a new discussion of the matter and for specified reasons. In addition, amendment of Terms of Office and Employment of Office Holders (who are not directors or controlling shareholders) requires the approval of the Remuneration Committee only, if the Remuneration Committee determines that the amendment is not material.

Aggregate Executive Compensation

The aggregate compensation, including share-based compensation, paid by us to all of our Office Holders as a group, with respect to the year ended December 31, 2014 was approximately $1.7 million. This amount includes approximately $96,000 set aside or accrued to provide pension, severance, retirement, vacation or similar benefits or expenses, but does not include business travel, relocation, professional and business association dues and expenses reimbursed to Office Holders, and other benefits commonly reimbursed or paid by companies in our industry. In addition to the seven members of the Board, the Company considers three other individuals, namely its former Chief Financial Officer, its VP Drug Development and its VP Regulatory Affairs & Project Management, to have been Office Holders in 2014.

As of December 31, 2014, options to purchase 940,977 of our ordinary shares granted to our Office Holders as a group were outstanding, of which options to purchase 746,331 of our ordinary shares were vested, with a weighted average exercise price of $0.51 per ordinary share. In addition, the Board approved the allocation of options to purchase 330,000 of our ordinary shares to certain Office Holders, of which (i) 310,000 are subject to shareholder approval and certain of which are also subject to obtaining a tax pre-ruling from the Israeli Tax Authority; and (ii) 20,000 are subject to obtaining a tax pre-ruling from the Israeli Tax Authority only. For outstanding equity-based awards granted to our Office Holders, see below under "Item 6. Directors, Senior Management and Employees—E. Share Ownership—Certain Information Concerning Equity Awards to Office Holders."

Individual Compensation of Covered Executives

The following table sets forth the compensation granted to the Company's Office Holders with respect to the year ended December 31, 2014. All amounts reported in the table reflect the cost to the Company, as recognized in its financial statements for the year ended December 31, 2014. The five individuals for whom disclosure is provided are referred to herein as "Covered Executives."

Information Regarding the Covered Executives	**Compensation for Services[1]**					
Name and Principal Position[1]	**Base Salary($)**	**Benefits and Perquisites ($)[2]**	**Cash Bonus ($)[3]**	**Equity-Based Compensation ($)[4]**	**Other ($)[5]**	**Total ($)**
Allen Baharaff (President and Chief Executive Officer and Director)	240,000	73,363	200,000	413,295	30,000	956,657
Maya Halpern (Chief Medical Officer and Director)	67,078	19,626	5,590	-	30,000	122,294
Antony Appleyard (Vice President Drug Development)	186,351	-	-	-	-	186,351
Shmuel Nir (Director)	-	-	-	94,970	30,000	124,970
William Marth (Director)	-	-	-	49,957	30,000	79,957

(1) Mr. Baharaff is a full-time employee of the Company; Dr. Halpern and Dr. Appleyard are part-time employees of the Company. Dr. Appleyard is employed through a service provider. Mr. Baharaff and Dr. Halpern also serve as members of our Board. Messrs. Nir and Marth serve solely as members of our Board. Cash compensation amounts denominated in currencies other than the Dollar were converted into Dollars at an exchange rate of NIS 3.58 = $1.00, which reflects the average conversion rate for fiscal year ended December 31, 2014.

(2) Amounts reported in this column include benefits and perquisites, including those mandated by applicable law. Such benefits and perquisites may include, to the extent applicable to the Covered Executives, payments, contributions and/or allocations for savings funds, pension, severance, vacation, car allowance, medical insurances and benefits, risk insurance (e.g., life, disability, accident), telephone, convalescence pay, relocation, payments for social security and other benefits and perquisites consistent with the Company's policies.

(3) Amounts reported in this column refer to the cash bonuses provided by the Company with respect to 2014, which have been provided for in the Company's financial statements for the year ended December 31, 2014 (including if such bonuses were paid during 2015). They exclude bonuses paid during 2014 which were provided for in the Company's financial statements for previous years. The amounts reported in this column do not include ad-hoc cash bonuses of $10,285 and $40,000 to Mr. Baharaff and Dr. Halpern, respectively, which were approved by the Board and the Remuneration Committee on December 30, 2014, and are subject to shareholder approval.

(4) Amounts reported in this column represent the expense recorded in the Company's financial statements for the year ended December 31, 2014 with respect to equity-based compensation. Assumptions and key variables used in the calculation of such amounts are discussed in Note 10 to the Financial Statements. For outstanding equity-based awards granted to Covered Executives see below under "Item 6. Directors, Senior Management and Employees—E. Share Ownership—Certain Information Concerning Equity Awards to Office Holders."

(5) Amounts reported in this column include payments made during 2014 and recorded in the financial statements for the year ended December 31, 2014 relating to directors' fees.

Compensation of Directors

As approved by our shareholders at our 2014 annual meeting of shareholders, in connection with their services as directors of the Company, each of our directors from time to time, including external directors, is entitled to an annual payment of $30,000, plus value-added tax, or VAT, if applicable, payable quarterly at the end of each quarter.

For the outstanding equity-based awards granted to our directors, see below under "Item 6. Directors, Senior Management and Employees—E. Share Ownership—Certain Information Concerning Equity Awards to Office Holders."

Compensation of External Directors

Each of our external directors is entitled to an annual amount of $30,000, plus VAT, if applicable, payable in quarterly installments at the end of each quarter. The compensation of external directors is also subject to the provisions of the Israeli regulations promulgated pursuant to the Companies Law governing the terms of compensation payable to external directors, or the Compensation Regulations, which provide that such compensation will not be less than the Minimum Amount (as such term is defined in the Compensation Regulations). According to the Compensation Regulations, the Minimum Amount is adjusted twice annually based on the Israeli Consumer Price Index and are a function of the Company's shareholders' equity. See also "Item 6. Directors, Senior Management and Employees—C. Board Practices—External Directors & Financial Experts" below.

Employment Agreements and Arrangements with Directors and Related Parties

We 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. These agreements also contain customary provisions regarding non-competition, confidentiality of information and assignment of inventions. However, the enforceability of the non-competition and assignment of inventions provisions may be limited under applicable law. See "Item 3. Key Information—Risk Factors—Risks Related to Our Business, Industry and Regulatory Requirements."

Employment Agreement with Our President and Chief Executive Officer

We entered into an employment agreement, dated December 23, 2013, with our President and Chief Executive Officer, Mr. Allen Baharaff, who is also a controlling shareholder, which was approved and ratified by our shareholders on December 30, 2013. Under the terms of his employment agreement, Mr. Baharaff is entitled to a gross monthly salary of $20,000. In addition, Mr. Baharaff will be eligible to receive (i) an annual bonus in an amount of two to six times his monthly base salary, to be determined based on the achievement of certain milestones set by our Board and (ii) upon the termination of his employment, special remuneration of nine times his gross monthly salary as consideration for certain noncompetition provisions contained in his employment agreement. Mr. Baharaff has received a special bonus of $200,000 in recognition of his efforts and contribution with respect to the consummation of our initial public offering. Mr. Baharaff will also receive other benefits required under Israeli law or that are customary for senior executives in Israel such as reimbursement for cellular telephone expenses, automobile maintenance expenses, and Company contributions equivalent to 5%, 8.33%, 2.5% and 7.5% of his gross monthly base salary towards certain pension, or a manager's insurance policy, severance, disability and tax-advantaged savings funds, or a study fund, respectively. Mr. Baharaff will also contribute 5% and 2.5% of his gross monthly salary towards the manager's insurance policy and study fund, respectively. Mr. Baharaff's employment agreement is terminable by either party upon 90 days' prior written notice, and contains customary provisions regarding noncompetition, confidentiality of information and assignment of inventions.

For cash bonuses granted to Mr. Baharaff see "Item 6. Directors, Senior Management and Employees— B. Compensation—Individual Compensation of Covered Executives." For outstanding equity-based awards granted to Mr. Baharaff see below under "Item 6. Directors, Senior Management and Employees—E. Share Ownership—Certain Information Concerning Equity Awards to Office Holders."

Employment Agreement with Our Chief Medical Officer

We entered into an employment agreement with Dr. Maya Halpern, our Chief Medical Officer and a member of our Board, dated December 23, 2013, on a part-time basis. Under her employment agreement, which became effective as of February 2014, Dr. Halpern is entitled to a gross monthly salary of NIS 20,000 (which is equivalent to US$ 5,602, based on an exchange rate of NIS 3.58 per US$ 1.00, which reflects the average exchange rate for the year ended December 31, 2014) per month. In addition, Dr. Halpern will be eligible to receive other benefits required under Israeli law or that are customary for senior executives in Israel, including entitlement for travel expenses and Company contributions equivalent to 6%, 8.33% and 7.5% of her gross monthly base salary towards certain pension, or a manager's insurance policy, severance and tax-advantaged savings funds, or a study fund, respectively. Dr. Halperin will also contribute 5.5% and 2.5% of her gross monthly salary towards the manager's insurance policy and study fund, respectively. The employment agreement is terminable by either party upon 60 days' prior written notice and contains customary provisions regarding noncompetition, confidentiality of information and assignment of inventions.

For cash bonuses granted to Dr. Halpern, see "Item 6. Directors, Senior Management and Employees— B. Compensation—Individual Compensation of Covered Executives." For outstanding equity-based awards granted to Dr. Halpern see below under "Item 6. Directors, Senior Management and Employees —E. Share Ownership—Certain Information Concerning Equity Awards to Office Holders."

2013 Incentive Share Option Plan

We maintain one equity-based incentive plan, our 2013 Incentive Share Option Plan, or our 2013 Plan. As of March 15, 2015, a total of 2,340,492 shares were reserved for issuance under our 2013 Plan, of which options to purchase 1,575,366 ordinary shares were issued and outstanding thereunder (i.e., were granted but not canceled, expired or exercised) and 435,126 shares remain unallocated for future equity awards pursuant to our 2013 Plan. In addition, the Board approved conditional grants of 330,000 options to certain of its Office Holders, which are not reflected in the issued and outstanding options or the unallocated share amounts set forth above. Our Board has approved an increase in the number of shares reserved for issuance under our 2013 Plan from 2,340,492 to 3,090,492, subject to shareholder approval under Israeli law. Our 2013 Plan, which was adopted by our Board on September 2, 2013, and approved by our shareholders in December 30, 2013 provides for the grant of options to purchase our ordinary shares and the issuance of restricted shares to our and our affiliates' respective directors, employees, office holders, service providers and consultants. Our 2013 Plan provides for such equity-based compensation under various and different tax regimes, including those detailed below.

The 2013 Plan is administered by our Board, which, on its own or upon the recommendation of our Remuneration Committee or any other similar committee of the Board, shall determine, subject to applicable law, the identity of grantees of awards and various terms of the grant. Consistent with our Compensation Policy, the 2013 Plan provides for granting options to purchase our ordinary shares pursuant to Section 102 of the Israeli Income Tax Ordinance, or the Ordinance, under the capital gains route, to directors, officers and employees who are Israeli residents holding)or have a right to hold or to purchase) less than 10% of our total share capital and do not have a right to receive 10% or more of the Company's profits. Subject to shareholder approval, our Board has approved an amendment to the 2013 Plan, which sets off the terms and conditions with respect to the issuance of restricted share units under the 2013 Plan.

Section 102 of the Ordinance allows Israeli employees, directors and officers, who are not controlling shareholders to receive favorable tax treatment for compensation in the form of shares or options. However, under this route we are not allowed to deduct any expense with respect to the issuance of the options or shares. Israeli non-employee service providers, consultants and shareholders who hold 10% or more of our total share capital or are otherwise controlling shareholders, may be granted options pursuant to Section 3(i) of the Ordinance, which does not provide for similar tax benefits. In order to comply with the terms of the capital gains route pursuant to Section 102 of the Ordinance, the granted options 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 grantee and should be held by the trustee for at least two years after the date of the grant. If such options or shares are sold by the trustee or are transferred to the grantee before the end of the two year period, then the grantee would be taxed at top marginal rates upon selling the shares.

For residents, or deemed residents, of the United States, the 2013 Plan provides grants, which are pursuant to Section 422 of the Internal Revenue Code of 1986, as amended, or the Code, as Incentive Stock Options, or ISOs, and any other participants which do not qualify for ISOs, as Non-statutory Stock Options, or NSOs, pursuant to the Code.

Section 422 of the Code allows employees, directors and officers, who are non-controlling shareholders (e.g., less than 10% shareholders) and are considered residents of the United States or those who are deemed to be residents of the United States for purposes of the payment of tax, or are otherwise subject to taxation in the United States with respect to the grant of awards, to receive favorable tax treatment for compensation in the form of shares or ISOs. 10% shareholders or persons which are not service providers will receive NSOs, which do not entitle them to receive similar tax benefits. Section 422(b) of the Code provides for the ISO track such that the individual does not have to pay ordinary income tax (nor employment taxes) on the difference between the exercise price and the fair market value of the shares issued (however, the holder may have to pay U.S. alternative minimum tax instead). However, if the shares are held for one year from the date of exercise and two years from the date of grant, then the profit (if any) made on sale of the shares is taxed as long-term capital gain. Section 422 of the Code requires that any grant of awards shall not be made at a price which is less than 100% of the fair market value of such awards on the date of the grant, all pursuant to the terms of Section 409A of the Code. However, under this ISO track, we are not allowed to deduct any expense with respect to the issuance of the options or shares. In order to comply with the terms of the ISO track, the option granted thereunder must meet the requirements of Section 422 of the Code when granted and at all times until the exercise thereof.

Options granted under the 2013 Plan will vest in accordance with the vesting dates as determined by the Board following the recommendation of the Remuneration Committee or any other similar committee of the Board with respect to each grant. Generally, options that are not exercised within ten years from the grant date expire, unless otherwise determined by the Board and the Remuneration Committee, as applicable, provided however, that, pursuant to our Compensation Policy, any equity-based awards to Office Holders must include both a minimum vesting period of not less than one year from the date of grant, and an exercise period of no more than ten years from the date of grant.

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 twelve 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 unexercised options will expire and terminate on the date of termination. If a grantee's employment or service is terminated for any other reason, the grantee may exercise his or her vested options within 90 days of the date of termination or within a longer period under specified circumstances. Any expired or unvested options shall return to the option pool reserved under the 2013 Plan for reissuance.

In the event of a merger or consolidation of our company subsequent to which we would no longer exist as a legal entity, or a sale of all, or substantially all, of our ordinary shares or assets or other transaction having a similar effect on us, or a Transaction, any unexercised options then outstanding will be cancelled. Notwithstanding the foregoing, the Board, or the relevant committee of the Board, may determine that the options will not be cancelled but will be assumed or substituted for an appropriate number of the same type of shares or other securities of the successor company as were distributed to the Company or the shareholders in connection with the Transaction. In addition, the Board, or the relevant committee of the Board, may determine to include in certain option agreements either a clause that provides for acceleration of vesting of all or part of the unvested options in the event of a Transaction or the occurrence of another event or a clause which provides that if the optionee's employment with the successor company is terminated by the successor company without cause within a certain period, not to exceed two years from the closing of such Transaction, all or part of the unvested options shall be accelerated.

C. Board Practices.

We are incorporated in Israel, and, therefore, we are subject to various corporate governance practices under Israeli law relating to such matters as external directors, independent directors, audit committee, remuneration committee and internal auditors. These Israeli law requirements are in addition to the requirements of the Listing Rules of the Nasdaq Capital Market and other relevant provisions of U.S. securities laws. Under such Listing Rules, a foreign private issuer may generally follow its home country practices for corporate governance in lieu of such comparable Listing Rules' requirements, except for certain matters such as composition and responsibilities of the audit committee and the SEC-mandated standards for the independence of its members. See below under "Item 16G. Corporate Governance" for further information.

Membership of the Board

Under our Articles, the Board consists of three classes of directors (not including the two external directors, each of whom are not part of any class) which are appointed for fixed terms of office in accordance with the Companies Law and our Articles, with one class being elected each year for a term of approximately three years by our shareholders at our annual general meeting.

Directors so elected cannot be removed from office by the shareholders until the expiration of their term of office. The directors do not receive any benefits upon the expiration of their term of office.

The three classes of directors are Class I Directors, Class II Directors and Class III Directors. The term of the initial Class I Directors will expire at the annual general meeting of shareholders to be held in 2015; the term of the initial Class II Directors will expire at the annual general meeting of shareholders to be held in 2016; and the term of the initial Class III Directors will expire at the annual general meeting of shareholders to be held in 2017. Dr. Halpern is the initial Class I Director; Mr. Shmuel Nir and Mr. Allen Baharaff are the initial Class II Directors; and Mr. William Marth and Mr. Chaim Hurvitz are the initial Class III Directors. In accordance with the Articles, any vacancies on the Board of, including unfilled positions, may be filled by a vote of a majority of the directors then in office, and each director chosen in this manner would hold office until the next annual general meeting of the Company (or until the earlier termination of his or her appointment as provided for in the Companies Law or the Articles).

The Articles provide that the minimum number of members of the Board is three and the maximum number is eleven. The Board presently comprises seven members, two of whom are external directors.

A nominee for service as a director in a public company may not be elected without submitting a declaration to the company, prior to election, specifying that he or she has the requisite qualifications to serve as a director, independent director or external director, as applicable, and the ability to devote the appropriate time to performing his or her duties as such.

A director, including an external director or an independent director, who ceases to meet the statutory requirements to serve as a director, external director or independent director, as applicable, must notify the company to that effect immediately and his or her service as a director will expire upon submission of such notice.

External Directors & Financial Experts

Under the Companies Law and the regulations promulgated pursuant thereto, Israeli companies whose shares have been offered to the public, or that are publicly traded outside of Israel, which we refer to as a public company, are required to appoint at least two natural persons as "external directors." No person may be appointed as an external director if such person is a relative of a controlling shareholder or if such person, a relative, partner or employer of such person, or anyone to whom such person is directly or indirectly subordinate, or any entity under such person's control, has or had, on or within the two years preceding the date of such person's appointment to serve as an external director, any affiliation with the company to whose board of directors the external director is proposed to be appointed, with any controlling shareholder of the company, with a relative of such controlling shareholder, or with any entity controlled by the company or by a controlling shareholder of the company, or, if the company has no controlling shareholder or a shareholder holding 25% or more of the company's voting rights, any affiliation, at the time of the appointment, to the chairman of the board of directors, the chief executive officer or the most senior financial officer of the company, or to a shareholder holding 5% or more of the outstanding shares or voting rights of the company. The term "affiliation" includes an employment relationship, a business or professional relationship maintained on a regular basis or control, as well as service as an office holder (as such term is defined in the Companies Law and which term includes a director), except for a term of a director appointed in order to serve as an external director of a company that is about to offer its shares to the public for the first time. The Israeli Minister of Justice, in consultation with the Israeli Securities Authority, may determine that certain matters will not constitute an affiliation, and has issued certain regulations with respect thereof.

In addition, no person may serve as an external director if: (i) the person's other positions or other business activities create, or may create, a conflict of interest with the person's service as an external director or interfere with the person's ability to serve as an external director; (ii) at the time such person serves as a non-external director of another company on whose board of directors a director of the reciprocal company serves as an external director; (iii) the person is an employee of the Israel Securities Authority or of an Israeli stock exchange; (iv) such person or such person's relative, partner, employer or anyone to whom such person is directly or indirectly subordinate, or any entity under such person's control, has business or professional relations with any person or entity he or she should not be affiliated with, as described in the previous paragraph, unless such relations are negligible; or (v) such person received compensation, directly or indirectly, in connection with such person's services as an external director, other than as permitted under the Companies Law and the regulations promulgated thereunder. If, at the time of election of an external director, all other directors who are not controlling shareholders of such company or their relatives, are of the same gender, then the designated external director must be of the other gender.

Pursuant to the Companies Law, an external director is required to have either financial and accounting expertise or professional qualifications according to criteria set forth in regulations promulgated under the Companies Law, provided that at least one of the external directors has financial and accounting expertise. The board of directors must make the determination as to the financial and accounting expertise, and as to the professional qualifications, of a director taking into consideration those criteria and matters set forth in the regulations. In addition, the boards of directors of public companies are required to make a determination as to the minimum number of directors who must have such financial and accounting expertise based on, among other things, the type of company, its size, the volume and complexity of the company's activities and the number of directors. The Board has determined that the minimum number of directors with financial and accounting expertise, in addition to the external director or directors who have such expertise, will be one, and that Mr. Marth qualifies as such. The external director who qualifies to have such expertise is Ms. Yaron-Eldar. Each of Ms. Yaron-Eldar and Mr. Marth qualifies as an audit committee financial expert pursuant to the applicable SEC rules, and accordingly as having the necessary financial sophistication as required by the Nasdaq Capital Market rules.

External directors are elected for a term of three years at the general meeting of shareholders by a simple majority, provided that the 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 as a result of an affiliation with a controlling shareholder, who are present and voting (abstentions are disregarded), or that the non-controlling shareholders or shareholders who do not have a personal interest in the matter as a result of an affiliation with a controlling shareholder who are present and voted against the election hold 2% or less of the voting power of the company.

External directors may be re-elected for two additional terms of three years each, provided that with respect to the appointment for each such additional three year term, one of the following has occurred: (i) the reappointment of the external director has been proposed by one or more shareholders holding together 1% or more of the aggregate voting rights in the company and the appointment was approved at the general meeting of the shareholders by a simple majority, provided that: (1)(x) in calculating the majority, votes of controlling shareholders or shareholders having a personal interest in the appointment as a result of a relationship with a controlling shareholder and abstentions are disregarded and (y) the total number of shares of shareholders who do not have a personal interest in the appointment as a result of a relationship with a controlling shareholder and/or who are not controlling shareholders, present and voting in favor of the appointment exceed 2% of the aggregate voting rights in the company, and (2) the external director so reappointed is not a related or competing shareholder, or a relative of such shareholder, at the time of the appointment, and does not and did not have, any affiliation with a related or competing shareholder, on or within the two years preceding such person's reappointment to serve as another term as external director. The term "related or competing shareholder" means the shareholder(s) proposing the reappointment or a shareholder holding 5% or more of the outstanding shares or voting rights of the company, provided that at the time of the reappointment, such shareholder(s), a controlling shareholder of such shareholder(s), or a company controlled by such shareholder(s), have a business relationship with the company or are competitors of the company; the Israeli Minister of Justice, in consultation with the Israeli Securities Authority, may determine that certain matters, under his conditions, will not constitute a business relationship or competition with the company; or (ii) the reappointment of the external director has been proposed by the board of directors and the appointment was approved by the majority of shareholders required for the initial appointment of an external director.

However, under regulations promulgated pursuant to the Companies Law, companies whose shares are listed for trading on specified exchanges outside of Israel, including the Nasdaq Capital Market, may elect external directors for additional terms that do not exceed three years each, beyond the three year terms generally applicable, provided that, if an external director is being re-elected for an additional term or terms beyond three year terms: (i) the audit committee and board of directors must determine that, in light of the external director's expertise and special contribution to the board of directors and its committees, the re-election for an additional term is to the company's benefit; (ii) the external director must be re-elected by the required majority of shareholders as described above; and (iii) the term during which the nominee has served as an external director and the reasons given by the audit committee and board of directors for extending his or her term of office must be presented to the shareholders prior to their approval.

Following termination of service as an external director, a public company, a controlling shareholder thereof and any entity controlled by a controlling shareholder, may not grant any benefit, directly or indirectly, to any person who served as an external director of such public company, or to his or her spouse or child, including, not appointing such person, or his or her spouse or child, as an office holder of such public company or of any entity controlled by a controlling shareholder of such public company, not employing such person or his or her spouse or child and not receiving professional services for pay from such person, either directly or indirectly, including through a corporation controlled by such person, all until the lapse of two years from termination of office with respect to the external director, his or her spouse or child; and until the lapse of one year from termination of office with respect to other relatives of the former external director.

Each committee of the Board that is authorized to exercise powers of a company's board of directors must include at least one external director. The audit and remuneration committees of a company's board of directors must include all of such company's external directors.

Under the Companies Law, an external director cannot be dismissed from office unless: (i) the board of directors determines that the external director no longer meets the statutory requirements for holding the office, or that the external director is in breach of his or her duty of loyalty to the company and the shareholders vote, by the same majority required for the appointment, to remove the external director after the external director has been given the opportunity to present his or her position; (ii) a court determines, upon a request of a director or a shareholder, to dismiss the external director after finding that such external director no longer meets the statutory requirements of an external director or that the external director is in breach of his or her duty of loyalty to the company; or (iii) a court determines, upon a request of the company or a director, shareholder or creditor of the company, to dismiss the external director after finding that such external director is unable to fulfill his or her duty or has been convicted of specified crimes.

Ms. Yaron-Eldar and Dr. Sidransky are the current external directors, appointed by our Board and approved by our shareholders to serve as such. Each external director will serve for an initial term of three years until June 2017.

Independent Directors Under the Companies Law

Under the Companies Law an "independent director" is either an external director or a director appointed or classified as such who meets the same non-affiliation criteria as an external director, as determined by the audit committee, and who has not served as a director of the company for more than nine consecutive years. For these purposes, ceasing to serve as a director for a period of two years or less would not be deemed to sever the consecutive nature of such director's service. An independent director may be removed from office in the same manner that an external director may be removed and, upon termination of service as an independent director, is subject to the same restrictions with respect to receipt of benefits, service as an office holder, employment and provision of professional services as are applicable to external directors.

Regulations promulgated pursuant to the Companies Law provide that a director in a public company whose shares are listed for trading on specified exchanges outside of Israel, including the Nasdaq Capital Market, such as the Company, who qualifies as an independent director under the relevant non-Israeli rules relating to independence standards for audit committee membership and who meets certain non-affiliation criteria, which are less stringent than those applicable to external directors, would be deemed an "independent" director pursuant to the Companies Law provided: (i) he or she has not served as a director for more than nine consecutive years; (ii) he or she has been approved as such by the audit committee; and (iii) his or her remuneration shall be in accordance with the Compensation Regulations. For these purposes, ceasing to serve as a director for a period of two years or less would not be deemed to sever the consecutive nature of such director's service.

Furthermore, pursuant to these regulations, such company may reappoint a person as an independent director for additional terms, beyond nine years, which do not exceed three years each, if the audit committee and the board of directors determine that in light of the independent director's expertise and special contribution to the board of directors and its committees, the reappointment for an additional term is to the company's benefit.

Committees of the Board

Our Articles also provide that the Board may delegate any, or all, of its powers to one or more committees of the Board, and may entrust to and confer upon a "managing director" such of its powers as it deems appropriate. However, the Companies Law provides that certain powers and authorities (for example, the power to approve the financial statements) may not be delegated and may be exercised only by the Board. Notwithstanding the foregoing, we currently do, and intend to continue to, comply with the corporate governance requirements of the Nasdaq Capital Market, except to the extent indicated elsewhere in this annual report, including as set forth under "Item 16G. Corporate Governance" below. The Companies Law requires public companies such as the Company to appoint an audit committee and a remuneration committee.

Audit Committee

The Companies Law requires public companies to appoint an audit committee comprised of at least three directors, including all of the external directors, the majority of whom must be independent directors under the Companies Law. The Companies Law further stipulates that the following may not be members of the audit committee: (i) the chairman of the board of directors; (ii) any director employed by or providing services on an ongoing basis to the company, to a controlling shareholder of the company or an entity controlled by a controlling shareholder of the company; (iii) a director whose livelihood depends on a controlling shareholder; and (iv) a controlling shareholder or any relative of a controlling shareholder.

The Companies Law further requires that: (i) the chairperson of the audit committee must be an external director; (ii) generally, any person who is not entitled to be a member of the audit committee may not attend the audit committee's meetings and voting sessions, unless such person was invited by the chairperson of the committee for the purpose of presenting a specific subject matter thereof; and (iii) the quorum required for the convening of meetings of the audit committee and for adopting resolutions by the audit committee be a majority of the members of the audit committee, provided that the majority of the members present are independent directors and at least one of them is an external director.

The responsibilities of the audit committee under the Companies Law include: (i) identifying flaws in the management of a company's business and making recommendations to the board of directors as to how to correct them; (ii) with respect to certain actions involving conflicts of interest and with respect to certain related party transactions, deciding whether such actions are material actions and whether such transactions are extraordinary transactions, respectively, all for the purpose of approving such actions or transactions; (iii) reviewing and deciding whether to approve certain related party transactions and certain actions involving conflicts of interest; (iv) reviewing the internal auditor's work program; (v) examining the company's internal control structure and processes, the performance of the internal auditor and whether the internal auditor has at his or her disposal the tools and resources required to perform his or her duties, considering, inter alia, the special needs of the company and its size; (vi) examining the external auditor's scope of work as well as the external auditor's fees and providing its recommendations to the appropriate corporate organ; (vii) providing for arrangements as to the manner in which the company will deal with employee complaints with respect to deficiencies in the management of the company's business and the protection to be provided to such employees; and (viii) with respect to related party transactions with a controlling shareholder, regardless of whether such transactions are extraordinary transactions, that prior to entering into such transaction, to establish the requirement of having a competitive process under the supervision of the audit committee or any individual, committee or body on its behalf and according to criteria established by the audit committee and to determine procedures for approving certain related party transactions with a controlling shareholder, which were determined by the audit committee to be non-extraordinary transactions, but which are not negligible transactions.

Our Board 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 the Nasdaq Capital Market, as well as the requirements for such committee under the Companies Law, as described below.

Our Audit Committee oversees the accounting and financial reporting processes of the Company. It also provides assistance to the Board in fulfilling its legal and fiduciary obligations with respect to matters involving the accounting, auditing, financial reporting and internal control functions of the Company. In carrying out its duties, our Audit Committee meets with management at least once a year, at which time, among other things, it reviews, and either approves or disapproves, the financial results of the Company for the immediately preceding fiscal year and conveys its conclusions in this regard to the Board. Our Audit Committee also monitors generally the services provided by the Company's external auditors to ensure their independence, and reviews all audit and non-audit services provided by them.

The Audit Committee's policy is to pre-approve all audit and non-audit services provided by the Company's external auditors. These services may include audit services, tax services and other consulting services. Additional services may be pre-approved by the Audit Committee on an individual basis. Once services have been pre-approved, the Company's external auditors and management then report to the Audit Committee on a periodic basis regarding the extent of services actually provided in accordance with the applicable pre-approval, and regarding the fees for the services performed. Such fees for 2014 were pre-approved by the Audit Committee in accordance with these procedures.

The Company's external and internal auditors also report regularly to our Audit Committee at its meetings, and our Audit Committee discusses with the Company's external auditors the quality, not just the acceptability, of the accounting principles, the reasonableness of significant judgments and the clarity of disclosures in the Company's financial statements, as and when it deems it appropriate to do so.

Under the provisions of the Sarbanes-Oxley Act, the audit committee is directly responsible for the appointment, compensation and oversight of the work of the company's external auditors. However, under Israeli law, the appointment of external auditors and their compensation require the approval of the shareholders of a public company. Pursuant to Israeli law, the shareholders may delegate the authority to determine the compensation of the external auditors to the board of directors. In addition, pursuant to the Companies Law, the audit committee is required to examine the external auditors' fees and to provide its recommendations with respect thereto to the appropriate corporate body. Accordingly, the appointment of the external auditors is required to be approved and recommended to the shareholders by our Audit Committee and approved by the shareholders. The compensation of the external auditors for audit services is required to be approved and recommended to the Board by our Audit Committee and approved by the Board. The Board has delegated its authority to approve the compensation of external auditors for non-auditing services to the Audit Committee.

Mr. Nir, Ms. Yaron-Eldar and Dr. Sidransky are the current members of our Audit Committee, with Ms. Yaron-Eldar serving as chairperson. Each of them is an "independent director" in accordance with the Nasdaq Capital Market corporate governance requirements, as affirmatively determined by our Board, and Ms. Yaron-Eldar and Dr. Sidransky also meet the qualifications for service as an "external director" under the Companies Law and the regulations promulgated thereunder, also as affirmatively determined by our Board and our shareholders. In addition, our Board has affirmatively determined that Ms. Yaron-Eldar also qualifies as an audit committee financial expert pursuant to the applicable SEC rules, and accordingly has the necessary financial sophistication as required by the Nasdaq Capital Market rules, and as a financial and accounting expert under the Companies Law.

Remuneration Committee

The Companies Law requires public companies to appoint a remuneration committee comprised of at least three directors, including all of the external directors, who must generally also constitute a majority of the members. All other members of the committee, who are not external directors, must be directors who receive compensation consistent with that of external directors and that is in compliance with the Compensation Regulations. In addition, the chairperson of the remuneration committee must be an external director.

The Companies Law further stipulates that directors who are not qualified to serve on the audit committee, as described above, may not serve on the remuneration committee either and that similar to the audit committee, generally, any person who is not entitled to be a member of the remuneration committee may not attend the remuneration committee's meetings. Our Board has adopted a remuneration committee charter setting forth the responsibilities of our Remuneration Committee, as described below.

The responsibilities of the remuneration committee under the Companies Law include: (i) making recommendations to the board of directors with respect to the approval of the compensation policy and any extensions thereto; (ii) periodically reviewing the implementation of the compensation policy and providing the board of directors with recommendations with respect to any amendments or updates thereto; (iii) reviewing and resolving whether or not to approve transactions with respect to the terms of office and employment of office holders; and (iv) resolving, under certain circumstances prescribed under the Companies Law, whether or not to exempt a transaction with a candidate for chief executive officer who meets non-affiliation criteria from shareholder approval.

Our Remuneration Committee also oversees the administration of the Company's various compensation plans and arrangements, in particular, the incentive compensation, deferred compensation and equity based plans of the Company (and to the extent appropriate, of the subsidiaries of the Company) and assists the Board in fulfilling its responsibilities relating to the compensation of directors, the Chief Executive Officer and other office holders of the Company. In carrying out these duties, our Remuneration Committee meets on an ad hoc basis. Under the Companies Law, our Remuneration Committee may need to seek the approval of the Board and the shareholders for certain compensation decisions as described above. Each member of our Remuneration Committee is an "independent director" in accordance with the Nasdaq Capital Market corporate governance requirements, as affirmatively determined by our Board. Mr. Nir, Ms. Yaron-Eldar and Dr. Sidransky are the current members of our Remuneration Committee, with Ms. Yaron-Eldar serving as chairperson.

Nominating Committee

Our Board does not currently have a nominating committee, as director nominees are presented by our Board to our shareholders based upon the nominations made by the Board itself, or in certain circumstances as prescribed by the Companies Law, by a shareholder or group of shareholders. Pursuant to the Listing Rules of the Nasdaq Capital Market, we currently intend to rely upon the exemption for foreign private issuers from the Nasdaq Capital Market corporate governance requirements related to independent director oversight of nominations to our Board and the adoption of a formal written charter or board resolution addressing the nominations process. See "Item 16G. Corporate Governance."

R&D Committee

Our R&D Committee, which was established by the Board on May 2014, advises and assists the Board in its oversight of our research and development programs, including the rationale and timeline of clinical trials and other studies, as well as market surveys in connection therewith. The R&D Committee operates in accordance with the purposes and objectives determined by the Board from time to time. Mr. Hurvitz, Dr. Sidransky and Mr. Marth are the current members of our R&D Committee, with Mr. Hurvitz serving as chairperson.

Internal Auditor

Under the 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. The role of the internal auditor is to examine, among other things, our compliance with applicable law and orderly business procedures. An internal auditor should comply with the requirements of the Companies Law and the Internal Audit Law, 5752-1992, and may not be:

(a) a person (or a relative of a person) who holds more than 5% of the Company's outstanding shares or voting rights;

(b) a person (or a relative of a person) who has the power to appoint a director or the general manager of the Company;

(c) an office holder, including a director, of the Company (or a relative thereof); or

(d) a member of the Company's independent accounting firm, or anyone on his or her behalf.

Pursuant to Israeli law, an internal auditor's tenure cannot be terminated without his or her consent, nor can he or she be suspended from such position unless the board of directors of the company has so resolved following the recommendations of the company's audit committee and, after providing the internal auditor with the opportunity to present his or her position to the board of directors of the company and to the audit committee.

On November 2, 2014, our Board appointed Mr. Alon Amit, CPA, from Raveh Ravid & Co. CPA, Tel Aviv, Israel, as the Company's internal auditor, effective as of January 1, 2015, for a period of two years.

Exculpation and Indemnification of Directors and Officers

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

Under the Companies Law, a company may indemnify, or undertake in advance to indemnify, an office holder for the following liabilities and expenses, imposed on office holder or incurred by office holder due to acts performed by him or her as an office holder, provided its articles of association include a provision authorizing such indemnification:

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

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

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

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

- a breach of the duty of loyalty to the company, provided that the office holder acted in good faith and had a reasonable basis to believe that such act would not prejudice the company;
- a breach of the duty of care to the company or to a third-party; and
- a financial liability imposed on the office holder in favor of a third-party.

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

- a breach of the duty of loyalty, except for indemnification and insurance for a breach of the duty of loyalty to the company in the event office holder acted in good faith and had a reasonable basis to believe that the act would not prejudice the company;
- a breach of the duty of care committed intentionally or recklessly, excluding a breach arising out of the negligent conduct of the office holder;
- an act or omission committed with intent to derive unlawful personal benefit; or
- a fine, monetary sanction, penalty or forfeit levied against the office holder.

Under the Companies Law, exculpation, indemnification and insurance of office holders require the approval of the remuneration committee, board of directors and, in certain circumstances, the shareholders, as described above under "Item 6—Directors, Senior Management and Employees—B. Compensation."

Our Articles permit us to exculpate, indemnify and insure our office holders to the fullest extent permitted by the Companies Law. Each of our office holders have entered into an indemnification agreement with us. In addition, have entered into agreements with each of our office holders, that became effective immediately upon consummation of our initial public offering, which superseded and replaced each indemnification agreement previously entered into by such office holders with the Company, exculpating them, to the fullest extent permitted by Israeli law, from liability to us for damages caused to us as a result of a breach of the duty of care and undertaking to indemnify them to the fullest extent permitted by Israeli law, including with respect to liabilities resulting from certain acts performed by such office holders in their capacity as an office holder of the Company, our subsidiaries or our affiliates. In accordance with each such new indemnification agreement, we agree to indemnify our office holders for certain liabilities resulting from our initial public offering. The indemnification is limited both in terms of amount and coverage.

In the opinion of the SEC, indemnification of directors and office holders for liabilities arising under the Securities Act, however, is against public policy and therefore unenforceable.

Agreements with Directors

Other than with our President and Chief Executive Officer, as detailed in "Item 7. Major Shareholder and Related Party Transactions—Related Party Transactions—Employment Agreements and Arrangements with Directors and Related Parties—Employment Agreement with Our President and Chief Executive Officer," we do not have written agreements with any director providing for benefits upon the termination of his or her services with our Company.

D. Employees.

As of December 31, 2014, we had 15 employees, of which 11 were full-time employees, two were part-time employees and two were consultants. Nine of such employees were involved in our product development operations and six served in general and administrative capacities. Thirteen of our employees were located in Israel and two of our research and development employees were located in the United Kingdom. The increase in the number of employees from 2013 by seven employees was the result of our growing activity in connection with our clinical studies, and drug development operations, which require more employees in research and development, as well as in administration and operations. In connection with our future U.S. clinical trials, we intend to hire a vice president for clinical operations, who we expect will be responsible for, among other things, establishing and building a clinical research infrastructure in the United States, including for the Phase III clinical trials, communications with the scientific and medical communities and physicians, which we believe may increase our operations and presence within the United States. In March 2015, we engaged George Tonelli to serve as our Vice President of Clinical Operations.

While none of our employees located in Israel are party to any collective bargaining agreements or represented by any labor unions, certain provisions of the Israeli labor laws and certain collective bargaining agreements between the Histadrut (General Federation of Labor in Israel) and the Coordination Bureau of Economic Organizations (including the Industrialists' Associations) are applicable to our employees by order of the Israel Ministry of Economics. These provisions primarily concern the length of the workday, minimum daily wages for professional workers, pension fund benefits for all employees, insurance for work-related accidents, procedures for dismissing employees, determination of severance pay and other conditions of employment. We generally provide our employees with benefits and working conditions beyond the required minimums. We have never experienced any employment-related work stoppages and believe our relationship with our employees is good.

E. Share Ownership.

As of March 15, 2015, there were 59 record holders of our ordinary shares holding an aggregate of 85.91% of our ordinary shares on a fully diluted basis.

Certain Information Concerning Ordinary Shares Owned by Office Holders

The following table sets forth information regarding beneficial ownership of our ordinary shares as of March 15, 2015 held by our directors and executive officers, individually and as a group.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to ordinary shares. Ordinary shares issuable under share options, warrants or other conversion rights currently exercisable or that are exercisable within 60 days after March 15, 2015 are deemed outstanding for the purpose of computing the percentage ownership of the person holding the options, warrants or other conversion rights, but are not deemed outstanding for the purpose of computing the percentage ownership of any other person. Percentage of shares beneficially owned is based on 11,100,453 ordinary shares outstanding on March 15, 2015, which does not include an aggregate of 2,340,492 ordinary shares that were either subject to outstanding equity awards granted or available for grant, of which: (i) 1,944,003 were subject to outstanding options (of which: (a) 1,239,752 were vested or will be vested within 60 days as of the date hereof; and (b) 330,000 were allocated by the Board to certain Office Holders and are subject to shareholder approval and/or obtaining a tax pre-ruling from the Israeli Tax Authority); and (ii) 435,126 remained available for future equity awards pursuant to our 2013 Plan.

	As of March 15, 2015	
	Number of ordinary shares beneficially owned	Percentage of ordinary shares beneficially owned
Allen Baharaff[1][3]	4,130,140	35.0%
Chaim Hurvitz[2][3]	1,003,873	9.0%
Dr. Maya Halpern	64,152	*
Shmuel Nir[3][4]	50,021	*
Dr. Maureen Graham	9,477	*
William Marth	5,720	*
Dr. Antony Appleyard	9,477	*
Josh Blacher[5]	4,000	*
George Tonelli[6]	—	*
Tali Yaron-Eldar	—	*
David Sidransky	—	*
All directors and executive officers as a group (11 persons)[6]	**5,276,861**	**44.6%**

* Less than 1%.

(1) Ordinary shares beneficially owned consist of (i) 3,420,823 ordinary shares, of which 3,416,823 are held through G. Yarom Medical Research Ltd., a company incorporated under the laws of the State of Israel, of which Mr. Baharaff is the controlling shareholder and the chairman of its Board of Directors and (ii) options to purchase 709,317 ordinary shares that are currently exercisable within 60 days from March 15, 2015, of which 567,162 have an exercise price per share of NIS 0.01 and will expire in September 2023, and 142,155 have an exercise price of $0.53 and will expire in September 2023. All such options were granted on December 30, 2013. Of the 4,130,140 ordinary shares, Mr. Baharaff exercises sole voting and dispositive power over 713,317 shares beneficially owned and shared voting and dispositive power with G. Yaron Medical Research Ltd. over 3,416,823 shares.

(2) Ordinary shares beneficially owned consist of 1,003,873 ordinary shares, of which 776,385 shares are held through Shirat HaChaim Ltd., a company incorporated under the laws of the State of Israel, of which Mr. Hurvitz is the controlling shareholder and the chairman of its Board of Directors. Of the 1,003,873 ordinary shares, Mr. Hurvitz exercises sole voting and dispositive power over 227,488 ordinary shares and shared voting and dispositive power with Shirat HaChaim Ltd. over 776,385 shares.

(3) All options included are either currently exercisable or will be exercisable within 60 days from the date hereof.

(4) Ordinary shares beneficially owned consist of (i) options to purchase 8,583 shares that are currently exercisable or will be exercisable within 60 days from the date hereof, all of which have an exercise price per share of $3.57, will expire in February 2024 and were granted on February 21, 2014, and (ii) 41,438 ordinary shares held through Tushia Consulting Engineers Ltd., of which Shmuel Nir is its controlling shareholder.

(5) On October 7, 2014, the Company and Mr. Morris mutually agreed to terminate the consulting agreement dated March 4, 2014, pursuant to which Mr. Morris served as the Company's Chief Financial Officer. The termination was effective December 31, 2014. On January 5, 2014, the Company announced the appointment of Josh Blacher, effective January 1, 2014, to replace Mr. Morris and serve as Chief Financial Officer.

(6) On March 6, 2015, the Company entered into a Consulting Agreement to engage Mr. Tonelli to provide consulting services in connection with the Company's clinical trials, subject to the Company's remuneration committee and Board approval. Such approvals were granted on March 30, 2015. In providing such services Mr. Tonelli, shall act as the Company's Vice President of Clinical Operations.

This table is based upon information supplied by officers and directors and is believed to be accurate. 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 shareholder's address is: c/o Galmed Pharmaceuticals Ltd., 8 Shaul Hamelech Blvd., Amot Mishpat Bldg., Tel Aviv, Israel 6473307.

Certain Information Concerning Equity Awards to Office Holders

The following table sets forth information, as of March 15, 2015, concerning all outstanding option awards to Office Holders. Mr. Morris, our former Chief Financial Officer, did not receive any equity awards. On March 6, 2015, the Company entered into a Consulting Agreement to engage Mr. Tonelli to provide consulting services in connection with the Company's clinical trials, subject to the Company's remuneration committee and Board approval. Such approvals were granted on March 30, 2015. In providing such services Mr. Tonelli, shall act as the Company's Vice President of Clinical Operations. As of March 15, 2015, Mr. Tonelli had not received any equity awards.

Name of Office Holder	Date of grant	Exercise price per share ($)	Shares subject to the option	Shares vested and unexercised	Shares unvested	Schedule date of expiration
Chaim Hurvitz[1]	December 30, 2014	$ 5.49	10,000[1][2]	0	10,000	Dec-30-2024
Allen Baharaff	December 22, 2013	NIS 0.01	266,085	266,085	0	Sep-2-2023
	December 22, 2013	$ 0.53	174,960	131,220	43,740	Sep-2-2023
	December 22, 2013	NIS 0.01	150,903	150,903	0	Sep-2-2023
	December 22, 2013	NIS 0.01	150,174	150,174	0	Sep-2-2023
	December 30, 2014	$ 5.49	140,000[1][2]	0	140,000	Dec-30-2024
Maya Halpern	December 22, 2013	$ 3.57	64,152	64,152	0	Sep-2-2023
	December 30, 2014	$ 5.49	120,000[1][2]	0	120,000	Dec-30-2024
William Marth	March 18, 2014	$ 3.57	17,166	4,290	12,876	Sep-02-2023
	December 30, 2014	$ 5.49	10,000[1]	0	10,000	Dec-30-2024
Shmuel Nir	February 21, 2014	$ 3.57	8,583	8,583	0	Sep-02-2023
	December 30, 2014	$ 5.49	10,000[1][2]	0	10,000	Dec-30-2024
Tali Yaron-Eldar	December 30, 2014	$ 5.49	10,000[1]	0	10,000	Dec-30-2024
David Sidransky	December 30, 2014	$ 5.49	10,000[1]	0	10,000	Dec-30-2024
Josh Blacher	December 30, 2014	$ 5.49	90,000	0	90,000	Dec-30-2024
Maureen Graham	December 22, 2013	$ 3.57	9,477	9,477	0	Sep-2-2023
	December 30, 2014	$ 5.49	10,000[1][2]	0	10,000	Dec-30-2024
Antony Appleyard	December 22, 2013	$ 3.57	9,477	9,477	0	Sep-2-2023
	December 30, 2014	$ 5.49	10,000[1][2]	0	10,000	Dec-30-2024

(1) This option grant is subject to shareholder approval, following the approval and recommendation of the Board and the Remuneration Committee, dated December 30, 2014.

(2) This option grant is subject to obtaining a tax pre-ruling from the Israeli Tax Authority.

ITEM 7. Major Shareholders and Related Party Transactions.

A. Major Shareholders.

Except as set forth in "Item 6. Directors, Senior Management and Employees—E. Share Ownership", to the best of our knowledge, no other person who we know beneficially owns 5.0% or more of the Company's ordinary shares outstanding as of March 15, 2015. None of our shareholders has different voting rights from other shareholders. Other than as described herein, to the best of our knowledge, we are not owned or controlled, directly or indirectly, by another corporation, by any foreign government or by any natural person or legal persons, severally or jointly, and we are not aware of any arrangement that may, at a subsequent date, result in a change of control of our company.

B. Related Party Transactions.

The following is a summary description of the material terms of those transactions with related parties to which we, or our subsidiaries, are party and which were in effect within the past fiscal year.

Share Purchase Agreement (February 2014)

On February 3, 2014 we entered into a share purchase agreement with certain of our shareholders and new investors, or the Share Purchase Agreement, pursuant to which we issued to such existing shareholders and new investors 560,224 ordinary shares at a price per share of $3.57 for a total investment amount of $2.0 million.

Registration and Information Rights Agreement

On December 30, 2013, in connection with the Reorganization, we entered into a registration and information rights agreement, on substantially the same terms as, and to replace, a prior investors' rights agreement entered into on December 21, 2011 between GHI and certain of its shareholders, or the Registration Rights Agreement. As of the date hereof, each of the holders of at least 1% of our ordinary shares is entitled to be a party to the Registration Rights Agreement, either as an original signatory or as an assignee or transferee of our ordinary shares, including Shirat HaChaim Ltd., which is an entity controlled by our Chairman, G. Yarom Medical Research Ltd., which is controlled by President and our Chief Executive Officer, David and Debora Goldfarb and Medgal Holdings S.A. We will refer to these shareholders, excluding Shirat HaChaim Ltd., as the Other Shareholders. The Registration Rights Agreement contains provisions regarding registration rights as set forth below.

Demand Registration Rights. At any time beginning six months following the effective date of our initial public offering, upon a request either Shirat HaChaim Ltd. or at least 40% of the registrable securities held by the Other Shareholders, we are required to use commercially reasonable efforts to register such requesting shareholders' ordinary shares under the Securities Act, but only if the aggregate offering price of the shares to be registered is at least $5,000,000. We are not required to effect more than two demand registrations; one registration upon the request of Shirat HaCahim Ltd. and the other upon a request of at least 40% of the registrable securities held by the Other Shareholders.

Piggyback Registration Rights. All of our shareholders that are a party to the Registration Rights Agreement have the right to request that we include their registrable securities in any registration statement that we file in connection with public offerings of our shares and resale registrations, except for certain excluded registrations, such as registrations of shares issued under employee benefit plans, a registration relating to a corporate reorganization or a registration on a form that does not include substantially the same information as would be required to be included in a registration statement covering the sales of registrable securities. If such public offering is underwritten, the right of any shareholder to include shares in the registration related thereto is conditioned upon the shareholder accepting the terms of the underwriting agreement between us and the underwriters, and then only in such quantity as the underwriters in their sole discretion determine will not materially and adversely jeopardize the success of such offering.

Form F-3 Registration. At any time after we become eligible under applicable securities laws to file a registration statement Form F-3, upon a written request of Shirat HaChaim Ltd. or the holders of at least 40% of the registrable securities held by the Other Shareholders, we will be required to register such shareholders ordinary shares under the Securities Act, but only if the aggregate offering price of the shares to be registered is at least $3,000,000. We are not required to effect more than two registrations on Form F-3 in any 12 month period.

Registration Preference. In the event that we register shares of our shareholders in a public offering or in a subsequent registration, Shirat HaChaim Ltd. has a preference over all other shareholders to register and sell its shares. In which case, the shares of all other shareholders to be registered will be reduced accordingly. However, in any registration initiated by us, the shares held by us or to be issued by us have such a preference over all other shareholders, including Shirat HaChaim Ltd.

Expenses. We have agreed to pay all expenses incurred in carrying out the above registrations, including the reasonable fees one counsel chosen by the selling shareholders that are a party to the Registration Rights Agreement, but excluding discounts or commissions payable to any underwriter; provided however, with respect to any registration initiated pursuant to a shareholder's demand rights, as set forth above, we will not be required to pay for any expenses if the registration is later withdrawn at the request of a majority holders of the shares to be registered, unless such holders agree to forfeit their right to each of their respective demand registrations.

The Registration Rights Agreement is silent with respect to term and termination provisions. However, it provides that we are not required to register shares of holders of less than 1% of our ordinary shares on a fully diluted basis if such shares may be sold pursuant to Rule 144 under the Securities Act.

Shareholders Rights Agreement

On December 30, 2013, in connection with the Reorganization prior to our initial public offering, we entered into a shareholders rights agreement, on substantially the same terms as, and to replace, a prior shareholders' rights agreement entered into on December 21, 2011 between GHI and certain of its shareholders, or the Shareholders Rights Agreement. Pursuant to the Shareholders Rights Agreement, the shareholders party thereto agreed to vote their ordinary shares for the election of our directors as follows: Two directors designated by G. Yarom Medical Research Ltd., one director designated by Shirat Hachaim Ltd., one director designated by the holders of the majority of the ordinary shares held by David and Debora Goldfarb and Medgal Holdings S.A. and additional directors (including any additional directors whose office may become vacated from time to time) designated by the majority vote of the directors then in office or by the shareholders of the Company at a general meeting. The Shareholders Rights Agreement was terminated upon the consummation of our initial public offering in March 2014.

Confirmation and Release Letter from the Beneficiaries of the late Professor Tuvia Gilat

The late Professor Tuvia Gilat, our co-founder, was employed by GHI, our predecessor, as its chief executive officer between January 2001 and December 2010, at which time he left due to severe illness. Professor Tuvia Gilat passed away in 2011. On December 18, 2011, we reached a final and conclusive settlement, or the Settlement, with all of Prof. Gilat's beneficiaries, which includes our current President and Chief Executive Officer and controlling shareholder, Mr. Allen Baharaff, pursuant to his last will and testament, or the Beneficiaries. The Settlement related to Prof. Gilat's rights and entitlements in connection with his employment with the Company and its predecessor, and the termination thereof, including, without limitation, all social benefit deductions under Israeli law. Following the approval and recommendation of the Audit Committee and the Board, on December 15, 2014, the shareholders approved to accelerate the payment due under the Settlement and to pay such amount from the Company's current net capital, as opposed to net profits, which was previously contemplated by the terms of the Settlement. The total Settlement amount outstanding, including interest, payable to the Beneficiaries was $279,999, which was fully paid to them during the first quarter of 2015.

Financing Agreement with GRD

Following the completion of our initial public offering in the United States, we provide financing to GRD from time to time, pursuant to which, the Company and GRD have executed several capital notes for an aggregate outstanding principal amount of $35.5 million. The par value of such notes is in NIS, and they bear no interest nor repayment date. Provided however, that no repayment shall be made before the fifth anniversary from the issuance date of each note.

Agreements with Directors and Officers

Employment and Consulting Agreements. We have entered into written employment or consulting agreements with certain of our Office Holders. These agreements provide for notice periods of varying duration for termination of the agreement by us or by the relevant Office Holder, during which time the Office Holder 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 these Office Holders. 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 certain of our Office Holders. Such option agreements may contain acceleration provisions upon certain merger, acquisition, or change of control transactions. We describe our 2013 Plan under "Item 6. Directors, Senior Management and Employees—B. Compensation—2013 Incentive Share Option Plan." If the relationship between us and an Office Holder is terminated, except for cause (as defined in the 2013 Plan and/or the applicable option award agreement), options that are vested will generally remain exercisable for 90 days after such termination.

C. Interests of Experts and Counsel.

Not applicable.

ITEM 8. Financial Information.

A. Consolidated Financial Statements and Other Financial Information.

See "Item 18. Financial Statements" for a list of all financial statements filed as part of this Annual Report on Form 20-F.

Legal Matters

We are neither party to any legal or arbitration proceedings, including those relating to bankruptcy, receivership or similar proceedings and those involving any third-party, nor any governmental proceedings pending or known to be contemplated, which may have, or have had in the recent past, significant effects on the company's financial position or profitability.

Dividend Policy

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 and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our Board may deem relevant.

Payment of dividends may also be subject to Israeli withholding taxes. See "Item 10. Additional Information—E. Taxation—Certain Israeli Tax Considerations" for additional information.

B. Significant Changes.

No significant changes with respect to our consolidated financial statements have occurred since December 31, 2014.

ITEM 9. The Offer and Listing.

9.A.4 Offer and Listing Details

Our ordinary shares have been listed on the Nasdaq Capital Market under the symbol "GLMD" since March 13, 2014. Prior to that date, there was no public trading market for our ordinary shares. Our initial public offering was priced at $13.50 per share. 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:

Annual Information:	**Low**	**High**
2014	$ 4.58	$ 14.00
Quarterly Information		
First Quarter 2014 (commencing March 13, 2014)	$ 10.85	14.00
Second Quarter 2014	6.38	12.44
Third Quarter 2014	5.83	11.48
Fourth Quarter 2014	4.58	8.56
Monthly Information:		
September 2014	$ 6.02	11.48
October 2014	6.09	8.56
November 2014	5.33	6.80
December 2014	4.58	6.85
January 2015	5.54	8.99
February 2015	6.33	10.00
March 2015 (through **15**)	10.85	14.00

9.B. Plan of distribution

Not applicable.

9.C. Market for Ordinary Shares

Our Ordinary Shares have been quoted on the NASDAQ Global Market since September 17, 2014 under the symbol "FOMX."

9.D. Selling shareholders

Not applicable.

9.E. Dilution

Not applicable.

9.F. Expenses of the issue

Not applicable.

ITEM 10. Additional Information.

A. Share Capital.

Not applicable.

B. Memorandum and Articles of Association.

Our original articles of association were registered with the Israeli Registrar of Companies at the time of incorporation of the Company on July 31, 2013, under our registration number 51-495351-2. At the 2014 annual general meeting of shareholders, our shareholders adopted our Articles, which became effective on the consummation of our initial public offering in the United States in March 2014, whereby the Company became a public company under the Companies Law. Under the Articles, the purpose of the Company is to engage in any lawful activity.

The following description of our share capital and provisions of our Articles are summaries and do not purport to be complete and are qualified in their entirety by the complete text of the Articles, which are filed as exhibits to this report and incorporated by reference herein, and by Israeli law.

Election of Directors

The Board consists of three classes of directors (not including external directors who do not form part of any class), with one class being elected each year by shareholders at the Company's annual general meeting for a term of approximately three years. In accordance with our Articles, directors so elected cannot be removed from office by the shareholders until the expiration of their term of office. Ordinary shares do not have cumulative voting rights. As a result, the holders of ordinary shares that represent a simple majority of the voting power represented at a shareholders' meeting and voting at the meeting have the power to elect all of the directors put forward for election, subject to specific requirements under the Companies Law with respect to the election of external directors. For further information as to these appointments, see "Item 6—Directors, Senior Management and Employees—C. Board Practices."

Under the Articles, a director shall vacate his or her office if that director dies; is declared bankrupt; is declared to be legally incompetent; resigns such office by notice in writing given to the Company; is not re-elected by the shareholders upon expiration of his or her term at the relevant annual general meeting of shareholders; or otherwise as provided in the Companies Law.

Our Articles provide that a director may, by written notice to the Company, appoint another person to serve as an alternate director provided that such appointment is approved by a majority of the directors then in office, and that such appointing director may remove such alternate director. Any alternate director shall be entitled to notice of meetings of the Board and of relevant committees and to attend and vote accordingly, except that the alternate has no standing at any meeting at which the appointing director is present or at which the appointing director is not entitled to participate as provided in the Companies Law. A person who is not qualified to be appointed as a director, or a person who already serves as a director or an alternate director, may not be appointed as an alternate director.

Unless the appointing director limits the time or scope of the appointment, the appointment is effective for all purposes until the earlier of (i) the appointing director ceasing to be a director; (ii) the appointing director terminating the appointment; or (iii) the occurrence, with respect to the alternate, of any of the circumstances under which a director shall vacate his or her office. The appointment of an alternate director does not in itself diminish the responsibility of the appointing director, as a director. An alternate director is solely responsible for his or her actions and omissions and is not deemed an agent of the appointing director. Under the Companies Law, external directors cannot generally appoint alternate directors, and a person who is not qualified to be appointed as an "independent" director may not be appointed as an alternate to an independent director. See "Item 6—Directors, Senior Management and Employees—C. Board Practices." At present, there are no effective appointments of alternate directors for our Board.

For discussions relating to certain compensation-related requirements of the Companies Law, external directors and financial experts, committees of the Board, and exculpation and indemnification of directors and officers, see "Item 6 - Directors, Senior Management and Employees".

Approval of Related Party Transactions under Israeli Law

Fiduciary Duties of Directors and Executive Officers

The Companies Law codifies the fiduciary duties that office holders owe to a company. Each person listed in the table under "Item 6. Directors, Senior Management and Employees—A. Directors and Senior Management" is an Office Holder under the Companies Law.

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

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

The duty of loyalty requires an office holder to act in good faith and for the benefit of a company, and includes a duty to:

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

Disclosure of Personal Interests of an Office Holder

The Companies Law requires that an office holder promptly disclose to the board of directors any personal interest that he or she may have concerning any existing or proposed transaction with a company, as well as any substantial information or document with respect thereof. An interested office holder's disclosure must be made promptly and in any event no later than the first meeting of the board of directors at which the transaction is considered. A personal interest includes an interest of any person in an act or transaction of a company, including a personal interest of one's relative or of a corporate body in which such person or a relative of such person is a 5% or greater shareholder, director or general manager or in which he or she has the right to appoint at least one director or the general manager, but excluding a personal interest stemming from one's ownership of shares in a 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 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.

Approval Procedure

If an office holder has a personal interest in a transaction, approval by the board of directors is required for the transaction, unless the articles of association of a company provide for a different method of approval. Our Articles do not provide for any such 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 the duty of loyalty. However, a company may not approve a transaction or action that is adverse to such company's interest or that is not performed by the office holder in good faith. Approval first by a 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 Office Holders' Terms of Office and Employment (which includes compensation, indemnification or insurance) generally require the approval of the remuneration committee, board of directors and, in certain circumstances, the shareholders, in that order, and must generally be consistent with the Company's Compensation Policy, as described under see "Item 6—Directors, Senior Management and Employees—B. Compensation."

Generally, a person who has a personal interest in a matter which is considered at a meeting of the board of directors or the audit committee may not be present at such a meeting or vote on that matter unless a majority of the directors or members of the audit committee have a personal interest in the matter, or unless the chairman of the audit committee or board of directors (as applicable) determines that he or she should be present in order to present the transaction that is subject to approval. Generally, if a majority of the members of the audit committee and/or the board of directors has a personal interest in the approval of a transaction, then all directors may participate in discussions of the audit committee and/or the board of directors on such transaction and the voting on approval thereof, but shareholder approval is also required for such transaction.

Transactions with Controlling Shareholders

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 a 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.

Under the Companies Law, an Extraordinary Transaction is defined as any of the following: (i) a transaction other than in the ordinary course of business; (ii) a transaction that is not on market terms; or (iii) a transaction that may have a material impact on a company's profitability, assets or liabilities.

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 under his or her control, require the approval of the audit committee, the board of directors and the shareholders of a company by a Special Majority, in that order.

Arrangements regarding the Terms of Office and Employment of a controlling shareholder who is an Office Holder, and the terms of employment of a controlling shareholder who is an employee of a company, require the approval of the remuneration committee, board of directors and the shareholders by a Special Majority, in that order, as further described above under "Item 6 —Directors, Senior Management and Employees—B. Compensation" with respect to Office Holders' compensation.

To the extent that any such transaction with a controlling shareholder is for a period extending beyond three years, approval is required once every three years, unless, with respect to extraordinary transactions with a controlling shareholder or in which a controlling shareholder has a personal interest, the audit committee determines that the duration of the transaction is reasonable given the circumstances related thereto.

Dividends and Dividend Policy

Dividends may be distributed only out of profits available for dividends as determined by the Companies Law, provided that there is no reasonable concern that the distribution will prevent the Company from being able to meet its existing and anticipated obligations when they become due. Generally, under the Companies Law, the decision to distribute dividends and the amount to be distributed is made by a company's board of directors. The Articles provide that the Board may from time to time declare, and cause the Company to pay, such dividends as may appear to it to be justified by the profits of the Company and that the Board has the authority to determine the time for payment of such dividends and the record date for determining the shareholders entitled to receive such dividends, provided the date is not before the date of the resolution to distribute the dividend. Declaration of dividends does not require shareholder approval.

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 and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our Board may deem relevant.

Payment of dividends may also be subject to Israeli withholding taxes. See "Taxation — Israeli Tax Considerations" for additional information.

Transfer of Shares

Ordinary shares which have been fully paid-up are transferable by submission of a proper instrument of transfer to the Company or its transfer agent together with the certificate of the shares to be transferred and such other evidence, if any, as the directors may require to prove the rights of the intending transferor in the transferred shares.

Our ordinary shares that are fully paid for are issued in registered form and may be freely transferred under our Articles, unless the transfer is restricted or prohibited by applicable law or the rules of a stock exchange on which the shares are traded. The ownership or voting of our ordinary shares by non-residents of Israel is not restricted in any way by our Articles or the laws of the State of Israel, except for ownership by nationals of some countries that are, or have been, declared as enemies of Israel.

Shareholder Meetings

The Articles provide that an annual general meeting must be held at least once in every calendar year, not later than 15 months after the last preceding annual general meeting, at such time and place as may be determined by the Board. The Board may, in its discretion, convene additional shareholder meetings and, pursuant to the Companies Law, must convene a meeting upon the demand of two directors or one quarter of the directors in office or upon the demand of the holder or holders of 5% of the Company's issued share capital and 1% of its voting rights or upon the demand of the holder or holders of 5% of its voting rights. All demands for shareholder meetings must set forth the items to be considered at that meeting. Pursuant to the Companies Law, the holder or holders of 1% of the Company's voting rights may request the inclusion of an item on the agenda of a future shareholder meeting, provided the item is appropriate for discussion at a shareholder meeting.

The agenda for a shareholder meeting is determined by the Board and must include matters in respect of which the convening of a shareholder meeting was demanded and any matter requested to be included by holder(s) of 1% of the Company's voting rights, as detailed above. According to regulations promulgated pursuant to the Companies Law and governing the terms of notice and publication of shareholder meetings of public companies, or the General Meeting Regulations, holder(s) of one percent or more of the Company's voting rights may propose any matter appropriate for deliberation at a shareholder meeting to be included on the agenda of a shareholder meeting, generally by submitting a proposal within seven days of publicizing the convening of a shareholder meeting, or, if the Company publishes a preliminary notice at least 21 days prior to publicizing the convening of a meeting (stating its intention to convene such meeting and the agenda thereof), within fourteen days of such preliminary notice. Any such proposal must further comply with the information requirements under applicable law and the Articles.

Pursuant to the Companies Law and regulations promulgated thereunder with respect to the convening of general meetings in a public company, shareholder meetings generally require prior notice of not less than 21 days, and for certain matters specified in the Companies Law, not less than 35 days. The function of the annual general meeting is to elect directors in accordance with the Articles, receive and consider the profit and loss account, the balance sheet and the ordinary reports and accounts of the directors and auditors, appoint auditors and fix their remuneration and transact any other business which under the Articles or applicable law may be transacted by the shareholders of a company in general meeting.

The quorum required for either an annual (regular) or an extraordinary (special) general meeting of shareholders consists of at least two shareholders present in person or by proxy holding shares comprising in the aggregate more than 33% of the voting rights of the Company. If a meeting is convened by the Board upon the demand of shareholders or upon the demand of less than 50% of the directors then in office or directly by such shareholders or directors and no quorum is present within half an hour from the time appointed, it shall be cancelled. If a meeting is otherwise called and no quorum is present within such time, the meeting is adjourned to the same day one week later at the same time and place or at such other time and place as the Board may determine and specify in the notice of the general meeting and it shall not be necessary to give notice of such adjournment. If a quorum is not present within half an hour from the time stated for such adjourned meeting, any shareholders present in person or by proxy at such meeting shall constitute a quorum. Generally, under the Companies Law and the Articles, shareholder resolutions are deemed adopted if approved by the holders of a simple majority of the voting rights represented at a meeting and voting unless a different majority is required by law or pursuant to the Articles. The Companies Law provides that resolutions on certain matters, such as amending a company's articles of association, assuming the authority of the board of directors in certain circumstances, appointing auditors, appointing external directors, approving certain transactions, increasing or decreasing the registered share capital and approving most mergers must be made by the shareholders at a general meeting. A company may determine in its articles of association certain additional matters in respect of which resolutions by the shareholders in a general meeting will be required.

Shareholder Duties

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

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

In addition, a shareholder also has a general duty to refrain from discriminating against other shareholders.

Certain shareholders have a further duty of fairness toward a company. These shareholders include any controlling shareholder, any shareholder who knows that it has the power to determine the outcome of a shareholder vote or a shareholder class vote and any shareholder who has the power to appoint or to prevent the appointment of an office holder of the company or other power towards the company. The Companies Law does not define the substance of this duty of fairness, except to state that the remedies generally available upon a breach of contract will also apply in the event of a breach of the duty to act with fairness.

Mergers and Acquisitions under Israeli Law

(i) Merger

Under the Companies Law, a merger is generally required to be approved by the shareholders and board of directors of each of the merging companies. If the share capital of the company that will not be the surviving company is divided into different classes of shares, the approval of each class is also required, unless determined otherwise by the court. Similarly, unless the court determines differently, a merger will not be approved if it is objected to by shareholders holding a majority of the voting rights participating and voting at the meeting, after excluding the shares held by the other party to the merger, by any person who holds 25% or more of the other party to the merger or by anyone on their behalf, including by the relatives of or corporations controlled by these persons. 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 any of the parties to the merger. Also, a merger can be completed only after all approvals have been submitted to the Israeli Registrar of Companies and 30 days have passed from the time that shareholder resolutions were adopted in each of the merging companies and 50 days have passed from the time that a proposal for approval of the merger was filed with the Israeli Registrar of Companies.

(ii) Special Tender Offer

The Companies Law also provides that, subject to certain exceptions, an acquisition of shares in a public company must be made by means of a tender offer if, as a result of the acquisition, the purchaser would become a holder of 25% or more of the voting power at general meetings. This rule does not apply if there is already another holder of 25% or more of the voting power at general meetings. Similarly, the Companies Law provides that, subject to certain exceptions, an acquisition of shares in a public company must be made by means of a tender offer if, as a result of the acquisition, the purchaser would become a holder of more than 45% of the voting power of the company. This rule does not apply if someone else already holds more than 45% of the voting power of the company.

(iii) Full Tender Offer

Under the Companies Law, a person may not acquire shares in a public company if, after the acquisition, he will hold more than 90% of the shares or more than 90% of any class of shares of that company, unless a tender offer is made to purchase all of the shares or all of the shares of the particular class. The Companies Law also provides (subject to certain exceptions with respect to shareholders who held more than 90% of a company's shares or of a class of its shares as of February 1, 2000) that as long as a shareholder in a public company holds more than 90% of the company's shares or of a class of shares, that shareholder shall be precluded from purchasing any additional shares. In order that all of the shares that the purchaser offered to purchase be transferred to him by operation of law, one of the following must have occurred: (i) the shareholders who declined or do not respond to the tender offer hold less than 5% of the company's outstanding share capital or of the relevant class of shares and the majority of offerees who do not have a personal interest in accepting the tender offer accepted the offer or (ii) the shareholders who declined or do not respond to the tender offer hold less than 2% of the company's outstanding share capital or of the relevant class of shares.

A shareholder that had his or her shares so transferred, whether he or she accepted the tender offer or not, has the right, within six months from the date of acceptance of the tender offer, to petition the court to determine that the tender offer was for less than fair value and that the fair value should be paid as determined by the court. However, the purchaser may provide in its offer that shareholders who accept the tender offer will not be entitled to such rights.

If the conditions set forth above are not met, the purchaser may not acquire additional shares of the company from shareholders who accepted the tender offer to the extent that following such acquisition, the purchaser would own more than 90% of the company's issued and outstanding share capital.

The above restrictions apply, in addition to the acquisition of shares, to the acquisition of voting power.

Anti-takeover Measures under Israeli Law

The Companies Law allows us to create and issue shares having rights different from those attached to our ordinary shares, including shares providing certain preferred rights, distributions or other matters and shares having preemptive rights. As of the date hereof, no preferred shares are authorized under our Articles. In the future, if we do authorize, create and issue a specific class of preferred shares, such class of shares, depending on the specific rights that may be attached to it, may have the ability to frustrate or prevent a takeover or otherwise prevent our shareholders from realizing a potential premium over the market value of their ordinary shares. The authorization and designation of a class of preferred shares will require an amendment to our Articles, which requires the prior approval of the holders of a majority of the voting power of our issued and outstanding shares at a general meeting of shareholders. The convening of the general meeting, the shareholders entitled to participate and the majority vote required to be obtained at such a meeting will be subject to the requirements set forth in the Articles and the Companies Law as described above in "— Shareholder Meetings."

Also, we have not adopted a rights plan, also known as a "poison pill." The legality of such rights plans as an additional anti-takeover measure has not been determined by the courts in Israel.

In addition, certain provisions of the Articles may have the effect of rendering more difficult or discouraging an acquisition of the Company deemed undesirable by the Board. Those provisions include: (i) limiting the ability of the Company's shareholders to convene general meetings of the Company (as discussed above); (ii) controlling procedures for the conduct of shareholder and Board meetings, including quorum and voting requirements; and (iii) the election and removal of directors. Moreover, the classification of the Board into three classes with terms of approximately three years each, and the requirement under Companies Law to have at least two external directors, who cannot readily be removed from office, may make it more difficult for shareholders who oppose the policies of the Board to remove a majority of the then current directors from office quickly. It may also, in some circumstances, together with the other provisions of the Articles and Israeli law, deter or delay potential future merger, acquisition, tender or takeover offers, proxy contests or changes in control or management of the Company, some of which could be deemed by certain shareholders to be in their best interests and which could affect the price some investors are willing to pay for ordinary shares.

Changes in Capital

On July 31, 2013, the Company's incorporation date, the registered share capital of the Company was NIS 500,000 divided into 50,000,000 ordinary shares, NIS 0.01 par value per share.

Our Articles enable us to increase or reduce our share capital. Any such changes are subject to the provisions of the Companies Law and must be approved by a resolution duly passed by our shareholders at a general meeting by voting on such change in the capital. In addition, transactions that have the effect of reducing capital, such as the declaration and payment of dividends in the absence of sufficient retained earnings or profits and an issuance of shares for less than their nominal value (under certain circumstances), require the approval of both our Board and an Israeli court.

C. Material Contracts

The following are summary descriptions of certain material agreements to which we are a party. The descriptions provided below do not purport to be complete and are qualified in their entirety by the complete agreements, which are attached as exhibits to this annual report on Form 20-F.

For a description of our material agreements relating to our strategic collaborations and research arrangements and other material agreements, please refer to "Item 4.B. Information on the Company—Business Overview—Strategic Collaborations, Research Arrangements and other Material Agreements." In addition, we have previously entered into the agreements described below, but we no longer deem these to be material to the Company.

Zora Biosciences Oy

On December 19, 2013, we entered into a memorandum of understanding with Zora Biosciences, or the Zora MOU, to explore opportunities to collaborate in order to develop a NASH clinical diagnostic tool, as well as a clinical diagnostic tool for patients receiving aramchol treatment. Zora performs lipidomic profiling analyses in order to generate molecular lipid quantification data.

According to the Zora MOU, in connection with our ARREST Study of aramchol, we will collect and provide to Zora liver tissue samples from biopsies and serum samples from the patients screened and enrolled in the Israeli-based centers in the trial and Zora will perform lipidomic profiling analysis based on such samples. Once Zora has performed its analysis, Zora is permitted to verify its results by comparing them to the results of the liver biopsies that will be taken from the trial participants and from their MRIs. We expect this to enable Zora to evaluate the performance of its lipidomic profiles and develop a NASH disease clinical diagnostic tool and generate lipidomic profiles correlated with disease progression of patients. We also expect that this will enable Zora to develop a clinical diagnostic tool for patients receiving aramchol treatment, which would be intellectual property owned by us.

We will not receive any financial payment from Zora. However, we will be obligated to pay to-be-agreed upon fees to Zora in respect of its lipidomic analysis activities, and if such activities generate patentable intellectual property for Zora, then we will receive a reimbursement of 40% of such fees.

According to the Zora MOU, we will own all clinical data and Zora will own all lipidomic data, each as generated by our collaboration. We also agreed to grant Zora a free license to use such clinical data only to develop biomarkers and related diagnostics in the field of NASH. Zora will grant to us a free license to use their lipidomic data generated by the clinical trial for developing a clinical diagnostic tool for patients receiving treatment with aramchol. Zora will also grant us a right of first discussion, exercisable upon completion of the ARREST Study, to enter into a business transaction with Zora, separate from the transaction and relationship contemplated in the Zora MOU, regarding the commercial exploitation of its NASH disease clinical diagnostic tool based upon the data generated during the collaboration. We agreed to enter into a definitive agreement with Zora on the basis of the principles detailed in the Zora MOU, but no such definitive agreement has been executed as of yet and at this stage we have no intention to pursue such an agreement. The Zora MOU is silent as to term, termination and whether or not it is binding.

Guangdong Xianqiang Pharmaceutical Co., Ltd.

On November 27, 2013, we entered into a non-binding memorandum of understanding, or the Xianqiang MOU, with Xianqiang, to explore collaborative opportunities to expand the potential market for aramchol into China.

According to the Xianqiang MOU, we expressed an interest in entering into a definitive agreement with Xianqiang that would grant it an exclusive, non-transferable, non-assignable and non-sublicenseable license to test, manufacture, sell, market and distribute aramchol in China, excluding Hong Kong, Taiwan and Macau, for the treatment of liver diseases only. Such license will be for such period and include such terms and conditions, including royalties, as will be agreed between the parties in such definitive agreement. Pursuant to such definitive agreement, all patent applications in connection with aramchol would be filed in our name and Xianqiang would finance all trials, test, clinical studies and other activities necessary to secure marketing approval of aramchol from the relevant regulatory authorities in China for the sale of aramchol in China. Thereafter, Xianqiang would fund the marketing, sales and distribution of aramchol in China. Furthermore, according to the Xianqiang MOU, the parties would agree on a development plan funded by Xianqiang, with Xianqiang owning the results generated in connection with such development plan. The parties agreed to negotiate and execute the relevant definitive agreements within sixty (60) days of entering into the Xianqiang MOU, but no such definitive agreement has been executed as of yet and at this stage we have no intention to pursue such an agreement.

Enterome Bioscience

On October 30, 2012, we entered into a memorandum of understanding with Enterome, or the Enterome MOU, to explore opportunities to collaborate in the field of gut microbiota and metabolic disorders by joining our efforts and expertise for the development of biomarkers and patient stratification tools. Enterome develops gut microbiota biomarkers based on quantitative metagenomic analysis for metabolic disorders and immune mediated diseases.

According to the Enterome MOU, in connection with our ARREST Study of aramchol, Enterome will be permitted to collect stool samples from the patients screened and enrolled in the trial and to perform gut microbiota metagenomic analysis from such samples. Once Enterome has performed its analysis, Enterome is permitted to verify its diagnostic results by comparing them to the results of the liver biopsies that will be taken from the trial participants and from their MRIs. We expect this to enable Enterome to evaluate the performance of its proprietary metagenomic profiles for stratifying patients and to generate metagenomic profiles correlated with patient disease progression. We, in turn, expect to use Enterome's findings to evaluate the correlation between aramchol's dose response data and patient metagenomic profiles in order to stratify potential patients for our future Phase III clinical trials, if any, and to identify NAFLD patients that are at risk of progression to NASH.

We will not receive any financial payment from Enterome and we are not obligated to make any financial payment to Enterome in respect of such activities.

According to the Enterome MOU, we will own all clinical data and Enterome will own all gut microbiota metagenomic data, each as generated by our collaboration. We also agreed to grant Enterome a free license to use such clinical data only to develop biomarkers and related diagnostics to stratify NAFLD patients according to their risk of developing NASH. This license will include the right to use the clinical data associated with the metagenomic data for medical and regulatory development, as well as commercial development. Enterome will grant to us a free license to use their metagenomic data generated by the clinical trial for scientific, clinical and regulatory purposes in developing aramchol, but not for commercial use for developing or promoting a diagnostic product. Enterome will also grant us a right of first refusal, exercisable upon completion of the PARREST Study, to enter into a business transaction with Enterome, separate from the transaction and relationship contemplated in the Enterome MOU, regarding the commercial exploitation of its metagenomic profiles and metagenomic data generated during the collaboration. We agreed to enter into a definitive agreement with Enterome on the basis of the principles detailed in the Enterome MOU, but no such definitive agreement has been executed as of yet and at this stage we have no intention to pursue such an agreement. The Enterome MOU is silent as to term, termination and whether or not it is binding.

Employment Agreements

See "Item 6. Directors, Senior Management and Employees—B. Compensation—Employment Agreements and Arrangements with Directors and Related Parties."

D. Exchange Controls.

There are no Israeli government laws, decrees or regulations that restrict or that affect our export or import of capital or the remittance of dividends, interest or other payments to non-resident holders of our securities, including the availability of cash and cash equivalents for use by us and our wholly-owned subsidiaries, except for ownership by nationals of certain countries that are, or have been, declared as enemies of Israel or otherwise as set forth under "Item 10. Additional Information—E. Taxation."

E. Taxation.

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

Certain Israeli Tax Considerations

The following is a brief summary of the material Israeli income tax laws applicable to us. This section also contains a discussion of material Israeli tax consequences concerning the ownership and disposition of our ordinary shares. This summary does not discuss all the aspects of Israeli tax law that may be relevant to a particular investor in light of his or her personal investment circumstances or to some types of investors subject to special treatment under Israeli law. Examples of this kind of investor include residents of Israel or investors 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 hereof and does not take into account possible future amendments which may be under consideration.

General Corporate Tax Structure in Israel

Israeli resident companies (as defined below), such as the Company, are generally subject to corporate tax at the rate of 26.5% of their taxable income, as of January 1, 2014 (and 25% in 2013).

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 an "Israeli resident" if it meets one of the following: (i) it was incorporated in Israel; or (ii) the control and management of its business are exercised in Israel.

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

The Law for the Encouragement of Industry (Taxes), 5729-1969, which we refer to as the Industry Encouragement Law, provides several tax benefits for "Industrial Companies," which are defined as Israeli resident-companies of which 90% or more of their income in any tax year is derived from an "Industrial Enterprise" that it owns, or an enterprise whose principal activity in a given tax year is industrial production. Eligibility for benefits under the Industry Encouragement Law is not contingent upon approval of any governmental authority.

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

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

Currently, we are not qualified as an Industrial Company within the meaning of the Industry Encouragement Law, and there can be no assurance that we will qualify as an Industrial Company in the future or that, even if we qualify as an Industrial Company, the benefits described above will be available to us at all.

Law for the Encouragement of Capital Investments, 5719-1959

The Law for the Encouragement of Capital Investments, 5719-1959, which we refer to as the Investment Law, provides certain incentives for capital investments in production facilities (or other eligible assets). The Investment Law was significantly amended effective April 1, 2005 and further amended as of January 1, 2011, or the 2011 Amendment. The 2011 Amendment introduced new benefits to replace those granted in accordance with the provisions of the Investment Law in effect prior to the 2011 Amendment.

Tax Benefits Under the 2011 Amendment

The 2011 Amendment canceled the availability of the benefits granted to Industrial Companies under the Investment Law prior to 2011 and, instead, introduced new benefits for income generated by a "Preferred Company" through its "Preferred Enterprise" (as such terms are defined in the Investment Law) as of January 1, 2011.

The definition of a Preferred Company includes a company incorporated in Israel that is not fully owned by a governmental entity, and that has, among other things, a Preferred Enterprise and is controlled and managed from Israel. Under a recent amendment announced in August 2013, or the 2013 Amendment, beginning in 2014 and in each year thereafter, a Preferred Company may only be entitled to reduced corporate tax rates of 16%, unless the Preferred Enterprise is located in a specified development zone, in which case the rate will be 9%. Income derived by a Preferred Company from a "Special Preferred Enterprise" (as such term is defined in the Investment Law) would be entitled, during a benefit period of ten years, to further reduced tax rates of 8%, or 5% if the Special Preferred Enterprise is located in a certain development zone.

As of January 1, 2014, dividends paid out of income attributed to a Preferred Enterprise are subject to withholding tax at source at the rate of 20% unless a different tax rate is provided under an applicable tax treaty. However, if such dividends are paid to an Israeli company, no tax is required to be withheld.

A Beneficiary Company may elect to file a notice until May 31st of each year in order to avail itself of the benefits of the 2011 Amendments to it pursuant to Sections 131 and 132 of the Income Tax Ordinance (New Version) - 1961, referred to herein as the Israeli Tax Ordinance, and such benefits will apply on the tax year subsequent to the year in which such notice was filed.

Currently, we are not entitled to receive the tax benefits described above and there can be no assurance that we will be entitled to receive such benefits at any time in the future. Furthermore, there can be no assurance that even if in the future we meet the relevant requirements for such tax benefits, that such tax benefits will be available to us at all.

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. Beginning in 2013, an additional tax at a rate of 2% may be imposed upon shareholders whose annual taxable income from all sources exceeds a certain amount.

A "Substantial Shareholder" is generally a person who alone, or together with his or her relative or another person who collaborates with him or her on a regular basis, holds, directly or indirectly, at least 10% of any of the "means of control" of a corporation. "Means of control" generally include the right to vote, receive profits, nominate a director or an officer, receive assets upon liquidation or instruct someone who holds any of the aforesaid rights regarding the manner in which he or she is to exercise such right(s), all regardless of the source of such right.

With respect to individuals, the term "Israeli resident" is generally defined under Israeli tax legislation as a person whose center of life is in Israel. The Israeli Tax Ordinance (as amended by Amendment Law No. 132 of 2002), states that in order to determine the center of life of an individual, consideration will be given to the individual's family, economic and social connections, including: (i) place of permanent residence; (ii) place of residential dwelling of the individual and the individual's immediate family; (iii) place of the individual's regular or permanent occupation or the place of his or her permanent employment; (iv) place of the individual's active and substantial economic interests; (v) 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: (i) the individual was present in Israel for 183 days or more in the tax year; or (ii) 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. Such presumption may be rebutted either by the individual or by the assessing officer.

Taxation of Israeli Resident Corporations on Payment of Dividends

Israeli resident corporations are generally exempt from Israeli corporate income tax with respect to dividends paid on ordinary shares held by such Israeli resident corporations as long as the profits out of which the dividends were paid were derived in Israel.

Capital Gains Taxes Applicable to Israeli Resident Shareholders

The income tax rate applicable to real capital gains derived by an Israeli individual resident from the sale of shares that were purchased after January 1, 2012, whether listed on a stock exchange or not, is 25%. However, if such shareholder is considered a Substantial Shareholder 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%. In addition, as noted above, beginning in 2013, an additional tax at a rate of 2% may be imposed upon shareholders whose annual taxable income from all sources exceeds a certain amount.

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 26.5% for corporations and up to 50% for individuals).

Taxation of Non-Israeli Shareholders on Receipt of Dividends

Non-Israeli residents are generally subject to Israeli income tax on the receipt of dividends paid on our ordinary shares at the rate of 25% (or 30% for individuals, if such person is a Substantial Shareholder at the time he or she receives the dividend or on any date in the 12 months preceding such date), which tax will be withheld at source, unless a different rate is provided under an applicable tax treaty between Israel and the shareholder's country of residence.

A non-Israeli resident who has dividend income derived from or accrued in Israel, from which the full amount of tax was withheld at source, is generally exempt from the duty to file tax returns in Israel in respect of such income; provided that (i) such income was not derived from a business conducted in Israel by the taxpayer and (ii) the taxpayer has no other taxable sources of income in Israel.

For example, under the Convention Between the Government of the United States of America and the Government of Israel with Respect to Taxes on Income, as amended, or 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 (as such term is defined in the Investment Law), subject to certain conditions. Where the recipient is a U.S. corporation owning 10% or more of the voting shares of the paying corporation during the part of the paying corporation's taxable year which precedes the date of payment of the dividend and during the entirety of its prior taxable year (if any) and the dividend is not paid from the profits of a Benefited Enterprise, the Israeli tax withheld may not exceed 12.5%, subject to certain conditions.

Capital Gains Income Taxes Applicable to Non-Israeli Shareholders

Non-Israeli resident shareholders are generally exempt from Israeli capital gains tax on any gains derived from the sale, exchange or disposition of our ordinary shares, provided that such shareholders did not acquire their shares prior to January 1, 2009 and such gains were not derived from a permanent business or business activity of such shareholders in Israel. However, non-Israeli corporations will not be entitled to the foregoing exemptions if an Israeli resident (i) has a controlling interest of more than 25% in such non-Israeli corporation or (ii) is the beneficiary of or is entitled to 25% or more of the revenues or profits of such non-Israeli corporation, whether directly or indirectly.

In addition, a sale of securities by a non-Israeli resident may be exempt from Israeli capital gains tax under the provisions of an applicable tax treaty. For example, under the U.S.-Israel Tax Treaty, the sale, exchange or disposition of our ordinary shares by a shareholder who is a U.S. resident (for purposes of the U.S.-Israel Tax Treaty) holding the ordinary shares as a capital asset and is entitled to claim the benefits afforded to such a resident by the U.S.-Israel Tax Treaty, or a Treaty U.S. Resident, is generally exempt from Israeli capital gains tax unless: (i) such Treaty U.S. Resident is an individual and was present in Israel for 183 days or more during the relevant taxable year; (ii) such Treaty U.S. Resident holds, directly or indirectly, shares representing 10% or more of our voting power of the Company during any part of the 12 month period preceding such sale, exchange or disposition, subject to certain conditions; or (iii) the capital gains arising from such sale, exchange or disposition are attributable to a permanent establishment of the Treaty U.S. Resident located in Israel, subject to certain conditions. In any such case, the sale, exchange or disposition of our ordinary shares would be subject to Israeli tax, to the extent applicable. However, under the U.S.-Israel Tax Treaty, such Treaty U.S. Resident would be permitted to claim a credit for such taxes against U.S. federal income tax imposed on any gain from such sale, exchange or disposition, under the circumstances and subject to the limitations specified in the U.S.-Israel Income Tax Treaty.

Regardless of whether shareholders may be liable for Israeli income tax on the sale of our ordinary shares, the payment of the consideration may be subject to withholding of Israeli tax at the source. Accordingly, shareholders may be required to demonstrate that they are exempt from tax on their capital gains in order to avoid withholding at source at the time of sale.

Estate and Gift Tax

Israeli law presently does not impose estate or gift taxes.

Pre-Ruling Regarding a Reorganization of Our Corporate Structure

In connection with the Reorganization, as detailed under "Item 4. Information on the Company—Historical Background and Corporate Structure" above, we obtained a pre-ruling from the Israeli Tax Authority. The Tax Pre-Ruling confirms that the transfer of shares and assets resulting in the Company as the parent company and 100% equity-owner of GRD, which holds all the Group's intellectual property, including the Company's patent portfolio, GIL and GTTI, is not taxable pursuant to the provisions of the Israeli Tax Ordinance as long as certain requirements are met. Pursuant to the Tax Pre-Ruling, certain restrictions under the Israeli tax laws will apply to the Company and its subsidiaries, as well as to those shareholders and option holders and other holders of rights in the share capital of the Company (on a fully diluted basis), who participated in the Reorganization and held such rights immediately after the consummation of the Reorganization, or the Rights Holders. In this section, each of the terms "Rights" and/or "share capital (on a fully diluted basis)" includes shares, options to purchase shares and any other "right" in "a body of persons" as such term is defined in the Israeli Tax Ordinance. These restrictions generally restrict these entities and Rights Holders from making any disposition of their Rights in the transferred assets and shares for a two year period following the consummation of the Reorganization, which ends in February 2016, or the Restriction Period. During the Restriction Period, these restrictions include the following:

- we may not sell or otherwise dispose of our intellectual property, other than out-licensing in the ordinary course of business;

- the Rights Holders immediately following the Reorganization must not change, subject to the following restriction and to the relief detailed below;
- the Rights Holders may not sell or otherwise transfer or dispose of more than 10% of their respective Rights, subject to the exemptions and relief detailed below;
- we must not sell or otherwise transfer or dispose of any of our shares in GTTI, GHI or GIL;
- we may not deduct for tax purposes any expenses related to the Reorganization; and
- during the two tax years following the end of the year in which the Reorganization was completed we may not offset losses (whether business or capital losses) incurred in the year in which the Reorganization was completed or in the years preceded that year up to the fair market value of the transferred asset.

Notwithstanding the foregoing restrictions, so long as the aggregate holdings of the Rights Holders, collectively, is 51% or more of the total share capital of the Company (on a fully diluted basis), then at any time during the Restriction Period, the following changes described below might be permitted under the Israeli Tax Ordinance and guidelines issued by the Israeli Tax Authorities:

- *Sale of Shares or Other Rights*. One or more of the Rights Holders will be allowed to sell more than 10% of its Rights in the Company, subject to the following:
  - other Rights Holders give their consent to such sale of Rights; and
  - the aggregate number of ordinary shares and other Rights sold by all Rights Holders, collectively as a group, will not exceed 10% of the total Rights then-outstanding.
- *Public Offering*. We may issue up to 49% of our share capital (on a fully diluted basis) following such issuance in a public offering of our ordinary shares involving the listing of such shares on a securities exchange, which included our initial public offering and the listing of our ordinary shares on the Nasdaq Capital Market.
- *Private Placement*. We may issue securities in a private placement to a person(s) who did not hold Rights in the Company prior to such issuance, or a New Investor, provided that such private placement either (i) is in an amount which does not exceed 20% of our total share capital (on a fully-diluted basis) then-outstanding following such issuance in one or more separate transactions or (ii) does not exceed, in the aggregate, 49% of our total share capital following such issuance, each New Investor will not receive more than 20% of our total share capital (on a fully-diluted basis) after such issuance and each New Investor does not participate in subsequent offerings or private placements, even if such New Investor purchased less than 20% in such preceding private placement.

If during the Restriction Period, we or the Rights Holders commit a Violation, the transfer of shares or other rights and/or assets in connection with the Reorganization will become subject to taxation based on the greater of the transferred assets' fair market value on the day of such Violation or taxes that, but for the Tax Pre-Ruling, would be payable in connection with the transfer of such assets and shares at the time of the Reorganization linked to the Israeli consumer price index linkage differentials and interest from the day of the actual transfer of such assets and shares until the day of payment of such taxes, unless the Israeli Tax Authority is satisfied that such Violation was a result of special circumstances beyond our control.

The foregoing restrictions do not apply to any sale of company securities issued after the date of the Tax Pre-Ruling to new investors who are not Rights Holders, including our ordinary shares issued to new investors who are not Rights Holders pursuant to the Share Purchase Agreement and the shares issued in connection with the initial public offering.

Certain U.S. Federal Income Tax Considerations

The following is a general summary of what we believe to be certain material U.S. federal income tax consequences relating to the purchase, ownership and disposition of our ordinary shares by U.S. Holders (as defined below). This summary is based on the Internal Revenue Code, or the Code, the regulations of the U.S. Department of the Treasury issued pursuant to the Code, or the Treasury Regulations, the income tax treaty between the United States and Israel, or the U.S.-Israel Tax Treaty, and administrative and judicial interpretations thereof, all as in effect on the date hereof and all of which are subject to change, possibly with retroactive effect, or to different interpretation. No ruling has been sought from the IRS with respect to any U.S. federal income tax consequences described below, and there can be no assurance that the IRS or a court will not take a contrary position. This summary is no substitute for consultation by prospective investors with their own tax advisors and does not constitute tax advice. This summary does not address all of the tax considerations that may be relevant to specific U.S. Holders in light of their particular circumstances or to U.S. Holders subject to special treatment under U.S. federal income tax law (including, without limitation, banks, insurance companies, tax-exempt entities, retirement plans, regulated investment companies, partnerships, dealers in securities, brokers, real estate investment trusts, certain former citizens or residents of the United States, persons who acquire our ordinary shares as part of a straddle, hedge, conversion transaction or other integrated investment, persons who acquire our ordinary shares through the exercise or cancellation of employee stock options or otherwise as compensation for their services, persons that have a "functional currency" other than the U.S. dollar, persons that own (or are deemed to own, indirectly, or by attribution) 10% or more of our shares, or persons that mark their securities to market for U.S. federal income tax purposes). This summary does not address any U.S. state or local or non-U.S. tax considerations, any U.S. federal estate, gift or alternative minimum tax considerations, or any U.S. federal tax consequences other than U.S. federal income tax consequences.

As used in this summary, the term "U.S. Holder" means a beneficial owner of our ordinary shares that is, for U.S. federal income tax purposes, (i) an individual citizen or resident of the United States, (ii) a corporation, or other entity taxable as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state thereof, or the District of Columbia, (iii) an estate the income of which is subject to U.S. federal income tax regardless of its source, or (iv) a trust with respect to which a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of its substantial decisions, or that has a valid election in effect under applicable Treasury Regulations to be treated as a "United States person."

If an entity treated as a partnership for U.S. federal income tax purposes holds our ordinary shares, the tax treatment of such partnership and each partner thereof will generally depend upon the status and activities of the partnership and such partner. A holder that is treated as a partnership for U.S. federal income tax purposes should consult its own tax advisor regarding the U.S. federal income tax considerations applicable to it and its partners of the purchase, ownership and disposition of our ordinary shares.

Prospective investors should be aware that this summary does not address the tax consequences to investors who are not U.S. Holders. Prospective investors should consult their own tax advisors as to the particular tax considerations applicable to them relating to the purchase, ownership and disposition of our ordinary shares, including the applicability of U.S. federal, state and local tax laws and non-U.S. tax laws.

Taxation of U.S. Holders

Distributions. Subject to the discussion below under "Passive Foreign Investment Company," a U.S. Holder that receives a distribution with respect to an ordinary share generally will be required to include the amount of such distribution in gross income as a dividend (without reduction for any Israeli tax withheld from such distribution) when actually or constructively received to the extent of the U.S. Holder's pro rata share of our current and/or accumulated earnings and profits (as determined under U.S. federal income tax principles). Any distributions in excess of our earnings and profits will be applied against and will reduce (but not below zero) the U.S. Holder's tax basis in its ordinary shares, and, to the extent they exceed that tax basis, will be treated as gain from the sale or exchange of our ordinary shares.

If we were to pay dividends, we expect to pay such dividends in NIS. A dividend paid in NIS, including the amount of any Israeli taxes withheld, will be includible in a U.S. Holder's income as a U.S. dollar amount calculated by reference to the exchange rate in effect on the date such dividend is received, regardless of whether the payment is in fact converted into U.S. dollars. If the dividend is converted to U.S. dollars on the date of receipt, a U.S. Holder generally will not recognize a foreign currency gain or loss. However, if the U.S. Holder converts the NIS into U.S. dollars on a later date, the U.S. Holder must include, in computing its income, any gain or loss resulting from any exchange rate fluctuations. The gain or loss will be equal to the difference between (i) the U.S. dollar value of the amount included in income when the dividend was received and (ii) the amount received on the conversion of the NIS into U.S. dollars. Such gain or loss will generally be ordinary income or loss and will be U.S. source income or loss for U.S. foreign tax credit purposes. U.S. Holders should consult their own tax advisors regarding the tax consequences to them if we pay dividends in NIS or any other non-U.S. currency.

Subject to certain significant conditions and limitations, any Israeli taxes paid on or withheld from distributions from us and not refundable to a U.S. Holder may be credited against the U.S. Holder's U.S. federal income tax liability or, alternatively, may be deducted from the U.S. Holder's taxable income. The election to deduct, rather than credit, foreign taxes, is made on a year-by-year basis and applies to all foreign taxes paid by a U.S. Holder or withheld from a U.S. Holder that year. Dividends paid on the ordinary shares generally will constitute income from sources outside the United States and be categorized as "passive category income" or, in the case of some U.S. Holders, as "general category income" for U.S. foreign tax credit purposes. Because the rules governing foreign tax credits are complex, U.S. Holders should consult their own tax advisors regarding the availability of foreign tax credits in their particular circumstances.

Dividends paid on the ordinary shares will not be eligible for the "dividends-received" deduction generally allowed to corporate U.S. Holders with respect to dividends received from U.S. corporations.

For taxable years beginning on or after January 1, 2013, certain distributions treated as dividends that are received by an individual U.S. Holder from a "qualified foreign corporation" generally qualify for a 20% reduced maximum tax rate so long as certain holding period and other requirements are met. A non-U.S. corporation (other than a corporation that is treated as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year) generally will be considered to be a qualified foreign corporation (i) if it is eligible for the benefits of a comprehensive tax treaty with the United States which the Secretary of Treasury of the United States determines is satisfactory for purposes of this provision and which includes an exchange of information program, or (ii) with respect to any dividend it pays on stock which is readily tradable on an established securities market in the United States. Dividends paid by us in a taxable year in which we are not a PFIC and with respect to which we were not a PFIC in the preceding taxable year are expected to be eligible for the 20% reduced maximum tax rate, although we can offer no assurances in this regard. However, any dividend paid by us in a taxable year in which we are a PFIC or were a PFIC in the preceding taxable year will be subject to tax at regular ordinary income rates (along with any applicable additional PFIC tax liability, as discussed below). As discussed below under "Passive Foreign Investment Company," we have determined that we are a PFIC and likely will continue to be a PFIC, at least until we develop a source of significant operating revenues.

The additional 3.8% "net investment income tax" (described below) may apply to dividends received by certain U.S. Holders who meet certain modified adjusted gross income thresholds.

Sale, Exchange or Other Disposition of Ordinary Shares. Subject to the discussion under "Passive Foreign Investment Company" below, a U.S. Holder generally will recognize capital gain or loss upon the sale, exchange, or other disposition of our ordinary shares in an amount equal to the difference between the amount realized on the sale, exchange, or other disposition and the U.S. Holder's adjusted tax basis (determined under U.S. federal income tax rules) in such ordinary shares. This capital gain or loss will be long-term capital gain or loss if the U.S. Holder's holding period in our ordinary shares exceeds one year. Preferential tax rates for long-term capital gain (currently, with a maximum rate of 20% for taxable years beginning on or after January 1, 2013) will apply to individual U.S. Holders. The deductibility of capital losses is subject to limitations. The gain or loss will generally be income or loss from sources within the United States for U.S. foreign tax credit purposes, subject to certain possible exceptions under the U.S.-Israel Tax Treaty. The additional 3.8% "net investment income tax" (described below) may apply to gains recognized upon the sale, exchange, or other taxable disposition of our ordinary shares by certain U.S. Holders who meet certain modified adjusted gross income thresholds.

U.S. Holders should consult their own tax advisors regarding the U.S. federal income tax consequences of receiving currency other than U.S. dollars upon the disposition of their ordinary shares.

Passive Foreign Investment Company

In general, a non-U.S. corporation will be treated as a PFIC for U.S. federal income tax purposes in any taxable year in which either (i) at least 75% of its gross income is "passive income," or (ii) on average at least 50% of its assets by value produce passive income or are held for the production of passive income. Passive income for this purpose generally includes, among other things, certain dividends, interest, royalties, rents and gains from commodities and securities transactions and from the sale or exchange of property that gives rise to passive income. Passive income also includes amounts derived by reason of the temporary investment of funds, including those raised in a public offering. Assets that produce or are held for the production of passive income include cash, even if held as working capital or raised in a public offering, marketable securities and other assets that may produce passive income. In determining whether a non-U.S. corporation is a PFIC, a proportionate share of the income and assets of each corporation in which it owns, directly or indirectly, at least a 25% interest (by value) is taken into account.

A foreign corporation's PFIC status is an annual determination that is based on tests that are factual in nature, and our status for any year will depend on our income, assets, and activities for such year. Based upon our review of our financial data, we have determined that we are currently a PFIC, and we likely will continue to be a PFIC, at least until we develop a source of significant operating revenues.

U.S. Holders should be aware of certain tax consequences of investing directly or indirectly in us due to our classification as a PFIC. A U.S. Holder is subject to different rules depending on whether the U.S. Holder makes an election to treat us as a "qualified electing fund," referred to herein as a "QEF election," for the first taxable year that the U.S. Holder holds ordinary shares makes a "mark-to-market" election with respect to the ordinary shares, or makes neither election. An election to treat us as a QEF will not be available if we do not provide the information necessary to make such an election. It is not expected that a U.S. Holder will be able to make a QEF election because we do not intend to provide U.S. Holders with the information necessary to make a QEF election.

QEF Election. One way in which certain of the adverse consequences of PFIC status can be mitigated is for a U.S. Holder make a QEF election. Generally, a shareholder making the QEF election is required for each taxable year to include in income a pro rata share of the ordinary earnings and net capital gain of the QEF, subject to a separate election to defer payment of taxes, which deferral is subject to an interest charge. An election to treat us as a QEF will not be available if we do not provide the information necessary to make such an election. It is not expected that a U.S. Holder will be able to make a QEF election because we do not intend to provide U.S. Holders with the information necessary to make a QEF election.

Mark-to-Market Election. Alternatively, if our ordinary shares are treated as "marketable stock," a U.S. Holder would be allowed to make a "mark-to-market" election with respect to our ordinary shares, provided the U.S. Holder completes and files IRS Form 8621 in accordance with the relevant instructions and related Treasury Regulations. If that election is made, the U.S. Holder generally would include as ordinary income in each taxable year the excess, if any, of the fair market value of our ordinary shares at the end of the taxable year over such holder's adjusted tax basis in such ordinary shares. The U.S. Holder would also be permitted an ordinary loss in respect of the excess, if any, of the U.S. Holder's adjusted tax basis in our ordinary shares over their fair market value at the end of the taxable year, but only to the extent of the net amount previously included in income as a result of the mark-to- market election. A U.S. Holder's tax basis in our ordinary shares would be adjusted to reflect any such income or loss amount. Gain realized on the sale, exchange or other disposition of our ordinary shares would be treated as ordinary income, and any loss realized on the sale, exchange or other disposition of our ordinary shares would be treated as ordinary loss to the extent that such loss does not exceed the net mark-to-market gains previously included in income by the U.S. Holder, and any loss in excess of such amount will be treated as capital loss. Amounts treated as ordinary income will not be eligible for the favorable tax rates applicable to qualified dividend income or long-term capital gains.

Generally, stock will be considered marketable stock if it is "regularly traded" on a "qualified exchange" within the meaning of applicable Treasury Regulations. A class of stock is regularly traded on an exchange during any calendar year during which such class of stock is traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. To be marketable stock, our ordinary shares must be regularly traded on a qualifying exchange (i) in the United States that is registered with the SEC or a national market system established pursuant to the Exchange Act or (ii) outside the United States that is properly regulated and meets certain trading, listing, financial disclosure and other requirements. Our ordinary shares are expected to constitute "marketable stock" as long as they remain listed on the Nasdaq Capital Market and are regularly traded.

A mark-to-market election will not apply to our ordinary shares held by a U.S. Holder for any taxable year during which we are not a PFIC, but will remain in effect with respect to any subsequent taxable year in which we become a PFIC. Such election will not apply to any PFIC subsidiary that we own. Each U.S. Holder is encouraged to consult its own tax advisor with respect to the availability and tax consequences of a mark-to-market election with respect to our ordinary shares.

Each U.S. Holder should consult its own tax adviser with respect to the applicability of the "net investment income tax" (discussed below) where a mark-to-market election is in effect.

Default PFIC Rules. A U.S. Holder who does not make a timely QEF election (we do not currently intend to prepare or provide the information that would enable a U.S. Holder to make a QEF election) or a mark-to-market election, referred to in this summary as a "Non-Electing U.S. Holder," will be subject to special rules with respect to (i) any "excess distribution" (generally, the portion of any distributions received by the Non-Electing U.S. Holder on the ordinary shares in a taxable year in excess of 125% of the average annual distributions received by the Non-Electing U.S. Holder in the three preceding taxable years, or, if shorter, the Non-Electing U.S. Holder's holding period for the ordinary shares), and (ii) any gain realized on the sale or other disposition of such ordinary shares. Under these rules:

- the excess distribution or gain would be allocated ratably over the Non-Electing U.S. Holder's holding period for such ordinary shares;
- the amount allocated to the current taxable year and any year prior to us becoming a PFIC would be taxed as ordinary income; and
- the amount allocated to each of the other taxable years would be subject to tax at the highest rate of tax in effect for the applicable class of taxpayer for that year, and an interest charge for the deemed deferral benefit would be imposed with respect to the resulting tax attributable to each such other taxable year.

If a Non-Electing U.S. Holder who is an individual dies while owning our ordinary shares, the Non-Electing U.S. Holder's successor would be ineligible to receive a step-up in tax basis of such ordinary shares. Non-Electing U.S. Holders should consult their tax advisors regarding the application of the "net investment income tax" (described below) to their specific situation.

To the extent a distribution on our ordinary shares does not constitute an excess distribution to a Non-Electing U.S. Holder, such Non-Electing U.S. Holder generally will be required to include the amount of such distribution in gross income as a dividend to the extent of our current or accumulated earnings and profits (as determined for U.S. federal income tax purposes) that are not allocated to excess distributions. The tax consequences of such distributions are discussed above under "Taxation of U.S. Holders—Distributions." Each U.S. Holder is encouraged to consult its own tax advisor with respect to the appropriate U.S. federal income tax treatment of any distribution on our ordinary shares.

If we are treated as a PFIC for any taxable year during the holding period of a Non-Electing U.S. Holder, we will continue to be treated as a PFIC for all succeeding years during which the Non-Electing U.S. Holder is treated as a direct or indirect Non-Electing U.S. Holder even if we are not a PFIC for such years. A U.S. Holder is encouraged to consult its tax advisor with respect to any available elections that may be applicable in such a situation, including the "deemed sale" election of Code Section 1298(b)(1) (which will be taxed under the adverse tax rules described above).

We may invest in the equity of foreign corporations that are PFICs or may own subsidiaries that own PFICs. If we are classified as a PFIC, under attribution rules, U.S. Holders will be subject to the PFIC rules with respect to their indirect ownership interests in such PFICs, such that a disposition of the ordinary shares of the PFIC or receipt by us of a distribution from the PFIC generally will be treated as a deemed disposition of such ordinary shares or the deemed receipt of such distribution by the U.S. Holder, subject to taxation under the PFIC rules. There can be no assurance that a U.S. Holder will be able to make a QEF election or a mark-to-market election with respect to PFICs in which we invest. Each U.S. Holder is encouraged to consult its own tax advisor with respect to tax consequences of an investment by us in a corporation that is a PFIC.

In addition, U.S. Holders should consult their tax advisors regarding the IRS information reporting and filing obligations that may arise as a result of the ownership of ordinary shares in a PFIC, including IRS Form 8621, Information Return by a Shareholder of a Passive Foreign Investment Company or Qualified Electing Fund.

The U.S. federal income tax rules relating to PFICs, QEF elections, and mark-to market elections are complex. U.S. Holders are urged to consult their own tax advisors with respect to the purchase, ownership and disposition of our ordinary shares, any elections available with respect to such ordinary shares and the IRS information reporting obligations with respect to the purchase, ownership and disposition of our ordinary shares.

Certain Reporting Requirements

Certain U.S. Holders are required to file IRS Form 926, Return by U.S. Transferor of Property to a Foreign Corporation, and certain U.S. Holders may be required to file IRS Form 5471, Information Return of U.S. Persons With Respect to Certain Foreign Corporations, reporting transfers of cash or other property to us and information relating to the U.S. Holder and us. Substantial penalties may be imposed upon a U.S. Holder that fails to comply. See the discussion regarding Form 8621, Information Return by a Shareholder of a Passive Foreign Investment Company or Qualified Electing Fund, above.

In addition, recently enacted legislation requires certain U.S. Holders to report information on IRS Form 8938, Statement of Specified Foreign Financial Assets, with respect to their investments in certain "foreign financial assets," which would include an investment in our ordinary shares, to the IRS.

U.S. Holders who fail to report required information could become subject to substantial penalties. U.S. Holders should consult their tax advisors regarding the possible implications of these reporting requirements arising from their investment in our ordinary shares.

Backup Withholding Tax and Information Reporting Requirements

Generally, information reporting requirements will apply to distributions on our ordinary shares or proceeds on the disposition of our ordinary shares paid within the United States (and, in certain cases, outside the United States) to U.S. Holders other than certain exempt recipients, such as corporations. Furthermore, backup withholding (currently at 28%) may apply to such amounts if the U.S. Holder fails to (i) provide a correct taxpayer identification number, (ii) report interest and dividends required to be shown on its U.S. federal income tax return, or (iii) make other appropriate certifications in the required manner. U.S. Holders who are required to establish their exempt status generally must provide such certification on IRS Form W-9.

Backup withholding is not an additional tax. Amounts withheld as backup withholding from a payment may be credited against a U.S. Holder's U.S. federal income tax liability and such U.S. Holder may obtain a refund of any excess amounts withheld by filing the appropriate claim for refund with the IRS and furnishing any required information in a timely manner.

New Legislative Developments

With respect to taxable years beginning on or after January 1, 2013, certain U.S. persons, including individuals, estates and trusts, will be subject to an additional 3.8% Medicare surtax, or "net investment income tax," on unearned income. For individuals, the additional net investment income tax applies to the lesser of (i) "net investment income" or (ii) the excess of "modified adjusted gross income" over $200,000 ($250,000 if married and filing jointly or $125,000 if married and filing separately). "Net investment income" generally equals the taxpayer's gross investment income reduced by the deductions that are allocable to such income. Investment income generally includes, among other things, passive income such as interest, dividends, annuities, royalties, rents, and capital gains. U.S. Holders are urged to consult their own tax advisors regarding the implications of the additional net investment income tax resulting from their ownership and disposition of our ordinary shares.

THE DISCUSSION ABOVE IS A GENERAL SUMMARY. IT DOES NOT COVER ALL TAX MATTERS THAT MAY BE OF IMPORTANCE TO A PROSPECTIVE INVESTOR. EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR ABOUT THE TAX CONSEQUENCES RELATING TO THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR ORDINARY SHARES IN LIGHT OF THE INVESTOR'S OWN CIRCUMSTANCES, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAWS.

F. Dividends and Paying Agents.

Not applicable.

G. Statements by Experts.

Not applicable.

H. Documents on Display.

You may read and copy this Annual Report on Form 20-F, including the related exhibits and schedules, and any document we file with the SEC without charge at the SEC's public reference room at 100 F Street, N.E., Room 1580, Washington, DC 20549. You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. The SEC also maintains an Internet website that contains reports and other information regarding issuers that file electronically with the SEC. Our filings with the SEC are also available to the public through the SEC's website at http://www.sec.gov.

As a "foreign private issuer," we are subject to the information reporting requirements of the Exchange Act that are applicable to foreign private issuers, and under those requirements file reports with the SEC. Those other reports or other information may be inspected without charge at the locations described above. As a "foreign private issuer," we are exempt from the rules under the Exchange Act related to the furnishing and content of proxy statements, and our officers, directors and principal shareholders will be exempt from the reporting and "short-swing" profit recovery provisions contained in Section 16 of the Exchange Act with respect to their purchases and sales of ordinary shares. Furthermore, as a "foreign private issuer," we are also not subject to the requirements of Regulation FD (Fair Disclosure) promulgated under the Exchange Act.

We maintain a corporate website at http://www.galmedpharma.com. Information contained on, or that can be accessed through, our website is not incorporated by reference into this annual report and does not constitute a part of this annual report. We have included our website address in this annual report solely as an inactive textual reference.

I. Subsidiary Information.

Not applicable.

ITEM 11. Quantitative and Qualitative Disclosures About Market Risk.

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, results of operations or cash flows due to adverse changes in financial market prices and rates, including interest rates and foreign exchange rates, of financial instruments.

Foreign Currency Exchange Risk

Our foreign currency exposures give rise to market risk associated with exchange rate movements of the Euro and NIS mainly against the U.S. dollar because a large portion of our expenses are denominated in Euros and NIS. Our Euro expenses consist principally of payments made to sub-contractors and consultants for preclinical studies, clinical trials and other research and development activities. Our NIS expenses consist principally of payments made to employees, sub-contractors and consultants for preclinical studies, clinical trials, professional services, other research and development activities and general and administrative activities. We anticipate that a large portion of our expenses will continue to be denominated in currencies other than the U.S. dollar. Our financial position, results of operations and cash flow are subject to fluctuations due to changes in foreign currency exchange rates. Our results of operations and cash flow are, therefore, subject to fluctuations due to changes in foreign currency exchange rates and may be adversely affected in the future due to changes in foreign exchange rates. Approximately 32% of our expenses are denominated in Euros. Changes of 5% and 10% in the U.S. dollar to Euro exchange rate will increase/decrease our operation expenses by 1.6% and 3.2%, respectively. Approximately 31% of our expenses are denominated in NIS. Changes of 5% and 10% in the U.S. dollar to NIS exchange rate will increase/decrease our operation expenses by 1.6% and 3.1%, respectively. To date, fluctuations in the exchange rates have not materially affected our results of operations or financial condition for the periods under review.

To date, we have not engaged in hedging 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 have an exposure to interest income sensitivity, which is affected by changes in the general level of Israeli interest rates. We currently do not hedge against interest rate exposure. Because of the short-term maturities of our cash equivalents and investment securities, we do not believe that an increase in market rates would have any significant impact on the realized value of our investment securities. If a 10% change in interest rates would not have a material effect on the fair value of our investment portfolio.

ITEM 12. Description of Securities Other Than Equity Securities.

A. Debt Securities.

Not applicable.

B. Warrants and Rights.

Not applicable.

C. Other Securities.

Not applicable.

D. American Depositary Shares.

Not applicable.

PART II

ITEM 13. Defaults, Dividend Arrearages and Delinquencies.

Not applicable.

ITEM 14. Material Modifications to the Rights of Security Holders and Use of Proceeds.

A. Not applicable.

B. Not applicable.

C. Not applicable.

D. Not applicable.

E. Use of Proceeds.

On March 18, 2014, we completed our initial public offering of 3,263,010 ordinary shares at a public offering price of $13.50 per share, which included 425,610 ordinary shares issued upon the exercise in full of the underwriters' option to purchase additional ordinary shares to cover over-allotments, for aggregate gross proceeds of approximately $44.1 million. Maxim Group LLC acted as sole book-running manager of the offering, and MLV & Co. and Feltl and Company acted as co-managers of the offering. The offer and sale of all of the shares in the offering were registered under the Securities Act pursuant to a registration statement on Form F-1, which was declared effective on March 12, 2014 (File No. 333-193792), and a registration statement on Form F-1 filed pursuant to Rule 462(b) of the Securities Act (File No. 333-194526).

We received aggregate net proceeds from the offering of approximately $39.9 million, after deducting approximately $3.1 million of underwriting discounts and commissions and approximately $1.1 million of estimated offering expenses directly payable by us. None of the underwriting discounts and commissions or other offering expenses were incurred or paid to our directors or officers or their associates or to persons owning ten percent or more of our ordinary shares or to any of our affiliates.

As of December 31, 2014, the net proceeds from our initial public offering were held in cash and cash equivalents, short-term deposits and marketable securities. Since then, we have deployed approximately $20.0 million into a variety of additional capital preservation investments, including short-term, investment grade, interest-bearing instruments, such as corporate debt securities, and certain short-term money market investments. We used approximately $750,000 of such net proceeds to pay for EndoPAT™ medical equipment purchased from Itamar. We have broad discretion in the use of the net proceeds from our initial public offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our ordinary shares.

We have no current understandings, commitments or agreements with respect to any material acquisition of or investment in any technologies, products or companies.

ITEM 15. Controls and Procedures.

Disclosure Controls and Procedures

We performed an evaluation of the effectiveness of our disclosure controls and procedures that are designed to ensure that information required to be disclosed in this Annual Report on Form 20-F and filed with the SEC is recorded, processed, summarized and reported timely within the time period specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by an issuer in the reports that it files or submits under the Exchange Act, is accumulated and communicated to the issuer's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. There can be no assurance that our disclosure controls and procedures will detect or uncover all failures of persons within our Company to disclose information otherwise required to be set forth in our reports. Nevertheless, our disclosure controls and procedures are designed to provide reasonable assurance of achieving the desired control objectives. Based on our evaluation, our management, including our President and Chief Executive Officer and Chief Financial Officer, have concluded that our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15(d) - 15(e) of the Exchange Act) as of the end of the period covered by this report are effective at such reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

This annual report does not include a report of management's assessment regarding internal control over financial reporting due to a transition period established by rules of the SEC for newly public companies.

Attestation Report of the Registered Public Accounting Firm

This annual report does not include a report of management's assessment regarding internal control over financial reporting due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the year ended December 31, 2014 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 16. [RESERVED]

ITEM 16A. Audit Committee Financial Expert.

Our Board has determined that Ms. Yaron-Eldar qualifies as an audit committee financial expert pursuant to the applicable SEC rules and that Ms. Yaron-Eldar is "independent" in accordance with the Nasdaq Capital Market corporate governance requirements. For information relating to Ms. Yaron-Eldar's qualifications and experience, see "Item 6. Directors, Senior Management and Employees—A. Directors and Senior Management."

ITEM 16B. Code of Ethics.

We have adopted a Code of Business Conduct and Ethics applicable to all of our directors and employees, including our President and Chief Executive Officer, Chief Financial Officer, controller or principal accounting officer or other persons performing similar functions, which is a "code of ethics" as defined in Item 16B of Form 20-F promulgated by the SEC and as required by the Nasdaq Capital Market Listing Rules, which refers to Section 406(c) of the Sarbanes-Oxley Act. Section 406(c) of the Sarbanes-Oxley Act provides that a "code of ethics" means such standards as are reasonably necessary to promote (i) honest and ethical conduct, including the ethical handling of actual or apparent conflicts of interest between personal and professional relationships; (ii) full, fair, accurate, timely and understandable disclosure in the periodic reports required to be filed by the issuer; and (iii) compliance with applicable governmental rules and regulation.

The full text of the Code of Business Conduct and Ethics **[is]** posted on our website at www.galmedpharma.com. Information contained on, or that can be accessed through, our website does not constitute a part of this prospectus and is not incorporated by reference herein. We will provide a copy of such code of ethics without charge upon request by mail or by telephone. If we make any amendment to the Code of Business Conduct and Ethics or grant any waivers, including any implicit waiver, from a provision of the Code of Business Conduct and Ethics, we will disclose the nature of such amendment or waiver on our website to the extent required by the rules and regulations of the SEC.

ITEM 16C. Principal Accountant Fees and Services.

Brightman Almagor Zohar & Co., a member firm of Deloitte Touche Tohmatsu Limited, an independent registered public accounting firm, served as our independent public accountants for the fiscal years ended December 31, 2013 and 2014, for which audited financial statements appear in this Annual Report on Form 20-F.

The following table presents the aggregate fees for professional services rendered by such accountants to us during their respective term as our principal accountants in 2013 and 2014.

	2014	2013
	(US$ in thousands)	(US$ in thousands)
Audit Fees (1)	60	60
Audit-Related fees (2)	141	-
All Other Fees (3)	13	-
Total	214	60

(1) Includes professional services rendered in connection with the audit of our annual financial statements and the review of our interim financial statements.

(2) Includes fees for our initial public offering in the United States in 2014.

(3) Includes professional fees related to an EU governmental incentive plan.

Audit Committee Pre-Approval Policies and Procedures

One of our Audit Committee's main roles is to assist the board of directors in fulfilling its responsibility for oversight of the quality and integrity of the accounting, auditing and reporting practices of the Company. The Audit Committee oversees the appointment, compensation, and oversight of the public accounting firm engaged to prepare or issue an audit report on the financial statements of the Company. [Our Audit Committee and Board have adopted a pre-approval policy for the engagement of our independent registered public accounting firm to perform certain audit and non-audit services. Pursuant to this policy, which is designed to assure that such engagements do not impair the independence of our auditors, the Audit Committee pre-approves annually a list of specific audit and non-audit services in the categories of audit services, audit-related services, tax services and other services that may be performed by our independent registered public accounting firm. Notwithstanding pre-approval by the Audit Committee of certain audit and non-audit services, our Board requires that the Audit Committee's chairperson approve any such audit or non-audit service in advance of engaging the service provider to provide such audit or non-audit service. 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.

Our shares are listed on the Nasdaq Capital Market under the symbol "GLMD." In addition to the corporate governance requirements of the Sarbanes-Oxley Act and the related rules implemented by the SEC, we must comply with the Listing Rules of the Nasdaq Capital Market. Under those Listing Rules, we may elect to follow certain corporate governance practices permitted under the Companies Law in lieu of compliance with corresponding corporate governance requirements otherwise imposed by the Listing Rules of the Nasdaq Capital 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 Capital Market, we follow the provisions of the Companies Law, rather than the Listing Rules of the Nasdaq Capital Market, with respect to the following requirements:

- *Distribution of certain reports to shareholders*. As opposed to the Listing Rules of the Nasdaq Capital Market, which require listed issuers to make certain reports, such as annual reports, interim reports and quarterly 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 plan to 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. See "Item 10. Additional Information—Documents on Display" for a description of our Exchange Act reporting obligations.

- *Nomination of directors.* With the exception of our external directors and directors elected by our Board due to vacancy, our directors are elected by an annual meeting of our shareholders to hold office until the next annual meeting following three years from his or her election. See "Item 6. Directors, Senior Management and Employees—C. Board Practices." The nominations for directors, which are presented to our shareholders by our Board, are generally made by the Board itself, in accordance with the provisions of our Articles and the Companies Law. One or more shareholders of a company holding at least 1% of the voting power of the company may nominate a currently serving external director for an additional three year term.

- *Compensation of officers*. We follow the provisions of the Companies Law with respect to matters in connection with the composition and responsibilities of our Remuneration Committee, Office Holder compensation and any required approval by the shareholders of such compensation. Israeli law and our Articles do not require that the independent members of our Board, or a remuneration committee composed solely of independent members of our Board, determine an executive officer's compensation, as is generally required under the Listing Rules of the Nasdaq Capital Market with respect to the Chief Executive Officer and all other executive officers of a company. Instead, our Remuneration Committee and conducts itself in accordance with the provisions governing the composition of and the responsibilities of a remuneration committee as set forth in the Companies Law. Furthermore, remuneration of Office Holders is determined and approved by our Remuneration Committee, and in general, by our Board as well, and in certain circumstances, by our shareholders, as detailed above. The requirements for shareholder approval of any Office Holder compensation, and the relevant majority or Special Majority for such approval, are all as set forth in the Companies Law. Thus, we seek shareholder approval for all corporate actions with respect to Office Holder compensation requiring such approval under the requirements of the Companies Law, including for our Compensation Policy and for certain Office Holder Compensation, rather than seeking approval for such corporate actions in accordance with Listing Rules of the Nasdaq Capital Market. All members of our Remuneration Committee are independent directors under applicable Nasdaq Capital Market and SEC rules, as affirmatively determined by our Board. See "Item 6. Directors, Senior Management and Employees—B. Compensation."

- *Independent directors*. Although Israeli law does not require that a majority of the directors serving on our Board be "independent," as defined under Nasdaq Capital Market Listing Rule 5605(a)(2), but rather requires we have at least two external directors who meet the requirements of the Companies Law, as described above under "Item 6. Directors, Senior Management and Employees—C. Board Practices—External Directors." A majority of our Board is independent based on the Nasdaq Capital Market rules. We are required, however, to ensure that all members of our Audit Committee are "independent" under the applicable Nasdaq Capital Market and SEC criteria for independence (as we cannot exempt ourselves from compliance with that SEC independence requirement, despite our status as a foreign private issuer) and we must also ensure that a majority of the members of our Audit Committee are "unaffiliated directors" as defined in the Companies Law. However, while not required by Israeli law our independent directors will conduct regularly scheduled meetings at which only such independent directors are present, as required by the Nasdaq Capital Market Listing Rules. Our Board has affirmatively determined that each of Mr. Nir, Ms. Yaron-Eldar, Mr. Marth and Dr. Sidransky qualifies as "independent" under the Nasdaq Capital Market independence standards.

- *Shareholder approval*. We will seek shareholder approval for all corporate actions requiring such approval under requirements of the Companies Law, rather than seeking approval for corporate actions in accordance with Nasdaq Capital Market Listing Rule 5635. In particular, under this Nasdaq Capital Market rule, shareholder approval is generally required for: (i) an acquisition of shares or 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 or 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 (or via sales by directors, officers or 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 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 remuneration 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 under "Item 6. Directors, Senior Management and Employees—C. Board Practices—Approval of Related Party Transactions under Israeli Law—Transactions with Controlling Shareholders," and (iii) terms of office and employment or other engagement of the controlling shareholder of the Company or such controlling shareholder's relative, which require the special approval described under "Item 6. Directors, Senior Management and Employees—B. Compensation" and "Item 6. Directors, Senior Management and Employees—C. Board Practices—Approval of Related Party Transactions under Israeli Law." In addition, under the Companies Law, a merger requires approval of the shareholders of each of the merging companies. See also "Compensation of officers" above.

ITEM 16H. Mine Safety Disclosure.

Not applicable.

PART III

ITEM 17. Financial Statements.

We have responded to Item 18 in lieu of responding to this item.

ITEM 18. Financial Statements.

Please refer to the financial statements beginning on page F-1. The following financial statements, financial statement schedules and related notes are filed as part of this Annual Report on Form 20-F, together with the report of the independent registered public accounting firm.

	Page
Report of Independent Registered Public Accounting Firm	F-1
Consolidated Balance Sheets	F-2
Consolidated Statements of Operations	F-3
Consolidated Statements of Comprehensive Loss	F-4
Consolidated Statements of Changes in Shareholders' Equity	F-5
Consolidated Statements of Cash Flows	F-6
Notes to Consolidated Financial Statements	F-7 - F-25

Deloitte.
Brightman Almagor Zohar

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Shareholders of
GALMED PHARMACEUTICALS LTD.

We have audited the accompanying consolidated balance sheets of Galmed Pharmaceuticals Ltd. ("the Company") and its subsidiaries as of December 31, 2014 and 2013, and the related consolidated statements of operations and changes in shareholders' equity (deficiency) and cash flows for each of the three years in the period ended December 31, 2014. These consolidated financial statements are the responsibility of the Company's board of directors and management. Our responsibility is to express an opinion on these consolidated 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. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audit 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 the management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements, present fairly, in all material respects, the financial position of the Company and its subsidiaries as of December 31, 2014 and 2013, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2014, in conformity with accounting principles generally accepted in the United States of America.

Brightman Almagor Zohar & Co.
Certified Public Accountants
A member firm of Deloitte Touche Tohmatsu Limited

Tel Aviv, Israel
March 31, 2014

Tel Aviv - Main Office	Trigger Foresight	Ramat-Gan	Jerusalem	Haifa	Beer-Sheva	Eilat
1 Azrieli Center	3 Azrieli Center	6 Ha-rakun	12 Sarei Israel	5 Ma'aleh Hashichrur	Omer Industrial Park	The City Center
Tel Aviv, 6701101	Tel Aviv, 6702301	Ramat Gan, 5252183	Jerusalem, 9439024	P.O.B. 5648	Building No. 10	P.O.B. 583
P.O.B. 16593				Haifa, 3105502	P.O.B. 1369	Eilat, 8810402
Tel Aviv, 6116402					Omer, 8496500	
Tel: +972 (3) 608 5555	Tel: +972 (3) 607 0500	Tel: +972 (3) 755 1500	Tel: +972 (2) 501 8888	Tel: +972 (4) 860 7333	Tel: +972 (8) 690 9500	Tel: +972 (8) 637 5676
Fax: +972 (3) 609 4022	Fax: +972 (3) 607 0501	Fax: +972 (3) 676 9955	Fax: +972 (2) 537 4173	Fax: +972 (4) 867 2528	Fax: +972 (8) 690 9600	Fax: +972 (8) 637 1628
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GALMED PHARMACEUTICALS LTD.
Consolidated Balance Sheets

U.S. Dollars in thousands, except share data and per share data

		As of December 31,	
		2014	2013
Assets			
Current assets			
Cash and cash equivalents	3	$ 23,736	$ 137
Short-term deposit	3	6,000	–
Marketable securities	3	2,250	–
Other accounts receivable	4	165	16
Total current assets		32,151	153
Property and equipment, net	5	774	13
Total assets		$ 32,925	$ 166
Liabilities and stockholders' equity (deficiency)			
Current liabilities			
Trade payables		875	1,355
Other accounts payable	6	243	334
Total current liabilities		1,118	1,689
Long-term liabilities			
Related parties	8	400	428
Total long-term liabilities		400	428
Stockholders' equity (deficiency)			
Ordinary shares, par value NIS 0.01 per share; Authorized 50,000 shares; Issued and outstanding: 11,100,453 shares as of December 31, 2014	10	32	–
Ordinary shares, par value $1 per share; Authorized 50,000 shares; Issued and outstanding: 9,739 shares as of December 31, 2013	10	–	10
Additional paid-in capital		68,116	25,681
Accumulated other comprehensive income		4	–
Accumulated deficit		(36,745)	(27,642)
Total stockholders' equity (deficiency)		31,407	(1,951)
Total liabilities and stockholders' equity (deficiency)		$ 32,925	$ 166

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

GALMED PHARMACEUTICALS LTD.
Consolidated Statements of Operations

U.S. Dollars in thousands, except share data and per share data

		Year ended December 31,		
		2014	**2013**	**2012**
Research and development, expenses	11	$ 6,664	$ 7,207	$ 2,443
General and administrative expenses	12	2,478	7,355	694
Capital loss		–	10	–
Total operating expenses		9,142	14,572	3,137
Financial expenses (income), net		(40)	2,912	6
Loss before income taxes		9,102	17,484	3,143
Income taxes	13	1	1	6
Net loss		$ 9,103	$ 17,485	$ 3,149
Basic and diluted net loss per share from continuing operations		$ 0.88	$ 3.45	$ 0.63
Weighted-average number of shares outstanding used in computing basic and diluted net loss per share *)		10,323,686	5,069,466	4,955,837

*) Retroactively adjusted to reflect the 729:1 share split, which occurred upon consummation of the Reorganization.

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

GALMED PHARMACEUTICALS LTD.
Consolidated Statements of Comprehensive Loss

U.S. Dollars in thousands, except share data and per share data

	Year ended December 31,		
	2014	**2013**	**2012**
Net loss	$ 9,103	$ 17,485	$ 3,149
Other comprehensive income:			
Net unrealized gain on available for sale securities	4	–	–
Comprehensive loss	$ 9,099	$ 17,485	$ 3,149

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

GALMED PHARMACEUTICALS LTD.
Consolidated Statements of Changes in Shareholder's Equity (Deficiency)

U.S. Dollars in thousands, except share data and per share data

	Ordinary shares		Additional paid-in	Capital	Accumulated other comprehensive	Accumulated	
	Shares	amount	capital	note	income	deficit	Total
Balance - January 1, 2012	6,853	$ 7	$ 4,239	$ 52	$ –	$ (7,008)	$ (2,710)
Capital note	–	–	–	3,672		-	3,672
Stock based compensation	–	–	208	–		–	208
Net loss	–	–	–	–		(3,149)	(3,149)
Balance - December 31, 2012	6,853	$ 7	$ 4,447	$ 3,724	$ –	$ (10,157)	$ (1,979)
Conversion of capital notes in December 2013	1,432	2	3,722	(3,724)	–	–	–
Stock-based compensation expenses	–	–	10,851	–	–	–	10,851
Conversion of loans, December 2013	1,408	1	6,541	–	–	–	6,542
Issuance of ordinary shares, December 2013	46	–	120	–	–	–	120
Net loss		–	–	–	–	(17,485)	(17,485)
Balance - December 31, 2013	9,739	$ 10	$ 25,681	$ –	$ –	$ (27,642)	$ (1,951)
Reorganization and stock split *)	7,099,731	20	25,671	–	–	(27,642)	(1,951)
Issuance of ordinary shares in February 2014	560,224	2	1,998	–	–	–	2,000
Issuance of ordinary shares upon initial public offering, net in March 2014 **)	3,263,010	9	39,847	–	–	–	39,856
Cashless exercise of options	177,488	1	(1)	–	–	–	–
Stock based compensation	–	–	601	–	–	–	601
Unrealized gain from marketable securities	–		–	–	4	–	4
Net loss	–		–	–	–	(9,103)	(9,103)
Balance - December 31, 2014	11,100,453	$ 32	$ 68,116	$ –	$ 4	$ (36,745)	$ 31,407

*) See also Note 1.

**) Net of offering costs in the amount of $4,204.

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

GALMED PHARMACEUTICALS LTD.
Consolidated Statements of Cash Flows

U.S. Dollars in thousands, except share data and per share data

	Year ended December 31,		
	2014	**2013**	**2012**
Cash flow from operating activities			
Net loss for the year	$ (9,103)	$ (17,485)	$ (3,149)
Adjustments required to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	9	4	5
Capital loss	–	10	–
Non-cash financial expenses due to convertible notes modification	–	2,878	–
Stock-based compensation expense	601	10,851	208
Changes in operating assets and liabilities:			
Decrease (Increase) in other accounts receivable	(149)	(2)	(11)
Increase (decrease) in trade payables	(480)	954	(89)
Increase (decrease) in other accounts payable	(91)	228	(103)
Increase (decrease) in related party	(28)	38	60
Net cash provided by (used in) operating activities	(9,241)	(2,524)	(3,079)
Cash flow from investing activities			
Purchase of property and equipment	(770)	(13)	(32)
Proceeds from sale of property and equipment	–	16	–
Investment in securities, available for sale	(2,246)	–	–
Investment in short-term deposit	(6,000)	–	–
Net cash provided by (used in) investing activities	(9,016)	3	(32)
Cash flow from financing activities			
Credit from bank	–	–	(9)
Receipt of short term loan from bank	–	–	26
Repayments of short-term loan from bank	–	(20)	(6)
Receipt of convertible notes	–	1,840	–
Issuance of ordinary shares	2,000	120	–
Issuance of ordinary shares upon IPO, net *)	39,856	–	–
Issuance of capital note	–	–	3,672
Net cash provided by financing activities	41,856	1,940	3,683
Increase (decrease) in cash and cash equivalents	23,599	(581)	572
Cash and cash equivalents at the beginning of the year	137	718	146
Cash and cash equivalents at the end of the year	$ 23,736	$ 137	$ 718
Non cash activity:			
Conversion of convertible loans into ordinary shares	–	$ 6,542	–
Conversion of capital note into ordinary shares	–	$ 3,724	–
Supplemental disclosure of cash flow information:			
	$ 4	–	–

*) Net of offering costs in the amount of $4,204.

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

GALMED PHARMACEUTICALS LTD.
Notes to Consolidated Financial Statements

Note 1 – General

Galmed Pharmaceuticals Ltd. (the "Company") is a clinical-stage biopharmaceutical company primarily focused on the development and commercialization of therapeutics for the treatment of liver diseases and cholesterol gallstones.

The Company was incorporated in Israel on July 31, 2013 and has not commenced operations until February 2, 2014. On February 2, 2014, upon a pre-ruling from the Israeli Tax Authorities, the Company underwent a reorganization (the "Reorganization") pursuant to which all of Galmed Holdings Inc.'s business, including shares in its fully owned subsidiary, Galmed 2000, which was incorporated in British virgin island) and net assets, was transferred to the Company. Contemporaneously, Galmed Pharmaceuticals Ltd. effected a stock split of 729:1. This Reorganization is considered a restructuring under common control in which the Company is the Successor (the "Successor") and Galmed Holdings Inc. (which, as of the date of the Reorganization, was owned in the same holding percentage by the same shareholders who owned the Company) is the predecessor (the "Predecessor").

Accordingly, the Company succeeded the Predecessor's activities and comparative amounts which is presented on these financial statements.

All the data in the accompanying notes regarding the amount of shares, options, warrants, capital notes, convertible notes, per share and par value is retroactively adjusted to reflect the 729:1 share split, which occurred upon consummation of the Reorganization.

The Company holds a wholly owned subsidiary, Galmed International Ltd., which was incorporated in Malta. Galmed International Ltd. holds a wholly owned subsidiary, Galmed Medical Research Ltd., which was incorporated in Israel.

The Company also holds a wholly owned subsidiary, Galmed Research and Development Ltd., which was incorporated in Israel.

Note 2 – Significant Accounting Policies

A. Basis of presentation

The consolidated financial statements have been prepared in accordance with United States Generally Accepted Accounting Principles ("U.S. GAAP").

B. Use of estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Note 2 – Significant Accounting Policies (Cont.)

C. Financial statement in U.S. dollars

The functional currency of the Company and its subsidiaries is the U.S dollar (the "dollar"), because the dollar is the currency of the primary economic environment in which the Company and its subsidiaries operate, and expect to continue operating in the foreseeable future. Transactions and balances denominated in dollars are presented in their original amounts. Non-dollar transactions and balances have been re-measured to dollars in accordance with the provisions of ASC 830-10, "Foreign Currency Translation." All transaction gains and losses from re-measurement of monetary balance sheet items denominated in non-dollar currencies are reflected in the statement of operations as financial income or expenses, as appropriate.

D. Principles of consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries: Galmed Research and Development Ltd, Galmed 2000 Inc., Galmed International Ltd., and Galmed Medical Research Ltd. All intercompany balances and transactions were eliminated upon consolidation.

E. Cash and cash equivalents

Cash equivalents are short-term, highly liquid investments that are readily convertible to cash with maturities of three months or less as of the date acquired.

F. Short-term bank deposits

Short-term bank deposits are deposits with maturities of more than three months but less than one year. The short-term bank deposits are presented at their cost. As of December 31, 2014, the Company's bank deposits were in U.S. dollars and bore interest at a weighted -average interest rate of 0.6%.

G. Marketable securities

Marketable securities are considered to be available for sale and are carried at fair value. Unrealized gains and losses, if any, are reported as a separate component of stockholders' equity. The cost of marketable securities classified as available for sale is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in interest income. Realized gains and losses, if any, are also included in other income, net. The cost of securities sold is based on the specific identification method.

Note 2 – Significant Accounting Policies (Cont.)

H. Property and equipment

Property and equipment are stated at cost, less accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets.

The annual depreciation rates are as follows:

	%
Office furniture and equipment	7
Computer software, electronic and medical equipment	15–33

I. Impairment of long-lived assets

The Company's and its subsidiaries' long-lived assets are reviewed for impairment in accordance with ASC 360-10, "Accounting for the Impairment or Disposal of Long-Lived Assets," 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 the assets 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 their fair value. During 2014 and 2013, no impairment losses were identified.

J. Severance pay

The Company's liability for severance pay is calculated in accordance with Israeli law, based on the most recent salary paid to each employee and the length of employment with the Company. Part of the liability is funded through individual insurance policies purchased from outside insurance companies, which are not under the Company's control. The Company employees are included under section 14 of the Severance Compensation Act, 1963 ("Section 14") for a portion of their salaries. According to Section 14, these employees are entitled to monthly deposits at a rate of 8.33% of their monthly salary, made in their name with such insurance companies. Under the Severance Compensation Act, 1963, payments in accordance with Section 14 release the Company from any future severance payments to those employees. The aforementioned deposits are not recorded as an asset in the Company's balance sheet.

Note 2 – Significant Accounting Policies (Cont.)

K. Fair value of financial instruments

The estimated fair value of financial instruments was determined by the Company using available market information and valuation methodologies. Considerable judgment is required in estimating fair values. Accordingly, the estimates may not be indicative of the amounts the Company could realize in a current market exchange.

The following methods and assumptions were used by the Company in estimating its fair value disclosures for financial instruments:

The carrying amounts of cash and cash equivalents, short-term bank deposits, marketable securities and trade payables approximate their fair value due to the short-term maturity of such instruments.

Fair value is an exit price representing the amount that would be received upon selling an asset or that would be 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 used by market participants in pricing an asset or a liability.

A three-tier fair-value hierarchy was established as a basis for considering such assumptions and for inputs used in the valuation methodologies in measuring fair value:

Level 1 - Observable inputs that reflect quoted prices (unadjusted) for identical assets or liabilities in active markets

Level 2 - Other inputs that are directly or indirectly observable in the marketplace; and

Level 3 - Unobservable inputs that are supported by little or no market activity

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.

Note 2 - Significant Accounting Policies (Cont.)

L. Convertible notes

The Company examines its issued convertible notes under ASC 470-20, "Debt with Conversion and Other Options," according to which the proceeds from the sale of debt securities with a conversion feature and or other options are allocated to each of the issued securities based on their relative fair value.

The Company also examined its issued convertible notes under ASC Topic 815, "Derivatives and Hedging," which generally provides criteria that, if met, require companies to bifurcate conversion options from their host instruments and account for them as freestanding derivative financial instruments. These three criteria are: (i) the economic characteristics and risks of the embedded derivative instrument are not clearly and closely related to the economic characteristics and risks of the host contract; (ii) the hybrid instrument that embodies both the embedded derivative instrument and the host contract is not re-measured at fair value under otherwise-applicable generally accepted accounting principles with changes in fair value reported in earnings; and (iii) a separate instrument with the same terms as the embedded derivative instrument would be considered a derivative instrument subject to the requirements of ASC Topic 815.

In determining whether an embedded derivative should be bifurcated, the Company considers all other scope exceptions provided by that topic. One scope exception particularly relevant to convertible instruments is whether the embedded conversion feature is both indexed to, and classified in, the Company's equity.

The Company further considered whether, under ASC 470-20-25, a beneficial conversion feature exists. If so, then the Company should have allocated the beneficial conversion feature to an equity component based on the benefit of the conversion terms granted to purchasers on the issuance date.

The Company examined and determined that no beneficial conversion feature exists under ASC 470-20. The Company also examined and determined that no derivative financial instrument exists that is subject to the requirements of ASC Topic 815 that should be bifurcated and separately accounted for as a derivative financial instrument.

Note 2- Significant Accounting Policies (Cont.)

M. Accounting for stock-based compensation

The Company applies ASC 718-10, "Share-Based Payment," which requires the measurement and recognition of compensation expense for all share-based payment awards made to employees and directors, including employee stock options under the Company's stock plans, based on estimated fair values. ASC 718-10 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 portion of the award that is ultimately expected to vest is recognized as expense over the requisite service periods in the Company's consolidated statement of operations.

The Company recognizes compensation expense for the value of non-employee awards, which have graded vesting, based on the accelerated attribution method over the requisite service period of each award, net of estimated forfeitures.

The Company recognizes compensation expenses for the value of employee awards, which have graded vesting, based on the straight-line method over the requisite service period of each of the awards, net of estimated forfeitures.

The Company estimates the fair value of restricted shares based on the market price of the shares at the grant date, and estimates the fair value of stock options granted using a Black-Scholes option-pricing model. The option-pricing model requires a number of assumptions, the most significant of which are the expected stock-price volatility and the expected option term (the time from the grant date until the options are exercised or expire).

The Company's calculations of the expected volatility were based upon actual historical stock-price movements over the period, which was equal to the expected option term. The expected option term was calculated for options granted to employees and directors in accordance with ASC-718-10-S99, using the "simplified" method, and grants to non-employees were based on the contractual term. Historically, the Company has not paid dividends, and has no foreseeable plans to do so. The risk-free interest rate is based on the yield from U.S. Treasury zero-coupon bonds with an equivalent term.

The following assumptions were used for the fiscal year 2014 and 2013 grants: dividend yield of 0.00% for both periods; risk-free interest rate between 0.91% and 1.68%; an expected life between five and six years; and a volatility rate ranging between 76% to 80%

N. Research and development expenses

Research and development expenses are charged to the statement of operations as incurred.

Note 2 - Significant Accounting Policies (Cont.)

O. Income taxes

The Company accounts for income taxes utilizing the asset and liability method in accordance with ASC 740, "Income Taxes." Current tax liabilities are recognized for the estimated taxes payable on tax returns for the current year. Deferred tax liabilities or assets are recognized for the estimated future tax effects attributable to temporary differences between the income-tax bases of assets and liabilities and their reported amounts in the financial statements and for tax loss carry forwards. Measurement of current and deferred tax liabilities and assets is based on provisions of enacted tax laws, and deferred tax assets are reduced, if necessary, by the amount of tax benefits, the realization of which is not considered more likely than not based on available evidence.

ASC 740-10 requires a two-step approach to recognizing and measuring uncertain tax positions. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. The second step is to measure the tax benefit as the largest amount that is more than 50% likely of being realized upon ultimate settlement.

P. Basic and diluted net loss per share

Basic net loss per share is computed based on the weighted-average number of shares outstanding during each year. Diluted net loss per share is computed based on the weighted-average number of shares outstanding during each year, plus the dilutive potential of the ordinary shares considered outstanding during the year, in accordance with ASC 260-10, "Earnings Per Share."

All outstanding stock options and warrants were excluded from the calculation of the diluted loss per share for the years ended December 31, 2014 and 2013 because all such securities have an anti-dilutive effect.

Note 3 – Investments

The following table summarizes the Company's cash, cash equivalents, and investments as of December 31, 2014 and 2013

	As of December 31, 2014			
	Cost Basis	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(in thousands)			
Cash and cash equivalents	$ 23,736	$ –	$ –	$ 23,736
Short-term deposit	6,000	–	–	6,000
Marketable securities	2,246	7	(3)	2,250
Total cash, cash equivalents and investments	$ 31,982	$ 7	$ (3)	$ 31,986

	As of December 31, 2013			
	Cost Basis	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(in thousands)			
Cash and cash equivalents	$ 137	$ –	$ –	$ 137
Total cash and cash equivalents	$ 137	$ –	$ –	$ 137

Note 4 – Other Accounts Receivable

	As of December 31	
	2014	2013
	(in thousands)	
Government institutions	$ 51	$ 11
Interest receivable	13	–
Prepaid expenses	101	5
	$ 165	$ 16

Note 5 – Property and equipment, net

	As at December 31	
	2014	2013
	(in thousands)	
Medical equipment	$ 750	$ –
Office furniture and equipment	5	3
Computer software and electronic equipment	45	27
	800	30
Accumulated depreciation	26	17
Net book value	$ 774	$ 13

Note 6 – Other Accounts Payable

	As of December 31	
	2014	2013
	(in thousands)	
Accrued expenses	$ 81	$ 236
Employees and related institutions	84	22
Accrued vacation *)	78	76
	$ 243	$ 334

*) Including inter alia due to a related party in the amount of $68 thousand and $70 thousand, as of December 31, 2014 and 2013, respectively.

Note 7 – Convertible Notes

From August through October 2013, the Company issued short-term convertible notes to various investors (the "Investors") in the aggregated amount of $1.84 million. Such notes were convertible into ordinary shares of the Company based on a price per share of $7.45. On December 1, 2013, the Company and the Investors signed an amendment that changed the conversion price per share to $3.57. The amendment was in line with a negotiation held simultaneously with an investor, which resulted in an issuance of ordinary shares (see note 10.A.5), reflecting a price per share of $3.57. The shares were issued at a discount from the Company's estimation regarding its own fair value due to the necessity of raising additional funds in order to finance its operational activity.

The Company applied the provisions of ASC 470-50, "Modifications and Extinguishments," to account for debt modification. The Company first determined that the exchange was not considered a troubled debt, mainly due to the fact that no concession was granted by the creditor. Based on the provisions of ASC 470-50, the Company determined that the exchange resulted in an extinguishment of the old convertible notes and the issuance of new convertible notes.

The Company recorded the new convertible notes by its measured fair value. The difference between the fair value of the new convertible notes and the net carrying amount of the extinguished notes, approximately $2.9 million—was recorded in the statement-of- operations report as a financial expense for the year ended December 31, 2013.

The Company measured the fair value of the new convertible notes according to present value techniques that are commensurate with valuation techniques used in valuation of convertible notes, which includes the fair value of the loan and the fair value of the conversion feature.

The following assumptions were used for measuring the fair value of the new convertible notes: dividend yield of 0.00%; risk-free interest rate of 1.71%; expected life of five years; volatility rate of 70%; and a discount rate of 20%.

On December 10, 2013, upon request of the convertible-notes holders, the notes fully converted into 515,403 ordinary shares with a par value of NIS 0.01.

In December 2013, upon request of the convertible-notes holders, the Company converted all of its outstanding convertible notes into 1,026,432 ordinary shares with a par value of NIS 0.01 per share.

Note 8 – Related Parties

A. Balances

1. On January 1, 2007, the Company entered into a consulting agreement with a consulting company (the "Consulting Company") owned by a member of the Company's Board of Directors, who is also the Company's CEO and a shareholder of the Company. The maximum monthly consideration for the services provided pursuant to the agreement is $10 thousand.

   In January 2012, the Consulting Company increased the scope of its services and, accordingly, the monthly fee was increased to $20 thousand. Later in 2012, the Consulting Company agreed to waive the majority of its 2012 fees.

   On December 23, 2013, the company entered into an employment agreement with its CEO, who and therefor the agreement with the Consulting Company was terminated.

   As of December 31, 2014, the Company had no debt, related to the mentioned Consulting agreement**.**

2. As of December 31, 2014 and 2013, the Company had an accrual in the amount of $255 thousand and $223 thousand, respectively, pursuant to an employment agreement with its CEO.

3. In December 2011, the Company signed an agreement with the beneficiaries of one of its cofounders, which stated that the beneficiaries are entitled to an aggregate amount of $263 thousand as a result of outstanding obligations of the Company owed to the late co-founder. Such amount is subject to annual interest equal to LIBOR + 1%.

   As of December 31, 2014 and 2013, the aggregated outstanding amount of the aforementioned liabilities was $280 thousand and $275 thousand, respectively.

B. Transactions

1. During 2013 and 2012, the Company recognized consulting fees and expenses owed to the Consulting Company in the amount of $10 thousand and $20 thousand, respectively.

2. During 2014, 2013 and 2012, the Company recorded salary expenses in the amount of $512 thousand, $34 thousand and $55 respectively, pursuant to an employment agreement with its CEO.

3. In 2012, the Company issued 241,299 options in order to purchase ordinary shares of the Company to the chairman of its board of directors. During 2014, 2013 and 2012, the stock-based compensation expenses with respect to the options amounted to $43 thousand, $101 thousand and $208 thousand, respectively. See also Note 10.A.7.

Note 8 – Related Parties (Cont.)

B. Transactions (Cont.)

4. During the years 2009 through 2011 and the year 2013, the Company received convertible notes in the amount of $1.2 million and $574 thousand, respectively, from various existing shareholders.

   In December 2013, upon the request of the convertible-notes holders, the notes were fully converted. See also Note 7.

5. In December 2013, the Company granted 806,274 options to purchase ordinary shares of the Company with a NIS 0.01 par value to certain directors. The options will vest over various periods not exceeding two years and will expire in September 2023. The exercise price is between $0.01 and $3.57 per share. As of December 31, 2014, the amount of vested Options is 762,534. The aggregate grant date fair value of such options is $7.8 million. During the year 2014 and 2013, with respect to the above-mentioned options, the Company recorded stock-based compensation expenses in the amount of $413 thousand and $7,0 nillion, respectively,. See also Note 10.

6. During 2014, the Company granted 685,749 options to purchase ordinary shares of the Company with a NIS 0.01 par value to certain directors. The options will vest over various periods not exceeding four years and will expire 10 years from the grant date. The exercise price is between $3.57 and $5.49 per share. The grant of 310,000 options to certain directors is subject to the approval of the general shareholders' meeting. As of December 31, 2014, the amount of vested Options is 21,456. The aggregate grant date fair value of such options, excluding the options that are waiting the general shareholders' meeting approval, is $285 thousand. During the year 2014 the Company recorded stock-based compensation expenses in the amount of $142 thousand with respect to the above-mentioned options. See also Note 10.

Note 9 – Commitments and Contingencies

In 2002, the Company entered an agreement with Aventis Pharma Deutschland GmbH. ("Aventis"), in which Aventis agreed that the Company will have the exclusive worldwide right to commercialize an invention covered by Israeli patent application 123998 and PCT/IL99/00173, and the Company agreed to pay Aventis a royalty of 10% in respect of all income that the Company or its affiliates may receive from the commercialization of such invention which is related to the prevention and treatment of gallstones.

Note 10 – Shareholders' Equity (Deficiency)

A. Ordinary shares

1. Ordinary shares confer upon the holders the right to receive notice to participate and vote in general meetings of the Company and the right to receive dividends, if declared.

2. During the period of September 11, 2000 (date of inception) through 2009, a total of 4,995,837 ordinary shares were issued by the Company in consideration of $4.2 million.

3. In December 2013, upon the request of convertible-notes holders, the Company converted all of its outstanding convertible notes into 1,026,432 ordinary notes.

4. In December 2013, upon the capital-notes holders' request, the Company converted all of its capital notes into 1,043,928 ordinary shares with a par value of NIS 0.01 per share.

5. On December 31, 2013, the Company signed an agreement with an investor in the Company in which the Company issued the investor 33,534 ordinary shares in consideration of $120 thousand.

6. On February 3, 2014, the Company entered into a share purchase agreement with certain of its shareholders and new investors, pursuant to which the Company issued to such existing shareholders and new investors 560,224 ordinary shares at a price per share of $3.57 for a total consideration in the amount of approximately $2 million.

7. During 2012, the Company granted Options to purchase 241,299 of its ordinary shares with a par value NIS 0.01 per share to the Chairman of its Board of Directors. On March 12, 2014, upon the IPO, the Chairman exercised the Options by way of a cashless exercise into 177,488 ordinary shares of the Company based upon the initial public offering price of $13.50 per share.

8. On March 12, 2014, the Company completed an initial public offering (the "IPO") and listed its ordinary shares on the NASDAQ Capital Market under the ticker symbol

   GLMD. In the IPO, the Company issued under 3.3 million shares to the market at a price of $13.50 per share (par value NIS 0.01 per share), for a total consideration of approximately $40 million, net of offering costs in the amount of approximately $4.2 million.

Note 10 – Shareholders' Equity (deficiency) (Cont.)

B. Capital notes

During the years 2012 and 2011, the Company signed share-purchase agreements with various investors, according to which the Company issued such investors capital notes in the aggregate amount of $3.7 million.

The capital notes are instruments of equity and not debt. The capital-notes holders had the right to convert the face-value amount of the capital notes, in whole or in part and without additional consideration, into ordinary shares of the Company; however, prior to such conversion, if at all, the capital notes (i) do not grant their holders with any of the rights of the Company's shareholders; (ii) have no maturity date, do not carry interest, are not linked to any index, and are not redeemable; and (iii) are not registered.

Accordingly, the Company classified such capital notes as an equity component. In 2013 the capital notes were fully converted into 1,043,298 ordinary shares.

C. Stock-based compensation

1. During 2002, the Company granted 38,637 Options to purchase ordinary shares of the Company to a service supplier (the "Service Supplier"). The Options were fully vested at the grant date, as set forth in the agreement signed by the parties. The options exercise price is $1.50 per share. As of December 31, 2014, all the aforementioned options were outstanding.

2. In December 2013, the Company granted 1,219,617 Options to purchase ordinary shares of the Company to certain consultants and directors. The options will vest over various periods not exceeding two years and will expire in September 2023. The option exercise price is between $0.01 and $3.57 per share. As of December 31, 2014, the amount of vested Options is 825,228.

3. In February 2014, the Company granted options to purchase 8,583 of its ordinary shares to a member of the board of directors. The options are fully vested and expire in September 2023. The exercise price is $3.57 per share, and the fair value of such options at the grant date was $95 thousand.

4. In March 2014, the Company granted Options to purchase 17,166 of its ordinary shares to a member of the board of directors. The options vest over three years and expire in September 2023. The exercise price is $3.57 per share, and the fair value of such options at the grant date was $190 thousand. As of December 31, 2014, the amount of vested options is 4,290.

Note 10 – Shareholders' Equity (deficiency) (Cont.)

C. Stock-based compensation (Cont.)

5. In December 2014, the Company granted 660 thousand Options to purchase ordinary shares of the Company to certain employees, consultants, and directors. The options will vest over four years and will expire in December 2024. The exercise price is $5.49 per share.

   The grant of 330 thousand options to certain employees and directors is subject to the approval of the general shareholders' meeting. As of December 31, 2014, none of such options were vested.

6. A summary of the status of the Company's option plans as of December 31, 2014 and 2013 and changes during the years then ended are presented below:

	December 31,			
	2014		2013 *)	
	Number of share options	Weighted average exercise price	Number of share options	Weighted average exercise price
Options outstanding at beginning of year	1,499,553	$ 1.17	279,936	$ 3.28
Granted **)	355,749	$ 5.35	1,219,617	$ 0.64
Exercised	(241,299)	$ 3.57	–	–
Outstanding at end of year	1,614,003	$ 1.70	1,499,553	$ 1.13
Options exercisable at year end	1,227,387	$ 1.40	1,331,154	$ 1.02

*) Retroactively adjusted to reflect the 729:1 share split, which occurred upon the consummation of the Reorganization.

**) Excluding grant of 330 thousand options subject to approval of the general shareholders' meeting.

As of December 31, 2014 and 2013, the weighted-average remaining contractual term of the outstanding and exercisable options, excluding the 38,637 Options granted in 2002 that have no expiration date, is 8.74 and 8.74 years, respectively.

Note 10 – Shareholders' Equity (Deficiency) (Cont.)

C. Stock-based compensation (Cont.)

As of December 31, 2014 and 2013, all of the outstanding and exercisable options are "in the money" with aggregate intrinsic value of $6.6 million and $115 thousand, respectively.

The unrecognized compensation expense calculated under the fair-value method for stock options expected to vest as of December 31, 2014 is approximately $1.9 million and is expected to be recognized over a weighted-average period of two years.

D. Warrants

During 2012, the Company granted an investor (the "Investor"), who is to assist the Company in creating business connections and opportunities; negotiating with third parties; and raising funds. For such services the Investor was granted 241,299 warrants to purchase ordinary shares of the Company with a par value of NIS 0.01. The warrants shall vest fully upon the occurrence of several performance conditions as set forth in the agreements signed by the parties. The exercise price would be $3.57. The warrants expired in May 2013.

Note 11 – Research and Development Expenses

	Year ended December 31,		
	2014	**2013**	**2012**
	(in thousands)		
Chemistry and formulation studies	$ 3,923	$ 2,081	$ 1,759
Salaries and benefits	573	–	–
Stock-based compensation	–	4,285	–
Research and preclinical studies	865	711	409
Clinical studies	1,148	128	171
Regulatory and other expenses	155	2	104
	$ 6,664	$ 7,207	$ 2,443

Note 12 – General and Administrative Expenses

	Year ended December 31,		
	2014	2013	2012
	(in thousands)		
Stock-based compensation	$ 601	$ 6,566	$ 208
Professional fees	625	496	1
Salaries and benefits	588	145	184
Traveling and conference costs	30	46	83
Rent and office-maintenance fees	284	46	38
Investor relations and business development	337	–	–
Other	13	56	67
	$ 2,478	$ 7,355	$ 694

Note 13 – Income Taxes

A. General

The Company is assessed for tax purposes on an unconsolidated basis. Each of the Company's subsidiaries is subject to the tax rules prevailing in its country of incorporation.

B. Corporate Taxation

Israeli subsidiary:

On July 30, 2013, the Knesset plenum approved, in a third reading, the budget bill and the bill to change the national priorities in 2013 and 2014 (the "Law"). In conjunction with this legislation there will be an increase of the corporate income-tax rate from January 1, 2014 to 26.5% (1.5% increase).

Maltese subsidiary:

Taxable income of Maltese companies is subject to tax at the rate of 35% in 2013 and 2014 ("Regular Tax Rate").

C. Net Operating Loss Carry forward

As of December 31, 2014, the Company had approximately $20.7 million net-operating-loss carry forwards, consisting of approximately $11.6 million of Maltese net-operating-loss carry forwards and approximately 9.1 million Israeli net-operating-loss carry forward. The Maltese and the Israeli loss carry forwards have no expiration date.

Note 13 – Income Taxes (Cont.)

D. 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 and its subsidiaries' assets are as follows

	As of December 31,	
	2014	2013
	(in thousands)	
Deferred tax assets		
Maltese subsidiary net-operating-loss carry forward	$ 4,058	$ 5,516
Israeli subsidiary net-operating-loss carry forward	2,381	–
Other reserves and allowances	107	115
Total deferred-tax assets	6,546	5,631
Valuation allowance	(6,546)	(5,631)
Net deferred-tax assets	$ –	$ –

Deferred-tax assets for carry forward losses in Malta and Israel are calculated using the applicable tax rate at the time of expected realization of the carry forward losses.

The Company has provided full valuation allowances in respect of deferred-tax assets. Management currently believes that it is more likely than not that those deferred taxes will not be realized in the foreseeable future.

D. Tax assessments

The Israeli subsidiary has received final tax assessments through the year ended December 31, 2010.

A reconciliation of the Company's effective tax expense to the Company's theoretical statutory tax benefit is as follows

Note 13 – Income Taxes (Cont.)

	Year ended December 31,		
	2014	**2013**	**2012**
	(in thousands)		
Loss before taxes on income, as reported in the consolidated statements of operations	$ 9,102	$ 17,484	$ 3,143
Statutory tax rate	26.5%	25%	25%
Theoretical tax benefit	2,412	4,371	786
Losses and other items for which a valuation allowance was provided or benefit from loss carry forwards	(2,412)	(4,371)	(786)
Other	1	1	6
Actual tax expense	$ 1	$ 1	$ 6

ITEM 19. Exhibits.

Exhibit No.	Description
1.1	Form of Amended and Restated Articles of Association of Galmed Pharmaceuticals Ltd. (English Translation) (1)
2.1	Specimen share certificate (1)
4.1	Registration and Information Rights Agreement, dated December 2013, by and among Galmed Pharmaceuticals Ltd., Shirat HaChaim Ltd., David & Debora Goldfarb, Medgal S.A. and G. Yarom Medical Research Ltd. (2)
4.2	Form of Indemnification Agreement (1)
4.3	Galmed Pharmaceuticals Ltd. 2013 Incentive Share Option Plan (2)
4.4	Agreement, dated 2002, by and between Galmed International Limited and Aventis Pharm Deutschland GmbH (2)
4.5	Personal Employment Agreement, dated December 23, 2013, by and between Galmed Medical Research Ltd. and Allen Baharaff (2)
4.6	Personal Employment Agreement, dated December 23, 2013, by and between Galmed Medical Research Ltd. and Maya Halpern (2)
4.7	Confirmation & Release Letter, dated December 18, 2011, from Beatrice Gilat, Jacob Gilat, Roni Gilat-Baharaff, Michael Gilat and Allen Baharaff to Galmed Medical Research Ltd. (2)
4.8	Equipment Purchase Agreement, dated September 24, 2014, between Itamar Medical Ltd. and Galmed Research and Development Ltd.*
4.9	Development and Manufacturing Services Agreement, dated January 27, 2015, between Galmed Research and Development Ltd. and Perrigo API Ltd.*
4.10	Investigator Initiated Clinical Trial Agreement, dated February 8, 2015, between Galmed Research and Development Ltd. and the University of California, San Diego*
8.1	List of subsidiaries of Galmed Pharmaceuticals Ltd. (1)
11.1	Code of Business Conduct and Ethics of Galmed Pharmaceuticals Ltd.
12.1	Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

Exhibit No.	Description
12.2	Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a) as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
13.1	Certification of Chief Executive Officer and Chief Financial Officer pursuant to Exchange Act Rules 13a-14(b) and 15d-14(b) and 18 U.S.C. Section 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

_____

(1) Incorporated herein by reference to Amendment No. 1 to the Registration Statement on Form F-1 filed with the SEC on February 28, 2014.
(2) Incorporated herein by reference to the Registration Statement on Form F-1 filed with the SEC on February 6, 2014.
* Portions of this exhibit were omitted and have been filed separately with the Secretary of the Securities and Exchange Commission pursuant to the Registrant's application requesting confidential treatment under Rule 24b-2 of the Exchange Act.

SIGNATURES

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

GALMED PHARMACEUTICALS LTD.

By: /s/ Allen Baharaff
Allen Baharaff
President and Chief Executive Officer

Date: March 31, 2015

Exhibit 4.8

CERTAIN PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND ARE SUBJECT TO A CONFIDENTIAL TREATMENT REQUEST. COPIES OF THIS EXHIBIT CONTAINING THE OMITTED INFORMATION HAVE BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION. THE OMITTED PORTIONS OF THIS DOCUMENT ARE MARKED WITH A [***].

EQUIPMENT PURCHASE AGREEMENT

This EQUIPMENT PURCHASE AGREEMENT (the "**Agreement**"), effective as of September 24th , 2014 (the "**Effective Date**"), is made by and between ITAMAR-MEDICAL LTD., a company organized under the laws of the State of Israel, having a place of business at 9 Halamish St., Industrial Park, Caesarea 38900, Israel, ("**Itamar**" or the "**Company**"), and GALMED RESEARCH AND DEVELOPMENT LTD., a company organized under the laws of the State of Israel with offices at 8, Shaul Hamelech Blvd., Tel Aviv 64733, Tel-Aviv, Israel ("**Galmed**").

WITNESSETH

WHEREAS, the Company wishes to enable Galmed to purchase certain Products as defined herein, all under the terms and conditions set forth herein.

NOW, THEREFORE, for and in consideration of the covenants and conditions hereinafter set forth, it is agreed by and between the parties as follows:

1. Sale of Products. Subject to the provisions of this Agreement, the Company, will sell Products ("Products") and subject to receiving certain study data as agreed between the parties in advance, will provide certain support to Galmed with regard to the Products, as set forth in **Exhibit A** hereto.

2 . Sale Process; Delivery; Upon signing the agreement Itamar will ship the Products into a location provided by Galmed in advance, in the quantity, as specified in **Exhibit A**. Any time Galmed wishes to purchase additional Products, it shall issue a written Purchase Order ("PO") to the Company detailing the type and number of Products required and the location to which these products are requested to be shipped. Such notification shall be delivered to the Company at least 30 days prior to the desired date of shipment. The cost of such additionally ordered Products is specified in **Exhibit B**.

3 . Consideration; Payment Terms; The consideration for the sale of Products and the payment terms are set forth in **Exhibit A** hereto. All prices set forth in **Exhibit A** and **Exhibit B** are based on delivery ex works, Itamar's Caesarea, Israel facilities, as that term is defined in Incoterms 2010, ICC Rules for the Use of Domestic and International Trade Terms, ICC Publication No. 715EF (the "**Delivery Point**"). Galmed assumes all risks of loss or damage to the Products from any cause, as well as any fees or taxes incurred after delivery.

4. Terms of Use.

4.1 Galmed will make sure that the Products are maintained in good operating condition, and are serviced and repaired when necessary to keep the Products in good operating condition. All use and maintenance must be done according to the Company's requirements or recommendations as described in the Product's Operating Manual provided by the Company. All maintenance must also comply with any legal and/or regulatory requirements. Galmed shall pay all costs related to compliance with the provisions of this Section.

4.2 The Company has a right, upon prior notice coordinated with Galmed to inspect the Products and to ensure compliance with the terms hereof.

4.3 The Products will not be altered, tampered with or modified without the Company's prior written consent.

5. All proprietary and sensitive information, disclosed by or on behalf of Galmed to the Company including any of the Company's representatives or learned by the Company and/or its representatives in connection with and in the course of performing of this Agreement, regardless of form, and any proprietary and sensitive information generated or resulting from the use of the Product ("Galmed's Confidential Information"), shall be treated as confidential both during the term of the Agreement and following its termination for a period of five (5) years. During such time period, the Company undertakes to maintain Galmed's Confidential Information in confidence and to use all reasonable efforts to ensure that its representatives maintain Galmed's Confidential Information in confidence, except as otherwise provided in this Agreement. The foregoing restrictions shall not apply to Galmed's Confidential Information which is, or becomes part of the public domain through no act or omission of the Company and/or was lawfully obtained by the Company from another source. The Company shall be liable for any breach of this section by any of its personnel, including by its representatives. Also, the Company shall not publicize the results of any non-public data derived from Galmed's "ARAMCHOL005 study" and "ARAMCHOL007 study" without Galmed's prior consent.

6. Warranty; Defects; Limitation of Liability.

6.1 EXCEPT AS SET FORTH IN THIS SECTION 6, THE COMPANY MAKES NO WARRANTIES OF ANY KIND HEREUNDER, WHETHER EXPRESS, IMPLIED OR ARISING FROM TRADE USAGE, CONTRACT, TORT OR OTHERWISE, INCLUDING ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

IN NO EVENT SHALL THE COMPANY BE LIABLE FOR SPECIAL, INDIRECT OR CONSEQUENTIAL DAMAGES OR LOST PROFITS OR REVENUES ARISING OUT OF THIS AGREEMENT OR IN CONNECTION WITH THE USE OR PERFORMANCE OF, OR RESULTS OBTAINED OR NOT OBTAINED FROM THE USE OF THE PRODUCTS, BY GALMED, HOSPITALS, OR OTHERWISE.

6.2 Subject to 4.1, 4.2, 4.3, 11, the Company hereby warrants to Galmed that: (1) each Product to be delivered hereunder will be free of defects in material and workmanship under normal use and service for a period of twenty seven months from the date of delivery (the "Warranty Period").

6.3 If, during the Warranty Period, a Product or any component of the Products becomes defective by reason of material or workmanship, and provided that Galmed immediately notifies the Company, the Company will as an option immediately repair the defect on site or supply a replacement which will be shipped within 48 hours and request the return of defective equipment to Company's premises for repair in accordance with Company's warranty and repair procedures.

6.4 The site coordinator in each site will receive the product in every site and check the Product for defects and whether the Product arrived in whole and will immediately notify Galmed and the Company if errors occurred and/or defected Products were identified. The Company's staff trainer shall then also check the Products for defects and whether the Product arrived in satisfactory condition and shall immediately notify Galmed and the Company if errors occurred and/or defected were identified.

6.5 The parties shall share the cost of shipping replacements and returning defected products.

6.6 This warranty shall not apply to any Products or component parts, that (a) have been damaged by improper operation, tampering with, improper maintenance, misuse, accident, or neglect, or were subject to any prohibited activities; (b) have been used in a manner not in accordance with the instructions supplied by the Company; (c) have had changes or repairs made without written authorization of the Company to do so; (d) were incorporated into another product without the prior written approval of the Company; or (e) were stored in conditions and/or for a period of time contrary to the guidelines of the Company which proves to be inadequate or unreasonable.

7. All rights and title to and/or interests in the results derived from using the Products by Galmed in the "ARAMCHOL005 and ARAMCHOL007 studies" are and shall be owned by and are and will be the exclusive property of Galmed, and shall be deemed the confidential information of Galmed.

8 . Indemnification. Galmed agrees to indemnify the Company and hold it harmless from and against any and all liability, fines, suits, claims, demands, actions, costs and expenses of any kind that arise or be claimed against the Company by any person as a result of an act of negligence or omission to use the Products by Galmed, its employees and service providers, including, but not limited to its obligations under Section 4 above, except for such damages or losses resulting from the use of the Products conducted in accordance with section 4 above.

9 . Default. If Galmed is in default on any provision of the terms of this Agreement, all of Galmed's payment obligations to the Company shall immediately become due and payable, and the Company may, without notice, decline to make further shipments, deliveries or terminate Galmed's outstanding POs, without affecting any other right or remedy the Company may have, including, but not limited to, any right to cancellation charges. For purposes of this Agreement, a "default" shall occur in the event that Galmed is more than five (5) days delinquent in any payment to the Company, becomes insolvent, is adjudicated bankrupt, petitions for or consents to any relief under any bankruptcy reorganization statutes, has a receiver appointed or makes an assignment for the benefit of creditors, or is otherwise unable to meet its financial obligations as they become due. Continued shipment by the Company following Galmed's default shall not constitute a waiver nor shall it affect Galmed's legal obligations hereunder.

10. Term and Termination of this Agreement.

10.1 This Agreement enters into effect on the Effective Date and shall remain in effect until the earliest of (i) the completion of Galmed's phase IIb clinical trial entitled ARAMCHOL005 and Galmed's receiving all final Core Lab reports from the Company and the Company receiving all data agreed between the parties in advance (ii) occurrence of termination by either party in an event of a breach of a material provision hereof that has not been remedied during a period of 14 days after the delivery of a notice thereof by the non-breaching party to the party in breach.

10.2 In any event of termination of this Agreement, except for event of a material breach by Galmed, the relevant provision of Section 3, 4, 5, 6, 8, 9, 10 and 12 of this Agreement shall remain in effect with respect to Products at such time.

1 1 . Assignment. Without the prior written consent of the Company, Galmed shall not (1) assign, transfer, pledge or hypothecate this agreement, or any part thereof, or any interest therein except to a successor in case of a merger, acquisition or as part of a transaction transferring all or substantially all the business or assets of Galmed or (2) sublet or lend the Products or permit them to be used by anyone other than Galmed, Galmed's employees and any of Galmed's agents conducting clinical studies.

12. Disclosure. Neither Party shall disclose, publicize or advertise in any manner the discussions or negotiations contemplated by the Agreement without the prior written consent of the other Party, except as may be required by law.

13. Governing Law; Disputes. This Agreement shall be governed by and construed in accordance with the laws of Israel. The competent courts and tribunals situated in Tel Aviv, Israel shall have sole and exclusive jurisdiction in any dispute or controversy arising out of or relating to this Agreement.

14. This Agreement is not intended by the parties to constitute or create a joint venture, pooling arrangement, partnership, agency, employer-employee relationship or a formal business organization of any kind.

15. Publication. The Company shall not publicize the data shared with the Company and results of any non-public data derived from Galmed's ARAMCHOL005 study and ARAMCHOL007 study without prior consent of Galmed.

16. This Agreement, together with the Exhibit(s), sets forth the entire agreement between the parties on the subject hereof and supersedes any previous agreement, understanding, memorandum, letter of intent or representation on the subject matter hereof. This Agreement may be amended only by written agreement signed by the duly empowered representatives of both parties.

17. Insurance. The Company warrants that it maintains, at its sole cost and expense, an adequate policies of general liability insurance in amounts of $1 million per occurrence and $2 million in the annual aggregate to insure its obligations hereunder.

IN WITNESS WHEREOF, each of the parties has caused this Agreement by a duly authorized representative on the dates entered herein below.

ITAMAR-MEDICAL LTD.		GALMED RESEARCH AND DEVELOPMENT LTD.
By:	/s/ Gilad Glick	By: /s/ Allen Baharaff
Name:	**Gilad Glick**	Name: Allen Baharaff
Title:	**CEO**	Title: CEO
Date:	24 November 2014	Date: 24 Sept 2014
By:	/s/ Shaul Sharoni	
Name:	**Shaul Sharoni**	
Title:	**CFO**	
Date:	24 November 2014	

EXHIBIT A
PRODUCTS AND PRICES

I. The Company's Product:

The Product includes:

1. EndoPAT kit composed of
   - EndoPAT device
   - Two hand supports
   - High pressure occluding cuff
   - Manometer
2. Preconfigured laptop with the EndoPAT software
3. A box of single-use EndoPAT probes includes 6 (Six) pairs of single use probes in the box – *one pair is required per test*
4. An envelope with the necessary equipment certificates and list of contents that are necessary for shipment (the "Shipment Documents")

In consideration for and subject to providing EndoPAT test results and study demographics to the Company that shall be used for internal purposes only, Galmed will be granted the following support at no additional cost:

1. A project manager will be assigned to the study at the Company and will serve as a focal point for the participating sites and Galmed.
2. The Company's representative's participation in and presenting at investigator's meetings will involve reimbursement of *travel costs only as pre-approved by Galmed*.
3. A hotline with a toll-free number for technical support will be provided to each participating study site at any reasonable time.
4. An on-site installation and staff training by the Company's experts for each participating site.
5. A core lab for the EndoPAT testing that includes:
   a. EndoPAT data analysis (test result) and test quality score (good, fair, inadequate) for each test.
   b. Fast feedback to sites on the first recordings of the study, to minimize the learning curve and prevent any sub-optimal performance entering the study.
   c. The Company shall submit a final Core Lab written report to Galmed, summarizing its data, findings and the results of deriving from the use of the Products in connection with Galmed's ARAMCHOL005 study and ARAMCHOL007 study, as well as a detailed interpretation of such data ("Core Lab Report"), within 30 days after data lock up of each study.

II. Quantity of Products to be provided by the Company to Galmed:

1. Sixty (60) EndoPAT devices including 60 envelops of Shipment Documents.
2. Sixty (60) Preconfigured laptop with the EndoPAT software
3. One hundred thirty two (132) boxes of single use EndoPAT probes

III. Total Cost to be paid by Galmed: A total cost of 750,000 USD, not including taxes, for the Products in Item II referenced above, provided that the agreement is signed and all Products specified in Item II above are shipped to Galmed by September 29th, 2014.

I. **Terms of payment:** Payment of the total cost referenced in Item II, including taxes shall be paid in full no later than December 30th, 2014.

EXHIBIT B

COST LIST FOR ADDITIONAL PRODUCTS THAT MAY BE PURCHASED BY GALMED UNDER THE TERMS OF THIS AGREEMENT

1. Additional EndoPAT device(s), each at [***] USD (a [***]% discount will be applied if the terms of the first order as specified in **EXHIBIT A** have been met).
2. Preconfigured laptop with the EndoPAT software at [***] USD (a [***]% discount will be applied if the terms of the first order as specified in **EXHIBIT A** have been met).
3. Box of 6 pairs of single use EndoPAT probes at [***] USD (a [***]% discount will be applied if the terms of the first order as specified in **EXHIBIT A** have been met).

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Exhibit 4.9

CERTAIN PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND ARE SUBJECT TO A CONFIDENTIAL TREATMENT REQUEST. COPIES OF THIS EXHIBIT CONTAINING THE OMITTED INFORMATION HAVE BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION. THE OMITTED PORTIONS OF THIS DOCUMENT ARE MARKED WITH A [***].

Development and Manufacturing Services Agreement

This Development and Manufacturing Services Agreement (the "**Agreement**") is made and entered into as of January 26, 2015 (the "**Effective Date**") by and between Perrigo API Ltd., an Israeli company, having its principal offices at 29 Lehi Street, Bnei Brak 51200, Israel ("**Perrigo**"), Galmed Research and Development Ltd. an Israeli company having its principal offices at 8, Shaul Ha'Melech Blvd., Tel Aviv 6473307, Israel ("**Galmed**"). The parties identified above are sometimes hereinafter individually referred to as a "**Party**" and collectively as the "**Parties**".

WHEREAS, Perrigo is in the business of development, production and marketing of various active pharmaceutical ingredients and finished dose formulation products and owns facilities for GMP manufacture of active pharmaceutical ingredients located at Neot Hovav, Israel ("**Perrigo's Facility**"); and

WHEREAS, Galmed is in the process of developing a novel final dosage pharmaceutical product for the treatment of Non Alcoholic Fatty Liver disorders, including Non-Alcoholic Steato-Hepatitis, named Aramchol (the "**Product**"), which is currently in clinical trials Phase IIb; and

WHEREAS, the active pharmaceutical ingredient contained in the Product (the "**API**") is currently manufactured for Galmed by Cambridge Major Laboratories Netherlands ("**CML**") in accordance with a manufacturing process that was developed by CML for Galmed and is owned by Galmed (the "**Manufacturing Process**") as generally defined in the Route Of Synthesis attached hereto as **Annex A** ; and

WHEREAS, Galmed and Perrigo wish to set forth the terms with respect to technology transfer, improvement of the Manufacturing Process and scale up to commercial scale of the API as set forth herein (hereinafter the "**Project**"); and

WHEREAS, the Parties wish to negotiate a definitive exclusive manufacturing and supply agreement, all as further detailed below;

Now Therefore, in consideration for the mutual covenants set forth herein and other good and valuable consideration, the receipt of which is hereby acknowledged, the Parties agree as follows.

1. Definitions

For the purpose of this Agreement, the terms set forth below will have the meaning given below.

"Affiliate" shall mean, with respect to any party hereto, any person, organization or entity directly or indirectly controlling, controlled by or under common control with, such party. For purposes of this definition only, "control" of another person, organization or entity shall mean the ability, directly or indirectly, to direct the activities of the relevant entity, and shall include, without limitation (i) ownership or direct or indirect control of fifty percent (50%) or more of the outstanding voting stock or other ownership interest of the other organization or entity, or (ii) possession of, or the power to elect or appoint fifty percent (50%) or more of the members of the governing body of the organization or other entity.

"Batch" means a batch of the API produced during the same cycle of manufacture.

"**Batch Record**" means the detailed production instructions for manufacture, production and control of a Batch, including documenting each step in the manufacture, processing, packing and labeling of the API, produced in accordance with GMP.

"Change of Control" means (i) consolidation or merger of a party or its ultimate parent company with or into any other company, or any other entity or person; (ii) corporate reorganization in which a party shall not be the continuing or surviving entity of such reorganization; (iii) sale, license or lease of all or substantially all of a party's assets; (iv) transaction or a series of related transactions in which a person or entity acquires more than fifty percent (50%) of the issued and outstanding shares, or fifty percent (50%) or more of the outstanding voting power of a party (treating any convertible preferred shares on an as-converted to ordinary share basis); (v) transaction or a series of related transactions in which a person or entity or "group," as such term is defined and interpreted under Rule 13d-5 of the U.S. Securities Exchange Act of 1934, as amended, acquires the right to control the appointment or the voting for the election of more than fifty percent (50%) of the directors of a party.

"**Confidential Information**" means any information and materials disclosed by a Party or an Affiliate of such Party or otherwise on its behalf (the "**Discloser**") to the other Party or its Affiliate(s) (the "**Recipient**"), regarding, without limitation, the technology, intellectual property, know-how, business, operations facilities and other affairs of the Discloser or affiliates thereof, whether disclosed in oral, written, electronic, visual or any other form, which information includes, but is not limited to: any information relating to or concerning the API or the Product, the processes and methods employed in the manufacture of API or the Product; Batch Records, Specifications; information related to Perrigo's Facilities or the CML facility; information related to manufacturing processes and/or technologies or to any products produced at Perrigo Facility or the CML facility; API Information; any prices and costs of the Parties; regulatory filings for the API or the Product; the Parties' business, regulatory plans and strategies, patent disclosures, patent applications, structures, models, techniques, formulas, processes, compositions, compounds, apparatus, designs sketches, photographs, plans, drawings, specifications, samples, reports, customer lists, price lists, studies, findings, inventions and other data and information disclosed or exchanged under this Agreement.

"**GMP**" shall mean all applicable good manufacturing practices as established by the respective Regulatory Authorities, as applicable for investigational new drugs in clinical phase III trials, including as established by the USFDA and EU-EMA (Investigational Medicinal Product) and as also adjusted as and in case required by the Regulatory Authorities in Colombia, Brazil, Peru, Chile and Mexico, as per their applicable guidelines for investigational new drugs in clinical phase III trials supplied by Galmed prior to the execution of this Agreement.

"**Intellectual Property**" means all patents and other patent rights, trade secrets, trademarks, service marks, registered designs, applications for any of the foregoing, trade and business names, unregistered trademarks and service marks, copyrights, rights in designs, inventions, developments, know-how, discoveries, improvements, methods, processes, techniques, specifications, models, procedures, rights under licenses, and rights of the same or similar effect or nature, in any part of the world, whether or not registered, published or unpublished, and registrations and applications for registration thereof, and all rights therein whether provided by international treaties or conventions or otherwise.

"**Invention**" means any concept, discovery, development, improvement, formula, process, composition of matter, formulation, method of use or delivery, specification, computer program or model (whether patentable or not) and any related and/or supporting documentation and data.

"**API Information**" all information and data relating to the API, including but not limited to formulae, methods of manufacture, product descriptions, test methods, validation of test methods, specifications, and all other supporting documentation, data and reports provided by Galmed to Perrigo, or developed or acquired by Perrigo or any of its affiliates during the term of this Agreement in connection with the manufacture and supply of API, including the information regarding the Process Stabilization the information regarding Scale Up, the Results and the Reports, as well as all applications, submissions, filings and correspondence of Galmed with or to FDA or any other governmental or Regulatory Authority with respect to the API.

"**Specifications**" means the specifications and technical characteristics of the API provided by Galmed as detailed in **Annex B,** as may be updated by Galmed from time to time in writing as set forth in Section 7A.1 below.

"**Regulatory Authority**" means any governmental authority (whether Federal, State, municipal or other), regulating the development, clinical testing , manufacture, packaging, labeling, storage, import, export, distribution, marketing, sale and/or intended use of the API in the United States (USFDA), the European Union (EMA) (and each of its respective member states), Colombia, Brazil, Peru, Chile and Mexico and any other additional country, as will be agreed upon by the Parties in writing.

"Qualified Person (**QP**)" pursuant to European Union pharmaceutical regulation (Directive 2001/83/EC for Medicinal products for human use), or pursuant to equivalent regulations by other Regulatory Authorities.

2. Scope and Purpose of this Agreement

2.1 This Agreement sets forth the terms upon which Perrigo will provide Galmed with services concerning the Project. For that purpose, the Parties agree that: (i) Galmed will transfer to Perrigo the documents, information, materials and know-how necessary to provide the services contemplated under this Agreement and establish the Manufacturing Process at Perrigo's Facility (the "**Technology Transfer**"); (ii) Perrigo will perform for Galmed certain laboratory studies for gap closing and stabilization of the current Manufacturing Process (the "**Process Stabilization"**), (iii) Perrigo will manufacture and supply 60kg GMP of the API at Perrigo's Facility (the "**Tech Transfer Batches** "); (iv) Perrigo will perform for Galmed additional laboratory studies for further improving and optimizing the Manufacturing Process the "**Process Improvement**"); and (v) Perrigo will scale up the Manufacturing Process to commercial scale, and manufacture and supply 900kg GMP of the API at Perrigo's Facility (the "**Scale Up Batches**"); all as more fully detailed below. Each of the foregoing shall be deemed a "stage" of the Project. For the avoidance of doubt, it is clarified that the Tech Transfer Batches and Scale Up Batches shall be, as per the Route of Synthesis detailed in **Annex A,** manufactured in Perrigo's Facility in Neot Hovav.

2.2 Subject to each Parties' performance of its obligation hereunder, and except as otherwise specifically agreed in this Agreement, the Parties agree to negotiate an exclusive commercial contract manufacturing and supply agreement for a minimum term of five years of commercial supply (the "**Supply Agreement**"), pursuant to which Perrigo will also provide further services to validate the Manufacturing Process and compile a DMF and will be assigned as Galmed's exclusive manufacturer and supplier of the API, as further set forth in Section 9 below. The supply of the API shall be made from Perrigo's Facility in Neot Hovav. Perrigo's Facility in India may be added as an additional manufacturing site as may be agreed upon in writing by the Parties and subject to a QP audit on behalf of Galmed, and subject to Galmed's agreement, at its sole discretion, which will not be unreasonably delayed or withheld. The foregoing undertaking is subject to the parties agreeing on the terms of the Supply Agreement, including, without limitation, the consideration and terms of supply.

2.3 Perrigo undertakes during the term of this Agreement and the Supply Agreement, not to directly or indirectly develop, manufacture or sell the API, except for Galmed. In addition, Perrigo shall not, during the term of this Agreement, provide any contract development and manufacturing services to any third party with respect to any cholic acid derivative investigational new drug.

3. Technology Transfer

3.1 To the extent not already provided to Perrigo at the date of this Agreement, Galmed will transfer to Perrigo (or shall cause CML to provide to Perrigo, as applicable) the documents, information, materials and know-how necessary to provide the services contemplated under this Agreement and establish the Manufacturing Process at Perrigo's Facility. The steps to be undertaken and their required time frames are set forth in a technology transfer protocol attached at **Annex C** (the "**Technology Transfer Protocol**").

3.2 Galmed acknowledges and agrees that the timely and complete transfer of the Galmed and/or CML deliverables under the Technology Transfer Protocol are essential for the timely start, performance and completion of the activities contemplated for the Technology Transfer and the Project. Any delay in the timeframes set forth in the Technology Transfer Protocol caused by Galmed or any third party on its behalf shall, to the extent reasonably possible and subject to Perrigo's production schedule, push forward the timeframes of the Project in the least amount of days. To the extent of any such delay, Perrigo undertakes to notify Galmed of such delay promptly upon its occurrence.

3.3 It is noted that Perrigo has already sent a qualified process engineer to CML's facility in the Netherlands for the purpose of observing the Manufacturing Process at CML's facility. Galmed will reimburse Perrigo for the travel and accommodation expenses of these two visits at actual cost, which is NIS 15,950 (Including VAT). In the event that Perrigo determines that an additional visit is required in order to observe additional critical aspects of the manufacturing cycle, Galmed will bear the additional travel and accommodation expenses of Perrigo's process engineer for such additional period, provided that these are reasonable and have been approved in advance by Galmed.

4. Process Stabilization

4.1 Perrigo will perform certain laboratory services with respect to the Process Stabilization in the scope defined and set forth in **Annex D** (the "**Process Stabilization Scope**") and, subject to the performance of Galmed's obligations detailed in Section 4.2 hereunder, in the timeframes set forth therein in **Annex D**. The Process Stabilization Scope will, subject to the provisions herein, be completed by April 30, 2015. Perrigo will perform the Process Stabilization Scope in a professional, timely and diligent manner, in accordance with the specifications set forth in the Process Stabilization Scope and the representations set forth in Section 12. For removal of doubt, without derogating from Perrigo's undertaking to perform its obligations set forth in **Annex D**, it is noted that Perrigo cannot warrant or guarantee the outcome of the Process Stabilization.

4.2 For Perrigo to perform the Process Stabilization, Galmed shall provide Perrigo with the necessary support, as detailed in the Process Stabilization Scope. Galmed's initial contact person for this shall be Dr. Mizhiritskii Michael, Galmed's CMC consultant, who may be replaced by Galmed from time to time by a written notice to be sent to Perrigo ("**Galmed's Consultant**").

4.3 Following the completion of the Process Stabilization, Perrigo will, in consultation with Galmed, prepare Batch Records for the implementation of the Manufacturing Process at Perrigo's Facility in Neot Hovav based on the existing batch records developed by CML and the outcome of the Process Stabilization Scope. In the framework of the preparation of the Batch Records as aforesaid, Galmed will request from CML to send a process engineer to Perrigo's Facility in Neot Hovav to assist with the preparation of the Batch Record, and Galmed will bear the costs and expenses of such visit, it being clarified that Galmed cannot guaranty that CML will agree to such visit. Galmed will approve and sign the Batch Records prior to manufacture of the Tech Transfer Batches by Perrigo as contemplated in Section 5.

5. Tech Transfer Batches

5.1 Following the completion of the transfer of the Manufacturing Process to Perrigo in accordance with the Technology Transfer Protocol and the completion of the Process Stabilization, Galmed shall purchase and Perrigo shall manufacture and deliver the Tech Transfer Batches to Galmed (60kg of the API) for the consideration set forth in Section 11.1.2, which will be manufactured in accordance with the Specifications and as further set forth in Section 12. The Tech Transfer Batches shall be used by Galmed only for conducting clinical trials for the Product and shall not be used otherwise for any commercial purpose or sale of the Product.

5.2 The Tech Transfer Batches shall be delivered by September 30, 2015. Delivery terms of the Tech Transfer Batches shall be according to Incoterms 2010 EXW ("ex works") Perrigo's Facility Neot Hovav, Israel.
Any delay in the timeframes of the Technology Transfer or the Process Stabilization Scope caused by Galmed shall, to the extent reasonably possible and subject to Perrigo's production schedule, push forward the timeframes of the Project in the least amount of days. To the extent of any such delay, Perrigo undertakes to notify Galmed of such delay promptly upon its occurrence.

As Perrigo intends to commence with the process of manufacturing the Tech Transfer Batches immediately following the execution of this Agreement, it is agreed that, except in the event of breach of this Agreement by Perrigo, Galmed shall be obliged to purchase the Tech Transfer Batches.

5.3 Galmed's Consultant shall be reasonably available, during normal business hours, during the production of the Tech Transfer Batches, to provide support to the critical production stages, either via phone, or to the extent Perrigo, in consultation with Galmed, shall deem necessary and in coordination with Galmed's Consultant, by being present at Perrigo's Facility (in Israel).

5.4 For the purpose of Section 5.3 above, it is clarified that Galmed cannot guaranty the cooperation of CML in the performance of its obligations under this Agreement, and any non-compliance and/or non-performance on part of CML under this Agreement shall not constitute a breach of this Agreement by Galmed. Galmed understands and acknowledges, however, that any such lack of cooperation by CML may cause delays in the timelines of the Project and any delay or inability to perform any of Perrigo's obligations due to such lack of cooperation shall not constitute a breach of this Agreement by Perrigo, provided that Perrigo undertakes to notify Galmed of such delay promptly upon its occurrence.

6. Process Improvement

Following the manufacture of the Tech Transfer Batches, Perrigo will perform certain laboratory services for the improvement and optimization of the Manufacturing Process in the scope defined and set forth in **Annex E** (the "**Process Improvement Scope**") and in the timeframes set forth therein. The Process Improvement Scope will be completed by March 31, 2016 (subject to delays caused solely by Galmed or any third party on its behalf, which will, to the extent reasonably possible and subject to Perrigo's production schedule, delay the aforementioned date in the least amount of days). Perrigo will perform the Process Improvement Scope in a timely, professional and diligent manner, however, for removal of doubt, it is noted that Perrigo cannot warrant or guarantee the successful outcome of the Process Improvement Scope.
During the Process Improvement Scope period, upon Galmed's request Perrigo shall keep Galmed informed of the progress of the Process Improvement (by way of an update by phone every two weeks, and monthly report, and a final report), and shall provide Galmed with all information it reasonably requests from time to time in connection therewith. In the final report with respect to the Process Improvement Scope, Perrigo shall put into writing all the information regarding the Process Improvement Scope as detailed in **Annex E**, including a detailed report on how the manufacturing process was made more efficient, the steps that were taken, a list of the suppliers, a list of other outsourced contractors, copies of lab reports, lab notebooks and logs, as well as any other information related to the Process Improvement Scope reasonably requested by Galmed.

Within a week following the completion of the Process Improvement, and prior to the manufacture by Perrigo of the Scale-Up Batches, Perrigo shall provide Galmed with a sample of the API produced, in order for Galmed to test such samples and confirm that it complies with the Specifications. Galmed shall test such samples and provide Perrigo with its written input within thirty (30) days from the receipt thereof.

7. Scale-Up Batches

7.1 Following the completion of the Process Improvement (whether successful or not), Galmed shall purchase and Perrigo shall manufacture and deliver the Scale-Up Batches (900 kg GMP of the API) from Perrigo, for the consideration set forth in Section 11.1.4, which will be manufactured in accordance with the Specifications and with the representations set forth in Section 12. The Scale-Up Batches shall be used by Galmed only for the purpose of conducting clinical trials for the Product and shall not be used otherwise for any commercial purpose or sale of the Product.

7.2 The first half of the Scale-Up Batches (450kg GMP) shall be delivered by June 30, 2016. The Second half of the Scale-Up Batches (450kg GMP) shall be delivered by August 15, 2016 (subject to delays caused solely by Galmed or any third party on its behalf, which, to the extent reasonably possible and subject to Perrigo's production schedule, will delay the aforementioned date in the least amount of days).

7.3 Delivery terms of the Scale-Up Batched shall be according to Incoterms 2010 EXW (“ex works”) Perrigo's Facility Neot Hovav, Israel.

7A. Additional Provisions and Regulatory Matters

With respect to the Tech Transfer Batches, the Scale-Up Batches and any other API manufactured by Perrigo under this Agreement, the following shall apply:

7A.1 The Specifications may be updated by Galmed from time to time due to regulatory changes or otherwise, by providing Perrigo with written notice and the updated Specifications. In such event, Perrigo shall notify Galmed within fourteen (14) days the estimated consequences of such changes, and whether or not such changes result in an increase to the timeframe or costs; in the event that such change results in an increase to the timeframe or costs, the parties shall discuss such change to timeframes or costs within five (5) days of receipt of Perrigo's reply as aforesaid. In the event that the Parties agree on a change to the Specifications as aforesaid, then **Annex B** shall be revised accordingly.

7A.2 During the Project, Perrigo shall send Galmed monthly written reports detailing the progress of the current stage of the Project, and the achievements to date (the "**Report**"). Said Report shall be in a format that is mutually acceptable to the Parties, and may include additional information reasonably requested by Galmed. Following the completion of each stage of the Project, Perrigo will provide Galmed with a written final report, setting forth in detail all the information regarding such stage. Without derogating from the above, to the extent that Galmed shall request to be informed of specific events relating to the progress of the Project, Perrigo shall provide Galmed with all material information it requests from time to time in connection therewith.

7A.3 Perrigo shall be responsible for testing the APIs in accordance with the protocols and test methods provided by Galmed or developed by Perrigo (and approved in writing by Galmed) during the Project for testing the API that Perrigo manufactures under this Agreement. Perrigo shall promptly inform Galmed of any deviations from the Specifications following such test methods and protocols. In addition, Perrigo shall provide Galmed with the results of such testing promptly upon their occurrence. Perrigo will also be responsible to ensure that each API Batch is appropriately labeled and traceable.

7A.4 Perrigo will deliver to Galmed one copy of the Batch Records with respect to each Batch of API manufactured and delivered to Galmed pursuant to this Agreement. Perrigo represents and warrants that all Batch Records and other documentation furnished to Galmed under this Agreement concerning the manufacture of the API will be accurate and complete. If Galmed requires supplemental documents from Perrigo in order to obtain or in connection with any Regulatory Authority approvals, Perrigo agrees to cooperate with Galmed and to make available to Galmed such additional or supplemental documentation in its possession as may reasonably be requested by Galmed. If further work is required from Perrigo with respect to the above, the Parties shall discuss in good faith the consideration that Perrigo will receive for performance of such additional work, provided that such consideration will be agreed in advance and in writing. Perrigo will retain originals of all Batch Records, any and all other records or documentation generated by it in connection with the manufacturing and testing of API under the terms of this Agreement.

7A.5 Regulatory Inspections. Perrigo agrees to notify Galmed promptly of any inspections by the FDA or other Regulatory Authorities which pertain to the API or the Perrigo Facility where the API is manufactured, and shall promptly and within seven (7) days of their receipt/sending provide to Galmed copies of all material reports, observations, notices, findings and replies to such findings and other material pertinent to such inspections all as may be relevant to the API. Perrigo shall have the right to redact from any such copies only such segments that do not relate in any manner to API and do not affect Perrigo's performance under this Agreement. Perrigo will allow, and will provide Galmed with any required authorization to allow, the FDA or any other Regulatory Authority to inspect, audit and review the facilities at which the APIs are manufactured and all procedures, practices, books, records, and documents to the extent requested by the FDA and any other Regulatory Authority relating to the API. Perrigo will permit Galmed representatives (subject to signing a confidentiality and non-use agreement) to be present during such inspections.

7A.6 Access to Perrigo's Facility. Galmed (or any party on Galmed's behalf) shall have the right, once every 36 months, or upon the occurrence of an event that Galmed determines requires inspection (such as adverse drug event, product complaint or other event that requires inspection in the course of Galmed's clinical trials), or as required by the drug manufacturer of the Product to conduct a QP audit (subject to such drug manufacturer signing of a standard confidentiality and non- use agreement), upon reasonable notice to Perrigo and during normal business hours, to audit Perrigo's Facilities for the API (to ensure that the APIs are being manufactured, packaged and stored in compliance with the Specifications, and all applicable laws and regulations, including without limitation, GMP and Galmed's quality and other standards). During such audits, Perrigo shall permit Galmed to contact and question the appropriate knowledgeable personnel of Perrigo. Perrigo will cooperate with Galmed with respect to a request to audit any Perrigo third party supplier or subcontractor involved in the manufacture and/or supply of the API ("**Perrigo's Suppliers**") responsible for manufacturing, packaging and storing the API. Perrigo shall make available to Galmed and its duly authorized representatives and agents (subject to the signing of a confidentiality and non-use agreement) all its and, subject to their approval, Perrigo's Suppliers' books, records and documents which in any way pertain to the manufacture or quality control, testing and compliance procedures of the API. It is clarified for the avoidance of doubt, that any audit as aforesaid shall not derogate in any manner from Perrigo's responsibility hereunder.

7A.7 Record Retention. Perrigo will retain originals of all Batch Records, financial records and all other records or documentation generated by it in connection with the processing and testing of API under the terms of this Agreement, and all records which are necessary in the event of a product recall or adverse drug event or product complaint, for not less than seven (7) years after the expiration date of the API to which the documentation relates and, if longer, such period as is required by applicable law.

8. API Acceptance

8.1 Galmed shall have the right to return any shipment to Perrigo, at Perrigo's expense, for visually detectable defects within thirty (30) days of receiving the API, or if Galmed determines that the API does not conform to the Specifications by testing and inspection in accordance with industry standards, within the earlier of fourteen (14) days following the completion of testing of the API by Galmed (or by the QP of Galmed's drug manufacturer) or three (3) months of delivery of the API.

8.2 Any disputes between the Parties as to whether all or any part of a shipment rejected by Galmed conforms to the API Specifications shall be first resolved between the Parties, which shall cooperate to mutually investigate the route-cause for the discrepancy in the analytical results (for example: repeating the analytical tests of the original sample, resampling and repeat the analytical tests, replace analytical instrument, the analyst performing the tests, and any other measures as will be decided between the Parties). If the Parties are unable to agree as to whether a rejected shipment conforms to the Specifications the dispute shall be finally resolved by a mutually acceptable third party independent expert (the "**Expert**"), who, if required according to said expert's discretion, may engage a third party analytical laboratory, which shall be referred to within fourteen (14) days of the Parties establishing the dispute. The determination of the said Expert shall be binding on the Parties, and all the expenses related to such testing and shipment, if required, will be borne by the Party at fault. In the event that the shipment was justifiably rejected, Galmed shall return the rejected shipment to Perrigo, which shall replace the rejected shipment (either by reprocessing or manufacturing of additional material). In the event that the Expert shall determine that the rejected shipment was unjustifiably rejected, Galmed shall [covered in one before previous sentence] pay for such shipment.

Galmed shall have the right to request Perrigo to reprocess/replace the API which is disputed prior to receiving the determination of the Expert. In that event, Galmed shall return the disputed shipment to Perrigo, and Perrigo will reprocess/replace the API and the costs of such reprocessed/replaced API shall be borne by the Party at fault according to the determination of the Expert.

CERTAIN PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND ARE SUBJECT TO A CONFIDENTIAL TREATMENT REQUEST. COPIES OF THIS EXHIBIT CONTAINING THE OMITTED INFORMATION HAVE BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION. THE OMITTED PORTIONS OF THIS DOCUMENT ARE MARKED WITH A [***].

9. Supply Agreement

9.1 As mentioned above, the Parties wish to negotiate a Supply Agreement, pursuant to which Perrigo will also provide further services to validate the Manufacturing Process and compile a DMF and will be assigned as Galmed's exclusive manufacturer and supplier of the API, subject to (i) the successful completion of Clinical Phases II and III of the Project and obtaining a marketing authorization for the marketing of the Product by a Regulatory Authority and (ii) agreement between the Parties on the terms of the Supply Agreement, as set forth in Section 9.2 below.

9.2 The fees for these additional services and the commercial terms of said Supply Agreement shall be discussed and agreed between the Parties in good faith. The contract manufacturing shall also take into account annual volumes of production. The Supply Agreement shall also include customary provisions and customary representations and warranties by the Parties, as well as the supply terms as applicable to such agreements, as shall be discussed between the parties in good faith.

9.3 For the avoidance of doubt, it is acknowledged that neither Party shall be under obligation to enter into the Supply Agreement, including in the event that the Parties do not agree on the terms of the Supply Agreement.

Furthermore, it is acknowledged that nothing in the foregoing shall limit Galmed's right to negotiate other proposals with third party manufacturers.

10. Project Management and Communication

The Parties will establish a Project management team, to which each Party will delegate at least one representative. Perrigo and Galmed will keep each other informed about the progress of the Project and the services contemplated hereunder, periodically discuss the progress and results and, if needed, jointly agree on adjustments to the annexures hereto.

11. Consideration

11.1 For the services contemplated hereunder Galmed shall pay Perrigo the following consideration:

11.1.1 Upon completion of the Technology Transfer and Process Stabilization Galmed shall pay to Perrigo [***] ([***]US Dollars.

11.1.2 For the manufacture of the Tech Transfer Batches (60kg of API) as per Section 5 above, Galmed shall pay Perrigo $[***] ([***] US Dollars) per kg of API, in two installments as follows:

(a) An advance payment of [***] ([***] US Dollars) shall be paid to Perrigo upon execution of this Agreement. Galmed acknowledges that the said advance payment will be used by Perrigo to purchase the materials necessary for the manufacture of the Tech Transfer Batches and is not refundable.

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(b) The balance amount shall be invoiced by Perrigo upon delivery of the Tech Transfer Batches ex works in accordance with Section 5.2.

11.1.3 Upon completion of the Manufacturing Process Improvement in accordance with Section 6 (and in accordance with **Annex E**), Galmed shall pay Perrigo [***] ([***] US Dollars).

11.1.4 For the manufacture of the Scale Up Batches as per Section 7 above, Galmed shall pay Perrigo [***] ([***] US Dollars) per kg of API, in two installments as follows:

(a) An advance payment equal to the costs of the purchase of the required raw materials, estimated at [***] ([***] US Dollars) shall be paid to Perrigo no later than six months prior to the then expected delivery of the Scale Up batches (the "**Advance Payment**"). Galmed acknowledges that the said advance payment will be used by Perrigo to purchase the materials necessary for manufacture of the Scale Up Batches and is not refundable. Alternatively, Galmed may, not later than seven months prior to the expected delivery of the Scale Up Batches notify Perrigo of its wish to make direct payments to the suppliers of the raw materials required for the manufacture of the API, in which case, such cost of direct payment to suppliers by Galmed will be reduced from the consideration due to Perrigo under this Section 11.1.4 of the Agreement.

(b) The balance amount shall be invoiced by Perrigo upon delivery of the Scale Up Batches ex works in accordance with Section 7.3.

Perrigo will make an effort to improve the quote for the price for the commercial supply under the Supply Agreement such that it will aim to be lower than [***] per kg of API, subject to the outcome and extent of the cost improvements achieved during the Manufacturing Process Improvement. It is clarified that the price of [***] per kg of API is not Galmed's target price, and that a competitive price is one of the considerations that are important to Galmed in deciding whether or not to enter into the Supply Agreement.

11.2 All payments to Perrigo by Galmed for work performed by Perrigo under the Agreement shall be made in New Israeli Shekels equivalent to the U.S Dollars amount at the official exchange rate applicable on the date of invoice. The above consideration is final and inclusive of all taxes and/or duties of whatever nature which are imposed or may be imposed with regard to the consideration, other than value added tax which will be added to all amounts mentioned in this Agreement, at the appropriate rate as required by law. Payments shall be made by wire transfer, money order or other method of payment approved in writing by Perrigo, within 30 (thirty) days of Perrigo's invoice for the same. Any payment due to Perrigo by Galmed that is not paid when it is due shall accrue interest, from the date when the same was due and payable, at the rate of 12 month LIBOR plus [***] (LIBOR as quoted by BBA – British Bankers' Association - http://www.bba.org.uk), compounded annually, payable on demand.

11.3 For removal of doubt it is noted that the full and timely payment of any part of the consideration hereunder is considered a material obligation. Without derogating from any of the rights available to Perrigo, it may withhold services until full payment for services/APIs is settled.

11.4 Payments to Perrigo shall be done without any deduction on account of taxes. Perrigo shall provide Galmed with a current and valid tax exemption certificate of the Israeli Tax Authority that indicates that no amount due to Perrigo under this Agreement needs to be withheld.

11.5 Galmed acknowledges that Perrigo shall exert a considerable effort in time and resources in providing the services contemplated under this Agreement and would have not entered into this Agreement unless for the obligation to purchase from it the Scale Up Batches and negotiate the Supply Agreement in good faith.

11.6 Perrigo acknowledges that Galmed is a clinical-stage company, and as such, time is of the essence, and it is dependent on the timely delivery of the Project and each of its stages under this Agreement by Perrigo (including timely delivery of the APIs), and would have not entered into this Agreement unless for Perrigo's foregoing acknowledgement as aforesaid, and its undertaking and obligation, subject to the provisions of this Agreement and the timely performance of Galmed's (and third parties on its behalf) obligation hereunder, to timely deliver the Project and each of its stages. The timely performance of Perrigo's obligations as aforesaid is considered a material obligation.

12. Warranty; Representations; **Undertakings**.

12.1 Representations Warranties and Undertakings of Perrigo. Perrigo represents, warrants and undertakes to Galmed that: (i) it is acknowledged that the Product that includes the API will be used to undergo clinical trials and accordingly, the API must comply with the GMP ; (ii) it shall obtain and maintain all necessary permits, registrations and licenses required, if required, to manufacture and supply the API under this Agreement, including without limitation FDA and any other applicable Regulatory Authority; (iii) it will comply in all material respects with all laws, rules and regulations applicable to the performance of its obligations under this Agreement, including all GMP of the Regulatory Authority applicable to its manufacture, labeling, packaging, storage and shipment of the API in effect from time to time as applicable for investigational new drugs in clinical Phase III trials; (iv) the API supplied pursuant to this Agreement shall fully conform with the Specifications, free of any defects, will be manufactured in compliance with GMP and other applicable laws, rules and regulations of the Regulatory Authorities as applicable for investigational new drugs in clinical Phase III trials and shall be capable of maintaining such until any expiration of shelf life date for the API; (v) Perrigo's Facility was audited by one or more third party QP audits in the last calendar quarter of 2014, and that there were no adverse findings discovered in any of the QP processes which have not been cured; (vi) it will perform the Services under this Agreement in a competent and professional manner, and the API shall be manufactured only by personnel who are highly qualified to provide services of the type of the Services; (vii) Perrigo has full right and authority to enter into this Agreement without the consent or approval of any third party.
Furthermore, Perrigo represents, warrants and undertakes towards Galmed that: (a) it has not during the last calendar year been found by the FDA or any other Regulatory Authority or any state or other authorized government official to have violated any statutes, rules, or regulations; or (b) it has not, during the last calendar year, received any relevant warning letter, observations, findings or the like from the FDA or other Regulatory Authority, which have not been cured; and Perrigo further undertakes to promptly notify Galmed in the event that it receives a warning letter, observations, findings or the like from the FDA or other Regulatory Authority during the term of this Agreement, to the extent that it relates to the API.

Other than the foregoing representations, Perrigo makes no representation or warranty regarding the Project or the API, including but not limited to warranties with respect to safety or effectiveness of the API and/or the Product. Galmed acknowledges and agrees that, Perrigo and Perrigo personnel (i) have not participated in and are not responsible for the invention, development, testing, clinical and/or safety evaluation of the API; (ii) have not evaluated and will not evaluate and are not responsible for the API's safety or suitability for use in humans or others; and (iii) have not participated in the development of the Manufacturing Process.

12.2 Representations and Warranties of Galmed. Galmed represents and warrants to Perrigo that, (i) to the best of its knowledge it has the requisite Intellectual Property rights related to the API and the Manufacturing Process; (ii) the performance of Perrigo's obligations under this Agreement shall not give rise to a cause of action by a third party against Perrigo for infringement or another violation of Intellectual Property rights relating to the API; (iii) it will comply in all material respects with all laws, rules and regulations, GMP, and Regulatory Authority regulations applicable to the API and the Product. Without derogating from the generality of the afore-mentioned, Galmed shall specifically comply with the U.S. Foreign Corrupt Practices Act ("FCPA"), the UK Anti-Bribery Act 2010 and any local anti-bribery and anti-corruption laws, a breach of which is considered for the purposes of this Agreement a material breach; and (iv) that it has full right and authority to enter into this Agreement without the consent or approval of any third party.

13. Confidential Information

Each Recipient will hold, and cause their respective representatives and advisers to hold at all times, any Confidential Information disclosed by the Discloser in strict confidence from any person (other than its affiliates or their representatives or advisers), and undertakes to maintain the Confidential Information in strict confidence and not to disclose or transfer it to others and not to make any use of the Confidential Information, for personal or other needs, without the prior written consent of the Discloser. Recipient shall use the same degree of care to preserve the secrecy and confidentiality of the Confidential Information and to avoid the unauthorized disclosure of the Confidential Information to third parties as it uses with respect to its own confidential, proprietary or trade secret information, but in any event no less than a reasonable degree of care.

Notwithstanding the foregoing, disclosure by the Recipient in the event such Recipient is compelled to disclose the Confidential Information by judicial or administrative authority and process shall not be deemed a breach of the confidentiality undertaking provided, however, if the Recipient becomes subject to a demand for discovery or disclosure of the Discloser's Confidential Information under lawful process, the Recipient (a) shall, to the extent permitted by law, give immediate notice to the Discloser prior to furnishing the Confidential Information so that the Discloser may seek an appropriate protective order, (b) shall not (unless expressly required) provide such disclosure until the Discloser has had the opportunity to obtain such protective order, (c) shall disclose only that portion of the Confidential Information which falls within the scope of such lawful process, and (d) shall cooperate in seeking reasonable protective arrangements requested by the Discloser.

The foregoing confidentiality undertaking shall not apply to the extent that:

13.1 The Confidential Information was in the public domain (either prior to or after the furnishing of such documents or information hereunder) through no fault and by reason other than a breach of this Agreement of such Recipient; or

13.2 The Confidential Information was already in the possession of a party as demonstrated by competent evidence or was later acquired by the Recipient from another legitimate source if the receiving party is not aware that such source is under an obligation to another party hereto to keep such documents and information confidential; or

13.3 It can be shown that the Confidential Information was independently developed by the Recipient without reliance on the Confidential Information disclosed by the Discloser; or

13.4 Information set forth in Section 14.2 below.

This Agreement does not constitute the conveyance of ownership with respect to or a license to any Confidential Information, except as otherwise provided in this Agreement. Upon the expiration or termination of this Agreement for any reason, each party agrees, except as otherwise provided in this Agreement, to return to the other party all documentation or other tangible evidence or embodiment of Confidential Information belonging to the other party and not to use same, unless otherwise agreed later.

This Section 13 shall survive the expiration or termination of this Agreement for a period of fifteen (15) years.

14. Public Disclosure

14.1 No disclosure (whether or not in response to an inquiry) of the terms and conditions of this Agreement shall be made by any Party hereto unless approved by the other Party prior to release. Such approval shall not be unreasonably denied or delayed.

14.2 Notwithstanding the foregoing, either Party may disclose such terms as are required to be disclosed in its publicly-filed financial statements or other public statements, pursuant to applicable securities laws, regulations and stock exchange rules; provided that, to the extent practicable, such Party shall provide the other Party with a copy of the proposed text of such statements or disclosure at least forty eight (48) hours in advance of the scheduled release or publication thereof to afford such other Party a reasonable opportunity to review and comment upon the proposed text (including redacted versions of this Agreement).

15. Intellectual Property Provision

15.1 Each Party acknowledges that all Confidential Information, background information and Intellectual Property rights ("**IPR**") owned, obtained or generated before or outside the Project by the other Party will at all times remain in the ownership of the other Party.

15.2 All Confidential Information such as raw data, information, test material, reference materials, and other Intellectual Property rights relating to the API and provided by Galmed to Perrigo pursuant to this Agreement shall remain the property of Galmed. Galmed grants Perrigo a non-exclusive, nontransferable, royalty free license, during the term of this Agreement, to use the foregoing in connection with the performance of the Services hereunder.

Furthermore, any Inventions specific to the API discovered by Perrigo in the course of this Agreement or any Inventions specific to the API discovered as a result of performing the Project or the Services, and the results and deliverables (as defined in **Annex D** and **Annex E**;) (collectively, the "**Results**") will be owned exclusively by Galmed and vested with Galmed, regardless of the Party that develops same, with the exception of the Perrigo Inventions (as defined below). Perrigo shall disclose the Results promptly to Galmed within the Report, and shall cooperate with Galmed in defending or taking steps necessary or as requested by Galmed to vest title to such Results in Galmed, at Galmed's expense. Galmed shall promptly reimburse Perrigo for any reasonable costs made in this respect. Only Galmed is entitled to acquire industrial and/or intellectual property rights anywhere in the world for its IPR (including, for the avoidance of doubt, the Results). Galmed will at all times have an unrestricted right to use the Results.

15.3 Perrigo will own all IPR and Inventions discovered in the course of this Agreement related to the research development and manufacturing methodologies which are not specific to the API (the "**Perrigo Inventions**"). The Perrigo Inventions shall, as far as generated or developed by Perrigo, become and remain the exclusive property of Perrigo and only Perrigo is entitled to acquire industrial and/or intellectual property rights anywhere in the world for its IPR. Where necessary, Galmed will co-operate in the acquisition of Perrigo Inventions by Perrigo, at Perrigo's expense. Notwithstanding the foregoing, subject to the payment by Galmed of the consideration for the Tech Transfer, Tech Transfer Batches and the Process Improvement, Perrigo hereby grants Galmed a non-exclusive, irrevocable, royalty free license, unlimited in time, to make use of the Perrigo Inventions solely for the purpose of manufacturing the API or the Product, either by Galmed, its Affiliates or any third party on Galmed's behalf (the "**License**"). The License shall be transferrable, solely in connection with or as part of an Assignment under Section 20.10 below, in which event the assignee shall receive a License at the same terms stipulated herein.

15.4 The Parties further acknowledge and agree that Galmed is engaging Perrigo as an independent contractor to manufacture and supply the API in accordance with the Specifications and this Agreement and that all API Information is and shall be the sole property of Galmed.
Galmed will grant Perrigo the right to use all such API Information and know-how owned or licensed by Galmed which is necessary for, and for the sole purpose of, the manufacture of the Products for Galmed, on and subject to the terms of and only for the duration of this Agreement.
Upon the termination of this Agreement, or upon Galmed's written request, Perrigo shall deliver to Galmed all the Batch Records and API Information relating to the manufacture of the API.

16. Indemnification and Limitation of Liability.

16.1 Galmed shall indemnify and hold harmless Perrigo and its Affiliates and their respective officers, directors, employees and agents (collectively "**Perrigo Indemnitees**") from and against any and all claims, damages, costs and expenses of any kind (including reasonable attorneys' and experts' fees) (collectively: "**Claims**") arising out of or resulting from any third party claims made or suits brought against Perrigo which arise or result from (i) the breach of any of Galmed's representations, warranties, covenants, obligations or agreements set forth in this Agreement; (ii) Galmed's negligence or willful misconduct in the performance of this Agreement; (iii) the use of the Product; except in the event of (i), (ii) or (iii) above, to the extent caused by the negligence or willful misconduct or breach of this Agreement by a Perrigo Indemnitee; or (iii) any third-party Intellectual Property infringement claims relating to the APIs or the Product.

16.2 Perrigo shall indemnify, defend and hold Galmed and its Affiliates and their respective officers, directors, employees and agents (collectively "**Galmed Indemnitees**") harmless from and against any and all Claims arising out of or resulting from any third party claims made or suits brought against Galmed which arise or result from (i) the breach of any of Perrigo's representations, warranties, covenants or agreements set forth in this Agreement, or (ii) Perrigo's negligence or willful misconduct in the performance of this Agreement; except in each case, to the extent caused by any Galmed Indemnitee's negligence or willful misconduct or breach of this Agreement.

16.3 In the event that any party seeks indemnification under the terms of this Section 16 (the "**indemnified party**"), it shall as soon as reasonably possible inform the other party (the "**indemnifying party**") in writing of the Claim, provided, however, that the failure to give such notification shall not affect the indemnification provided hereunder except to the extent the indemnifying party shall have been actually prejudiced as a result of such failure. The indemnified party shall permit the indemnifying party to assume direction and control of the defense of the Claim and shall cooperate as requested (at the expense of the indemnifying party) in the defense of the Claim. The indemnifying party shall not settle any Claim with the indemnified party's prior written consent, which consent shall not be unreasonably withheld or delayed.

16.4 **EACH PARTY HEREBY AGREES THAT SUBJECT TO APPLICABLELAW, AND EXCEPT IN THE EVENT OF (I) BREACH OF CONFIDENTIALITY OBLIGATION UNDER THIS AGREEMENT, OR (II) FRAUD OR WILLFUL MISCONDUCT, THE OTHER PARTY'S LIABILITY TO SUCH PARTY FOR ANY AND ALL INJURIES, CLAIMS, LOSSES, EXPENSES, OR DAMAGES, WHATSOEVER, ARISING OUT OF OR IN ANY WAY RELATED TO THE WORK PERFORMED BY PERRIGO UNDER THE AGREEMENT, FROM ANY CAUSE OR CAUSES, INCLUDING, BUT NOT LIMITED TO, NEGLIGENCE, ERRORS, OMISSIONS OR STRICT LIABILITY, SHALL NOT EXCEED THE SUM OF TWO MILLION USD ($2,000,000).**

16.5 **EXCEPT IN THE EVENT OF (I) BREACH OF CONFIDENTIALITY OBLIGATION UNDER THIS AGREEMENT, OR (II) FRAUD OR WILLFUL MISCONDUCT IN NO EVENT SHALL EITHER PARTY BE LIABLE TO THE OTHER OR ANY OF ITS AFFILIATES FOR ANY CONSEQUENTIAL, INCIDENTAL, INDIRECT, SPECIAL, PUNITIVE OR EXEMPLARY DAMAGES (INCLUDING, WITHOUT LIMITATION, LOST PROFITS, BUSINESS OR GOODWILL) SUFFERED OR INCURRED BY SUCH OTHER PARTY OR ITS AFFILIATES IN CONNECTION WITH THIS AGREEMENT, EVEN IF ADVISED OF THE POSSIBILITY OF SUCH DAMAGES.**

17. Security and Safety Procedures.

Galmed and CML personnel authorized to have access to the Perrigo facility in connection with the work performed by Perrigo under the Agreement shall abide by the security and safety procedures established by Perrigo. Galmed shall be liable for any breaches of security and/or safety by Galmed or CML personnel. All Galmed personnel shall agree to abide by Perrigo policies and standard operating procedures established by Perrigo.

18. Force Majeur

Neither Party will be liable for any failure to perform or for delay in performance resulting from any cause beyond its reasonable control, strikes, lockouts, labour troubles, restrictive government or judicial orders, or decrees, riots, insurrection, war, terror, or Acts of God, provided that payment of sums due shall not be excused due by any such force majeure. A Party seeking to claim Force Majeure must give the other party prompt notice of the Force Majeure with reasonably full particulars and an estimate of the extent and duration of its delay in performance, or inability to perform, and use all possible diligence to remove the Force Majeure as quickly as possible. If the delay continues beyond sixty (60) days after the notice given, the Parties must meet to discuss in good faith a mutually satisfactory resolution of the problem and if unable to achieve such resolution within a further 14 days, either Party may elect to terminate this Agreement by fourteen (14) days prior written notice to the other.

19. Term and Termination

19.1 This Agreement is valid from the date of signature by both Parties and shall remain in force and effect for the duration of the provision of the services contemplated hereunder.

19.2 This Agreement may be terminated by either Party upon thirty (30) days prior written notice in the event of a breach of term of this Agreement by the other Party, provided that the breach is not cured within such 30 day notice period.

19.3 This Agreement may be terminated by either Party upon thirty (30) days prior written notice to the other Party if the other Party is declared bankrupt, becomes insolvent, ceases its business activities or has been operating under court appointed receivership.

19.4 Galmed shall have the right, at any time, on thirty (30) days prior written notice to Perrigo, subject to the provisions of this Agreement, to terminate this Agreement, in the event that due to the failure or inconclusive results in clinical trials that it is conducting or will conduct, or in any other event that Galmed shall decide at its discretion to finally not proceed with the commercialization of the Product.

19.5 In the event of a substantial delay by either party in the timeline of the Project (of more than three months in total), the parties shall discuss in good faith a new timeframe for the Project. In the event that the parties cannot agree on such new timeframe, the other Party may terminate this Agreement with fourteen (14) days prior written notice.

19.6 In the event of a Change of Control of Perrigo, or in the event that Perrigo publically announces that it has entered into an agreement pursuant to which a Change of Control of Perrigo will occur, Galmed shall have the right, but not the obligation to terminate this Agreement on thirty (30) days prior written notice to Perrigo. In the event that Galmed chooses not to terminate this Agreement, Perrigo's rights and obligations shall be fulfilled by Perrigo's successors.

19.7 In the event of a change of control of Galmed, including without limitation the license by Galmed of substantially all of Galmed's rights in the Product or IPR related to the Product, Galmed shall, subject to the payment of a break-up fee of two-hundred and fifty thousand USD ($250,000) and subject further to the full payment of the consideration for the Tech Transfer Batches, have the right, but not the obligation to terminate this Agreement on thirty (30) days prior written notice to Perrigo.

19.7 Notwithstanding anything to the contrary in this Agreement, except in the event of termination of the Agreement by Galmed in accordance with Section 19.2 above due to a breach by Perrigo, Galmed shall remain obliged to pay Perrigo for the Tech Transfer and the Tech Transfer Batches as per and subject to the terms of Sections 5.2, 11.1.1 and 11.1.2 and subject to the terms thereof (including, for the avoidance of doubt, delivery of the Tech Transfer Batches in accordance with Sections 5.1 and 5.2).

19.8 The termination of this Agreement for any reason shall be without prejudice to, and shall not affect any other rights of either Party and all such rights of both shall survive any such termination. In addition, any termination of this Agreement shall not release the Parties from liabilities and obligations accrued until the time of termination. Notwithstanding anything to the contrary that may be contained herein, in the event of the termination or expiration of this Agreement, Sections 7A.5 (Regulatory Inspections), 7A.6 (Access to Perrigo's Site), 7A.7 (record retention), 12 (representations and warranties) 13 (confidentiality), 15 (intellectual property), 16 (indemnification and limitation on liability), 19 (term and termination) and 20 (miscellaneous) shall survive the termination or expiration of this Agreement and continue in effect. Furthermore, the obligation of Galmed to pay any amounts which are due under the Agreement as of the date of termination shall survive termination of this Agreement.

20. Miscellaneous

20.1 Severability: In the event that any part, article, paragraph, sentence, section or clause of this Agreement shall be held to be invalid or otherwise unenforceable, the invalid or unenforceable provision shall be deemed deleted, and the remaining part of the Agreement shall continue in the full force and effect. If any tribunal or court of competent jurisdiction deems any provision hereof unenforceable, such provision shall be modified only to the extent necessary to render it enforceable and this Agreement shall be valid and enforceable and the Parties hereto agree to be bound by and perform same as thus modified

20.2 Independent Contractors. Nothing in this Agreement shall create any relationship of agency, joint venture, partnership employer/employee or similar relationship between the Parties. Each Party is an independent contractor of the other Party.

20.3 Amendments. Any amendment or supplement to this Agreement shall be effective only if made in writing and signed by both Parties

20.4 Waiver. A waiver by either Party of any term or condition of this Agreement in any one instance shall not be deemed or construed to be a waiver of such terms or conditions for any similar instance in the future or of any subsequent breach hereof

20.5 Entire Agreement. This Agreement sets forth the entire agreement between the Parties regarding the subject matter hereof and supersedes all prior agreements, whether written or oral, between the Parties with respect to such subject matter.

20.6 Further Assurances. The Parties agree to execute any and all documents reasonably necessary and to cooperate with each other in order to consummate, implement and give full force and effect to the obligations of the Parties under this Agreement. Perrigo shall transfer all documentation in Perrigo's possession, as may be reasonably necessary by Galmed from time to time for regulatory purposes; and any documentation (including the API Information) in its possession reasonably required by Galmed in the event transferring the API Information, including following the termination of this Agreement. Furthermore, Perrigo undertakes to reasonably cooperate with Galmed following the termination of this Agreement in the technology transfer of the manufacturing process of the API from Perrigo to a third party, including transferring the API Information and manufacturing procedure from Perrigo to another facility of a third party, in consideration for the payment to Perrigo of reasonable fees for any additional work that may be required and time actually spent in connection therewith (including reimbursement of expenses), to be agreed by the Parties at such time. Additional scope of work (not specifically described in this Section 20.6 or elsewhere in this Agreement), may be agreed upon by the Parties in writing.

20.7 Notices. Any notice or other communication required or permitted to be delivered to any Party under this Agreement shall be in writing and shall be deemed properly delivered, given and received when delivered (by hand, by registered mail, by courier or express delivery service or by facsimile) to the address for such Party first set forth above (or to such other address or facsimile telephone number as such Party shall have specified in a written notice given to the other Parties hereto). Furthermore, day to day correspondences may be sent by email with confirmation receipt.

20.7 Equitable Remedies. Each of the Parties acknowledges and agrees that, in the event of a breach or threatened breach of this Agreement by any Party or the failure of a Party to perform in accordance with the specific terms hereof, the other party hereto maybe irreparably damaged and that monetary damages may not provide an adequate remedy. Accordingly, it is agreed that, in addition to any and all other rights which may be available, at law or in equity, the non-breaching party shall be entitled to seek injunctive relief and/or specifically to enforce the terms and provisions hereof in any court of competent jurisdiction.

20.8 Remedies Cumulative. The rights and remedies given in this Agreement to a non-defaulting party shall be deemed cumulative, and the exercise of one of such remedies shall not operate to bar the exercise of any other rights and remedies reserved to a non-defaulting party under the provisions of this Agreement or, subject to the provisions of this Agreement, given to a non-defaulting party at law or in equity.

20.9 Governing Law

This Agreement shall be construed in accordance with, and governed in all respects by, the laws of the State of Israel. The competent courts of Tel Aviv shall have exclusive jurisdiction over any dispute between the Parties arising hereunder or in connection herewith (including non-contractual claims), which cannot be promptly resolved on an amicable basis.

20.10 Assignment

This Agreement shall be binding upon and inure to the benefit of the parties hereto and their respective successors and permitted assigns.
Galmed shall be entitled, at any time, to assign this Agreement to an Affiliate of Galmed, provided Galmed shall remain jointly responsible for any and all financial liabilities hereunder, or to a successor in case of a merger, acquisition or as part of a transaction transferring all or substantially all the business or assets of Galmed relating to this Agreement (collectively, an "**Assignment**").
Subject to Section 19.5 above, Perrigo shall not assign its rights and obligations under this Agreement without first obtaining the written consent of Galmed.

[Signature Page Follows]

IN WITNESS WHEREOF, the Parties have executed this Agreement on the date first written above.

PERRIGO API LTD.:

By: /s/ Yoav Grinberg

Name: Yoav Grinberg

Title: General Manager

Date: 27/1/2015

GALMED RESEARCH AND DEVELOPMENT LTD.:

By: /s/ Chaim Hurvitz

Name: Chaim Hurvitz

Title: Chairman

Date: 1/27/15

By: /s/ Allen Baharaff

Name: Allen Baharaff

Title: CEO

Date: 27.1.2015

Annex A

Route of Synthesis

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Aramchol
IND 79,200

Galmed Pharmaceuticals Ltd.
CONFIDENTIAL

TABLE OF CONTENTS

3.2.S.2.2	Description ofManufacturing Process and Process Controls	2

LIST OF FIGURES

Figure 1.	Synthetic Route B	2
Figure 2.	Flow Chart for Route B Step i	5
Figure 3.	Flow Chart for Route B Step ii	6
Figure 4.	Flow Chart for Route B Step iii (Part A, [***])	7
Figure 5.	Flow Chart for Route B Step iii (Part B, [***])	8
Figure 6.	Flow Chart for Route B Step iv	10
Figure 7.	Flow Chart for Route B Step v	11

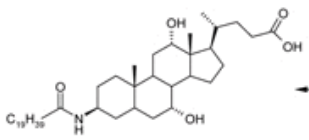
3.2.S.2.2 Description of Manufacturing Process and Process Controls

Aramchol is a conjugated bile acid formed by the amide coupling of the carboxylic acid in Arachidic acid (C20:0) to an amine containing derivative of cholic acid. The starting materials are derived from cholic acid and arachidic acid. To date Aramchol has been manufactured by two similar synthetic routes.

The present synthetic route is described by Route B (Figure 1). In this scheme the starting material is [***] which is purchased from an approved supplier. Aramchol is then synthesized *via* a five step process as described below and in the flow charts in Figure 2 to Figure 7. Current processes afford approximately [***] Kg of Aramchol per reaction / lot. The contents of several lots can be pooled into a final batch which is then controlled by final release testing.

Figure 1. Synthetic Route B

[***]



[***]

[***]

[***]

3.2.S Drug Substance

Step i

[***]

Step ii

An [***] is charged with [***] [***]. The reactor is rinsed with [***] and then the reaction is [***] to obtain a slight reflux. The reaction is [***]. In process control testing is performed to determine the extent of conversion. [***] is dosed into the reaction whilst maintaining the [***]. The [***] of the reaction is monitored and is stirred. The [***] by-product is [***] and the [***] is retained. An [***] [***] of the [***] is performed. [***] is charged to the reactor and is concentrated by [***] prior to addition of [***]. The contents of the reactor are concentrated again and then [***] which effects a solvent switch to begin to induce crystallisation. The contents of the reactor are then concentrated once more and then [***] is added. The contents of the reactor [***] and the resulting crystalline mass is collected by filtration. The cake is washed with [***] and then the [***] product is dried on the filter. In process control testing is performed for purity; [***] ; LOD, Karl Fischer analysis and then dry [***] product is discharged.

Step iii

[***] (product from step ii) and [***] is charged into an [***]. The suspension [***] to obtain a solution. [***] is charged to the reactor and the [***] solution is stirred. The reaction is [***] and then [***] is charged to the reactor. The reaction is [***] with stirring. The contents of the reactor are filtered on a [***] and the [***] is washed with [***]. A phase separation is performed and the lower organic layer is collected and dried with [***]. The [***] is removed by [***] and the [***] is charged into a reactor and part of the [***] solvent is removed by [***]. In process testing of the solution of [***] is performed for purity.

3.2.S Drug Substance

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[***] is charged to the [***] in the reactor. The lines of the reactor are rinsed with [***]. A solution of [***] is dosed into the reactor. The dosing line is rinsed with [***]. The reaction is stirred at [***]. In-process testing is performed to determine the extent of conversion. A solution of [***] (as much as is required to complete conversion) is dosed in to the reactor. The dosing line is rinsed with [***]. The reaction is stirred at [***]. In-process testing is performed to determine the extent of conversion to [***]. [***] is charged to the reactor and the [***] is stirred. Once the layers have separated the lower organic layer is collected and [***] is removed by [***]. [***] is charged to the reactor. Further [***] is removed by [***]. The contents of the reactor are [***] and then [***] is charged to the reactor. Further [***] is removed by [***] . [***] is charged to the reactor and the contents of the reactor are [***] to obtain a solution. The solution is [***] to induce crystallisation. If crystallization does not occur then [***] must be added. The solution/slurry is [***]. The crystalline mass is [***] and is then isolated by [***] and the cake is [***] with [***] and then [***] . In process testing is performed to determine purity. Crude [***] is discharged from the filter and is then dissolved in [***]. The solution is [***] to allow crystallization. The solution is [***] and is then [***]. The product is collected by filtration and the cake is washed with [***]. The pure [***] is dried on the filter. In process testing is performed for LOD and purity. Pure and dry [***] [***] is discharged.

Step iv

[***], water and [***] is charged into an [***]. [***]
[***] is charged to the reactor. The dosing lines of the reactor are [***].

The reaction is stirred at [***]. In-process testing is performed to determine the extent of conversion. To the reaction concentrated [***] is added and the [***]. The reaction is [***] and then the [***]. The [***] are collected by filtration and the cake is washed with [***]. Crystalline product is dried on the filter. In process control testing is performed for purity. The crystalline cake is [***] with [***] at [***] [***]. The product is collected and dried on the filter with [***]. In-process testing is performed for LOD and purity.

Pure [***] is discharged from the reactor.

In some instances full release testing then takes place on [***] once it has been discharged from the reactor. However, the [***] active substance can be [***] prior to release testing.

Step v

[***] are transferred to an [***] configured such that fumes pass through an [***]. The reaction is [***]. [***] is dosed into the reaction, keeping the [***]. The reactor dosing lines are rinsed with [***]. The reaction is stirred and reaction progress monitored. The reaction is [***] to in-process testing is performed to determine the extent of conversion prior to discharge of [***] solution for use in step [***].

3.2.S Drug Substance

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Figure 2. Flow Chart for Route B Step i

[***]

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Figure 3. Flow Chart for Route B Step ii

[***]

3.2.S Drug Substance

Figure 4. Flow Chart for Route B Step iii (Part A, [***])

[***]

3.2.S Drug Substance

Figure 5. Flow Chart for Route B Step iii (Part B, [***])

[***]

3.2.S Drug Substance

[***]

3.2.S Drug Substance

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Figure 6. Flow Chart for Route B Step iv

[***]

3.2.S Drug Substance

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Figure 7. Flow Chart for Route B Step v

[***]

3.2.S Drug Substance

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Annex B

Specifications

Analytical R&D

Annex B – API Specifications

Material name: Aramchol

Stage: End Product

Identification code: **3ARMCN0 Ed. 01**
Project code: ARMC

INTERNAL RELEASE AND SHELF LIFE SPECIFICATION

Superseded Ed. No.: N/A from: N/A

Changes:

This document is Perrigo Company confidential and proprietary information. Individuals printing a copy of a Perrigo procedural document are responsible for ensuring that it is the most current revision.

Material name: Aramchol

Stage: End Product

Identification code: **3ARMCN0 Ed. 01**
Project code: ARMC

INTERNAL RELEASE AND SHELF LIFE SPECIFICATION

Approvals	Name	Signature	Date
Issued by Analytical R&D Department			
Approved by Synthetic R&D Manager			
Approved by QC Manager			
Approved by QA Engineer			

Test	Requirement	Method
Description	White to off white powder	ARMC-01
Identification:		
a)HPLC	Complies with Retention time of RS	ARMC-06
b) IR	IR absorption spectrum of the test sample complies with the IR spectrum of the RS	ARMC-02
c) XRD	XRD-gram corresponds to reference	ARMC-03
d) Melting point	[***]	ARMC-04
Water content	Not more than [***]	ARMC-05
Residue on ignition*	Not more than [***]	ARMC-09
Assay by HPLC (as is)	[***]	ARMC-06

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Test	Requirement	Method
Related substances:		
RRT [***]	Not more than [***]	
RRT [***]	Not more than [***]	
RRT [***]	Not more than [***]	ARMC-07
RRT [***]	Not more than [***]	
RRT [***]	Not more than [***]	
RRT [***]	Not more than [***]	
RRT [***]	Not more than [***]	
RRT [***]	Not more than [***]	
RRT [***]	Not more than [***]	
RRT [***]	Not more than [***]	
Any other unknown	Not more than [***]	
Total	Not more than [***]	
Residual solvents:*		
[***]	Not more than [***]	
	Not more than [***]	
	Not more than [***]	ARMC-08
	Not more than [***]	
	Not more than [***]	
	Not more than [***]	
Heavy Metals:*		
[***]	Not more than [***]	
	Not more than [***]	ARMC-10
	Not more than [***]	
	Not more than [***]	
[***]Content	Not more than [***]	ARMC-11
[***]	Not more than [***]	ARMC-12
PSD*	Report value [***]	ARMC-13

* Not to be performed for stability studies.

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Legend of impurities:

Perrigo Name	Chemical Formula	Chemical Name

Annex C

Technology Transfer Protocol

Document No.:

Ed. 1

TECHNOLOGY TRANSFER PROTOCOL

Name of the API	**Aramchol**	
Technology Provider	CML, Netherlands for Galmed Ltd.	
Prepared by	Anat Shatkin Process Engineer Perrigo API	Sign / Date
Reviewed by	Raya Abu Process department Perrigo API	Sign / Date
	Silvina Guernik Quality control manager Perrigo API	Sign / Date
	Revital ben Daniel R&D manager Perrigo API	Sign / Date
	Shira Webshat Facility manager Perrigo API	Sign / Date
	Alex Rutman Quality control Perrigo API	Sign / Date
Approved by	Name Galmed	Sign / Date
Issued by	Anat Shatkin Process Engineer Perrigo API	Sign / Date

INDEX

Sr. No.	Contents	Page No.
1.	Objective / Purpose	**3**
2.	Scope	**3**
3.	Distribution	**3**
4.	Responsibilities	**4**
5.	Receiving team's Responsibilities	**6**
6.	List of current process documents to be received from CML	**8**
7.	List of materials to be received from CML	**11**
8.	Transfer plan	**12**
9.	Production plan	**13**
10.	Critical and Important Process Parameters	**14**
11.	Comparison of the process equipment, analytical laboratory instruments & risk analysis	**15**
12.	Acceptance criteria for the success of transfer	**19**
13.	Annexure A- Standards requirements	**20**
14.	Annexure B- Representative samples requirements	**20**
15.	Annexure C- Method transfer requirements	**21**
16.	Annexure D- Raw materials requirements	**21**
17.	Annexure E- In process requirements	**22**
18.	Annexure F- Bill of materials	**24**

1. Objective / Purpose:

The Objectives / Purpose of this protocol are:

- To establish and provide guidelines for technology transfer of the Aramchol process from CML to Perrigo API (PAPI).
- To provide the plan for the various activities to be completed during the technology transfer.
- To provide acceptance criteria for the success of the technology transfer.

2. Scope:

Aramchol was developed by Galmed LTD and is currently produced in CML, Netherlands.

This plan covers the technology transfer of Aramchol from CML, Netherland to Perrigo API, Neot Hovav (PAPI).
[***]

3. Distribution:

- QA (Perrigo API)- Original
- Process Manager (Perrigo API)- Copy
- QC (Perrigo API)- Copy
- R&D (Perrigo API)- Copy
- Production Manager at each site- Copy
- Business Development (Perrigo API)- Copy
- Core team members at each site- Copy

4. Responsibilities:

The members of technology transfer and receiving teams and the responsibilities for various activities are given below:

4.1. Team from the Receiving Site- PAPI:

The team from the receiving site shall drive the total technology transfer activity.

Team Leader: **Yael Gafni – R&D Project Manager**

[***]

Core Team	Responsible for	Phone	Email
Anat Shatkin	Process	[***]	[***]
Shiran Yehoshua Magal	Manufacturing	[***]	[***]
Shira Webshat	Manufacturing	[***]	[***]
Silvina Guernik	QC	[***]	[***]
Roza Marcu	QC	[***]	[***]
Alex Rutman	QA	[***]	[***]
Yakir Geron	QA	[***]	[***]
Mali Lahav	Raw materials & Procurement	[***]	[***]
Yulia Rudinski	Ecology	[***]	[***]
Yair Markowitz	Safety	[***]	[***]
Revital Ben-Daniel	Analytical & Synthetic R&D	[***]	[***]

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4.2. Team from Transferring Site- CML:

The team from the transferring site shall provide all the documents & information related to the product for the successful technology transfer.

Team Leader: Production manager, Remy Litjens

(Phone:_____ , E-mail: [***])

(Please add the team members' names, phone and email)

Core Team	Responsible for	Phone	Email
	Process		
	Manufacturing		
	QC		
	QA		
	Raw materials & Procurement		
	Ecology		
	Safety		
	Analytical Development		
	…..		

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5. Receiving Team's Responsibilities- PAPI:

5.1. For the transfer of process:

Name	Department	Responsible for
Raya Abu Anat Shatkin Shira Webshat Shiran Yehoshua-Magal	Manufacturing R&D	[***]
Yulia Rudinski	Ecology	[***]
Yair Markovitz	Safety	[***]

5.2. For the transfer of analytical methods:

Name	Department	Responsible for
Silvina Guernik Roza Marcu	QC R&D	[***]

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5.3. For the Transfer of QA & Regulatory documents:

Name	Department	Responsible for
Alex Rutan	QA	[***]
Yakir Geron	QA	[***]

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6. List of Current Process documents to be received from CML:

Sr. No.	Description	Target date	Responsibility	Status
1.	[***]	[***]	[***]	[***]
2.	[***]	[***]	[***]	[***]
3.	[***]	[***]	[***]	[***]
4.	[***]	[***]	[***]	[***]
5.	[***]	[***]	[***]	[***]
6.	[***]	[***]	[***]	[***]
7.	[***]	[***]	[***]	[***]
8.	[***]	[***]	[***]	[***]
9.	[***]	[***]	[***]	[***]
10.	[***]	[***]	[***]	[***]
11.	[***]	[***]	[***]	[***]
12.	[***]	[***]	[***]	[***]
13.	[***]	[***]	[***]	[***]
14.	[***]	[***]	[***]	[***]
15.	[***]	[***]	[***]	[***]
16.	[***]	[***]	[***]	[***]
17.	[***]	[***]	[***]	[***]
18.	[***]	[***]	[***]	[***]
19.	[***]	[***]	[***]	[***]
20.	[***]	[***]	[***]	[***]
21.	[***]	[***]	[***]	[***]
22.	[***]	[***]	[***]	[***]

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Sr. No.	Description	Target date	Responsibility	Status
23.	[***]	[***]	[***]	[***]
24.	[***]	[***]	[***]	[***]
25.	[***]	[***]	[***]	[***]
26.	[***]	[***]	[***]	[***]
27.	[***]	[***]	[***]	[***]
28.	[***]	[***]	[***]	[***]
29.	[***]	[***]	[***]	[***]
30.	[***]	[***]	[***]	[***]
31.	[***]	[***]	[***]	[***]
32.	[***]	[***]	[***]	[***]
33.	[***]	[***]	[***]	[***]
34.	[***]	[***]	[***]	[***]
35.	[***]	[***]	[***]	[***]
36.	[***]	[***]	[***]	[***]
37.	[***]	[***]	[***]	[***]
38.	[***]	[***]	[***]	[***]
39.	[***]	[***]	[***]	[***]
40.	[***]	[***]	[***]	[***]

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7. List of materials to be received <u>from CML for QC</u>:

Sr. No.	Description	Required quantity	Target date	Responsibility
From R&D/ QC/ Production				
1.	[***]	[***]	[***]	[***]
2.	[***]	[***]	[***]	[***]

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8. Transfer plan:

Sr. No.	Parameter	Responsibility	Target date
1.	[***]	[***]	[***]
2.	[***]	[***]	[***]
3.	[***]	[***]	[***]
4.	[***]	[***]	[***]
5.	[***]	[***]	[***]
6.	[***]	[***]	[***]
7.	[***]	[***]	[***]
8.	[***]	[***]	[***]
9.	[***]	[***]	[***]
10.	[***]	[***]	[***]
	[***]		[***]
	[***]		[***]
11.	[***]	[***]	[***]
	[***]		[***]
	[***]		[***]
12.	[***]	[***]	[***]
13.	[***]	[***]	[***]
14.	[***]	[***]	[***]

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Sr. No.	Parameter	Responsibility	Target date
15.	[***]	[***]	[***]
16.	[***]	[***]	[***]

9. Production plan:

Type	Batch size (RM Input)	Batch size (output)	Number of batches
[***]	[***]	[***]	[***]

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10. Critical and important Process Parameters:

[***]

11. Comparison of process equipment, analytical laboratory instruments & risk analysis:

During the assessment of risks due to change in Process equipments and Instruments & controls (given below), we shall ensure that the changes do not affect the critical process parameters (given above).

11.1. Comparison of Process Equipment: (please enter here the equipment used along the process for each step in the CML column; please include details such as the volume of the vessels, material of construction, filtration area, etc.)**- prepared in a separate file during the visit to CML**

Process step	Equipment (CML)	Equipment (PAPI)	Comments, Risk assessment, actions required
[***]			
[***]			
[***]			
[***]			
[***]			
[***]			
[***]			
[***]			
[***]			

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11.2. Comparison of Instrumentation & control system: (please enter here the equipment used along the process in the CML column. Add rows if needed)

Critical process automation	Related Equipment (CML)	Related Equipment (PAPI)	Comments, Risk assessment, actions required
[***]			
[***]			
[***]			
[***]			
[***]			
[***]			
[***]			
[***]			
[***]			

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11.3. Comparison of analytical laboratory instruments: (please enter here the equipment used along the process in the CML column)

Test	Instrument (CML)	Instrument (PAPI)	Comments, Risk assessment, actions required
[***]			
[***]		[***]	
[***]		[***]	
[***]		[***]	
[***]		[***]	
[***]		[***]	
[***]		[***]	
[***]		[***]	
[***]		[***]	
[***]		[***]	
[***]		[***]	
[***]		[***]	
[***]		[***]	
[***]		[***]	
[***]	[***]	[***]	[***]
[***]		[***]	
[***]			
[***]			
[***]			
[***]			
[***]		[***]	

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12. Acceptance criteria for the success of transfer:

[***]

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13. Annexures:

Annexure A

ARAMCHOL – Standards Requirements

Sr. No.	Name	CML Code	Qty (gr)
1	[***]	[***]	[***]
2	[***]	[***]	[***]
3	[***]	[***]	[***]
4	[***]	[***]	[***]
5	[***]	[***]	[***]
6	[***]	[***]	[***]
7	[***]	[***]	[***]
8	[***]	[***]	[***]

Annexure B

ARAMCHOL – Representative Samples Requirements

Sr. No.	Name	CML Code	Qty (gr)
1	[***]	[***]	[***]
2	[***]	[***]	[***]
3	[***]	[***]	[***]
4	[***]	[***]	[***]
5	[***]	[***]	[***]
6	[***]	[***]	[***]
7	[***]	[***]	[***]
8	[***]	[***]	[***]
9	[***]	[***]	[***]

Annexure C

ARAMCHOL – Method Transfer Requirements

Sr. No.	Name	CML Code	Qty (gr)
1	[***]	[***]	
2	[***]	[***]	

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Annexure D

ARAMCHOL – Raw Materials Requirements

Sr. No.	Name	Requirement from CML	Remarks
1	[***]	[***]	[***]
2	[***]	[***]	[***]
3	[***]		[***]
4	[***]	[***]	
5	[***]	[***]	
6	[***]	[***]	[***]
7	[***]	[***]	[***]
8	[***]		[***]

Annexure E

ARAMCHOL – In-Process Requirements

Sr. No.	Name	Requirement from CML	Remarks
1	[***]	[***]	[***]
2	[***]	[***]	[***]
3	[***]	[***]	[***]
4	[***]	[***]	[***]
5	[***]	[***]	[***]
6	[***]	[***]	
7	[***]	[***]	[***]
8	[***]	[***]	[***]
9	[***]	[***]	[***]
10	[***]	[***]	[***]
11	[***]	[***]	[***]

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Annexure F- Bill of materials

[***]

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Annex D

Process Stabilization Scope

Aramchol

Process Stabilization Scope of Work

Stage 1 of production – [***]

[***]

Stage 2 of production – [***]

[***]

Stage 3 of production – [***]

[***]

Stage 4 of production – [***]

[***]

Analytical Development Scope

[***]

General

- The studies described above will be carried out over a period of **[***]**. Additional 1 month lead time for ordering advanced intermediates / starting materials is required.
- **[***]** will be ordered from Glamed's current source **[***]**
- **[***]** will be ordered from **[***]** (Galmed's current source) **[***]**.
- 3 final lab samples of about 30gr will be produced
- Once completed, an evaluation will be carried out to decide whether process can be transferred directly to **[***]** or pilot scale up **[***]** is recommended first. Such pilot scale up will require **[***]** of additional work.

Other Working Assumptions

- All analytical standards will be supplied by Galmed / CML.
- Galmed will provide API sample that was used for passing the TOX study. This sample will serve as a standard to set the API specifications.

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- Any method that will be developed by Perrigo API will be applied on this standard.
- The API specifications will be set in accordance with the impurity profile of this sample.

- Any new impurity that will be discovered throughout Perrigo API campaign that was not observed in the batch that was used for TOX study is not quoted in the suggested quotation and will be re-quoted.
- **[***]**. Galmed would define the scope of Solid State study if required.

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Annex E

Process Improvement Scope

Aramchol

Process Improvement Scope of Work

Stage 1 of production – [***]

[***]

Stage 2 of production – [***]

[***]

Stage 3 of production – [***]

[***]

Stage 4 of production – [***]

[***]

General (All Production Stages):

[***]

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Exhibit 4.10

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Investigator-Initiated Clinical Trial Agreement

This Clinical Trial Agreement ("Agreement") is made and entered into effective as of the full execution hereof ("Effective Date"), by and between The Regents of the University of California, a California constitutional corporation, on behalf of its San Diego campus, located at 9500 Gilman Drive, La Jolla, CA 92093, California ("Institution"), and Galmed Research and Development Ltd., a private company having its principal place of business at 8, Shaul Hamelech Blvd., Tel Aviv, 6473307, Israel ("Company"), (each may be individually referred to as a "Party" and collectively, as "the Parties").

Whereas, Dr. Rohit Loomba, M.D., an employee of Institution ("Principal Investigator"), desires to conduct a clinical study ("Study") under a protocol entitled "Aramchol Versus Placebo for the Treatment of HIV-associated NAFLD" UCSD#20150180 ("Protocol"), a copy of which is attached hereto as **Exhibit A;**

Whereas, Principal Investigator has authored the Protocol and Institution and Principal Investigator have the expertise and facilities to conduct the Study;

Whereas, Company is providing financial support in accordance with the budget attached hereto as **Exhibit C** for use in the Study;

Whereas, the Study is intended to advance scientific and medical knowledge and Institution considers the Study to be research done in the public interest;

Now, therefore, in consideration of the mutual promises set forth in this Agreement, the Parties hereby agree as follows:

1. Scope of Work.

1.1 Principal Investigator. The Institution shall conduct the Study under the direction of the Principal Investigator. Principal Investigator may appoint such other appropriate and qualified institution employees to provide services on behalf of Institution to conduct such Study ("Study Staff"). If Principal Investigator becomes unable or unwilling to continue to conduct the Study, and a mutually acceptable substitute Principal Investigator ("Substitute Investigator") is not identified by the parties, then either Party shall have the option to terminate the Study upon thirty (30) days prior written notice and pursuant to Section 8.4 below. Upon the approval of such Substitute Investigator by the Parties as aforesaid, although not a party, the Substitute Investigator shall execute this Agreement as having read and understood Principal Investigator obligations under the agreement, and shall be considered as the "Principal Investigator" for any purpose under this Agreement.

1.2 Institution as Study Sponsor. If applicable, Institution and Principal Investigator shall act as "Sponsor" of the Study, as such term is defined by the U.S. Food and Drug Administration ("FDA") Federal Code of Regulations.

1.3 Study Staff. Institution, through Principal Investigator, shall supervise Study Staff in their performance of the Study and ensure that all Study Staff are qualified to perform the duties assigned to such person. Institution shall take reasonable steps to inform Study Staff of their obligations under this Agreement.

1.4 Conduct of the Study. Institution shall, and shall cause the Principal Investigator and Study Staff (collectively, "Study Team") to, conduct the Study in accordance with this Agreement, the Protocol, and all applicable federal and state laws and regulations ("Applicable Law"); provided, however, that Institution may deviate from the Protocol and such instructions to the extent that the safety of Study subjects so requires. For clinical Studies, such conduct includes compliance with International Conference on Harmonization Good Clinical Practice (ICH GCP), but only to the extent that the ICH GCP guidelines comport with FDA regulations, the Helsinki Declaration, rules and regulations for protecting the rights, safety and welfare of human subjects and for the control of new drugs under investigation, including relevant data protection laws, the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, as well as all applicable laws and regulations pertaining to the protection of the personal data of subjects ("Rules and Regulations").

1.5 Manner of Conduct. Institution represents that it and the Principal Investigator have the requisite skills, knowledge, experience and human resources to undertake and conduct the Study in accordance with the provisions of this Agreement. Principal Investigator and Institution represent and warrant, that they, and the Study Staff have all training, information, licenses, approvals or certifications necessary for safely, adequately and lawfully performing the Study, and all such training, licenses, approvals or certifications shall be properly maintained throughout the course of the Study.

1.6 Investigational New Drug Application ("IND")/Investigational Device Exemption ("IDE"). To the extent required to do so by Applicable Law, Institution will obtain and maintain an IND/IDE pursuant to FDA regulations.

1.7 IRB Approval. Institution shall obtain approval of the Study, the Protocol, and an informed consent from the appropriate institutional review board ("IRB") and shall seek any other approvals required for the Study from applicable safety or review boards or other authorities.

1.8 Informed Consent. Prior to a Study subject's participation in Study, Institution shall obtain from each Study subject participating in the Study or such Study subject's legal representative an informed consent, which includes a waiver of medical confidentiality, signed by the Study subject or his or her legal representative, unless such signature is waived by the IRB. Institution shall ensure that such informed consent shall be granted only under circumstances that provide the prospective Study Subject (or his or her legal representative) with reasonable and sufficient opportunity to consider whether or not to participate in the Study and that minimize the possibility of coercion or undue influence. Such written informed consent shall be obtained in compliance with all Applicable Law, standards and guidelines. Institution shall further ensure that each Study subject shall execute an authorization form intended to give the Study subject's permission to use his or her personal data as necessary to accomplish the goals of the Study.

1.9 Protocol Ownership and Changes to the Protocol. Company acknowledges that Investigator is the author of the Study Protocol and research design of the Study. The Protocol and research design of the Study is the property of the Institution. Institution shall inform Company of any changes to the Protocol. Protocol changes shall be in writing and will not take effect until approved by the IRB.

1.10 Multi-Center Study. In the event of a multi-center Study, Institution agrees that each site involved in the Study (each a "Study Site" and collectively "Study Sites") shall enter into a written agreement with Institution regarding its participation in the Study. Institution and Investigator shall be solely responsible for the conduct of the Study at all Study Sites, and shall ensure that the Study Sites comply with the terms and conditions of this Agreement and all Applicable Laws. Upon request by Company, Institution and Investigator shall provide a list of participating sites and any updates thereto. Institution shall prepare the form of the agreement to be used with the Study Sites, which shall afford Company all rights as set forth in this Agreement.

1.11 Provision of Study Drug and Study Supplies. Company shall provide to Institution, without cost, a certain quantity agreed by the parties of Company's study drug called Aramchol, to conduct the Study pursuant to the Protocol ("Study Drug"), as well as any other compounds, comparator drugs, and/or equipment (collectively, "Study Supplies") which is agreed by the Company and specified in the Protocol. Company shall also provide Institution with written instructions and prescriptions governing the administration of the Study Drug, and Institution shall maintain proper and complete records concerning the administration of the Study Drug as well as maintain an inventory log regarding the current inventories of the Study Drug and shall verify that such log is completed and updated on an ongoing basis. Institution and the Principal Investigator shall not modify or reverse engineer the Study Drug and will maintain, safeguard and store the Study Drug in a safe and secure manner consistent with ICH GCP and in strict compliance with the Protocol, Applicable Law and the Rules and Regulations, and keep or cause to be kept records of all Study Drug received, used, dispensed, disposed of and/or returned to Company. All Study Supplies, including the Study Drug, provided for the purpose of carrying out the Study may not be used for any other purpose whatsoever. Principal Investigator and Institution are responsible for the security and accountability of all such Study Supplies. Where Company requests, Institution shall store the Study Drug in Institution's pharmacy (the "Pharmacy"). In such case, the Study Drug shall be stored according to the instructions of Company, in compliance with the Pharmacy's practice and policy regarding storage of drugs.

2 Access and Auditing.

2.1 Access to Study Data. Upon prior written request to Institution, at mutually agreeable times during Institution's regular business hours, and subject to the terms of this Agreement and Applicable Law, Company or its agents may access Institution's Study data in the form in which it is available, except that direct identifiers of any Study subject, including, but not limited to. Study subject's name, birth date, street address, telephone, social security or health plan beneficiary numbers ("Direct Identifiers") shall not be made available to Company. In the event Study data contains Direct Identifiers, such Direct Identifiers shall be redacted. Company shall be responsible for all costs to Institution for making such Study data available, including any costs associated with redaction.

2.2 Compliance with HIPAA and CMIA . The Parties shall comply with all Applicable Laws governing patient privacy and confidentiality of health information, including without limitation the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") and its implementing regulations, and the State of California Confidentiality of Medical Information Act ("CMIA"). The Parties shall take all actions necessary to comply with such laws and regulations, including agreeing to amend this Agreement as necessary for compliance.

Adverse Event Reporting. Institution is solely responsible for reporting adverse events in the course of a Study in accordance with Applicable Law and the Protocol to the FDA or other regulatory authorities. Institution shall provide Company with a copy of any adverse event reports as they are submitted to the FDA or other authority. In the event of a Serious Adverse Event, Institution and the Study Staff will immediately take all measures at their disposal to evaluate the risk to the other Study subjects and will agree on which measures to take in order to mitigate that risk.

2.3 Debarment. Institution certifies that it will not knowingly use the services of any Study Staff to perform services in connection with the Study who is (i) debarred, disqualified or banned from conducting clinical studies under the Generic Drug Enforcement Act of 1992, as amended, or (ii) excluded, debarred or suspended from participation in, or is otherwise ineligible to participate in, any federal health care program or federal procurement or non-procurement program. Institution further certifies that neither it, or the Principal Investigator nor any person or entity it utilizes to perform services pursuant to this Agreement, has been convicted of a criminal offense that falls within the ambit of 42 U.S.C. § 1320a-7(a) or is otherwise related to the provision of healthcare items or services. Institution agrees to inform Company as soon as practicable in writing of any change to this certification.

2.4 Information and Regulatory Authority Audits. Each of Institution and Company shall notify and provide the other with copies of any inquiries, correspondence or communications to or from any governmental or regulatory authority related to the Study at Institution as soon as practicable after their receipt. In addition, if any governmental or regulatory authority: (i) contacts Institution or the Principal Investigator with respect to the Study; (ii) conducts, or gives notice of its intent to conduct, an inspection at Institution; or (iii) takes, or gives notice of its intent to take, any other regulatory action with respect to any activity of Institution or Principal Investigator which could reasonably be expected to impact any data or clinical activity under the Study; the Principal Investigator must promptly notify the Company of the contact or notice. The Principal Investigator shall provide the Company with copies of all information and documentation applicable to the Study issued by any governmental or regulatory authority and any proposed response. The Company will have the right to review and comment in advance on any responses, which pertain to the Study Drug. Furthermore, Institution and Principal Investigator shall provide the Company within two weeks following the inspection a written report of the inspection, noting with specificity each Study-related record or document provided to or reviewed by the regulatory authority. The Parties shall use reasonable efforts to properly address and will cure any and all non-compliance issues. Institution and the Principal Investigator will consult with and inform the Company of the actions taken and the responses provided to any report or correspondence issued by any governmental authority which could reasonably be expected to impact the Study Drug.

3. Compensation

Company shall make payments to Institution in accordance with the payment schedule attached hereto as **Exhibit B** ("the Payment Schedule") and the budget attached hereto as **Exhibit C** ("Budget"). All payments shall be provided to Institution within 30 days of the end of the calendar month during which Institution's invoice is received by Company. Company shall also make payments to Institution in accordance with Section 7 of this Agreement. The Parties agree that all such payments made by Company to Institution reflect fair market value for the research performed hereunder.

4. Ownership of Data and Intellectual Property

4.1 Study Data. All rights, title and interest in Study data shall be the sole and exclusive property of the Institution. Company shall have the right to use in its sole discretion, for any legal purpose consistent with the informed consents, including publication and regulatory filings, any Study data provided to Company, at Company's request. Company shall own the completed Case Report Forms (CRFs) and the data therein that is provided to Company by Institution, Institutions shall maintain the original CRFs for regulatory compliance and any other Institution required purpose consistent with Institution policies.

4.2 Final Report. Within 60 days following completion of the Study, Institution shall provide Company with a final report of the research results of the Study. Company shall have the unlimited right to use, copy and disseminate the final report for any legal purpose. The Principal Investigator shall prepare and maintain, both during and following the performance of the Study, current, complete and accurate written records, accounts, notes, reports and data of the Study, including CRFs, in accordance with the Protocol. Such materials and data shall be maintained in accordance with Section 5 below.

4.3 Study Inventions. Institution shall own all patentable inventions and discoveries conceived and reduced to practice in the direct performance of the Study ("Study Inventions"). Institution shall promptly disclose such Study Inventions to Company.

4.4 Grant of License and Option to License. To the extent legally able, Institution agrees to grant to Company a non-exclusive, worldwide, royalty-free, fully paid up, transferrable and sublicensable (including through multiple chains) license to use, import, export, have made, make, commercialize or sell Institution's interest in all Study Inventions and Institution's Confidential Information as required to exploit the Study Inventions. Also, to the extent legally able, Institution shall grant Company a time-limited first right to negotiate an exclusive, worldwide license to Institution's rights in any Study Invention on commercially reasonable terms and conditions agreed between the Parties in advance and in good faith. Company will advise Institution in writing within ninety (90) days of Institution's written notification to the Company of a disclosure of Study Invention whether or not it wishes to secure an exclusive commercial license ("Election Period"). Company shall have one hundred and eighty (180) days from the date of election to enter into a license agreement with Institution ("Negotiation Period"). In the event it is necessary in the opinion of the Institution to file a patent application to protect a Study Invention during the Negotiation Period in geographies agreed between the parties, Company will reimburse Institution for reasonable incurred patent costs during such period.

4.5 No Rights to Other Proprietary Interests. Nothing contained in this Agreement shall be deemed to grant either directly or by implication, estoppel, or otherwise, any rights under any patents, patent applications or other proprietary interests, whether dominant or subordinate, or any other invention, discovery or improvement of either party, other than the specific rights covering Study Inventions under this Agreement.

5. Confidentiality

5.1 Institution Confidential Information. Institution shall only disclose confidential information necessary for Company's support of the Study. "Institution Confidential Information" shall mean and include all data and other information which are disclosed by the Institution to Company, for the purposes of conducting Study which is marked as "Confidential" at the time of disclosure, or (i) in the case of oral disclosures, identified at the time of such oral disclosure as confidential and reduced to writing and marked as "Confidential" within thirty (30) days of oral disclosure; (ii) if not marked, regarded as confidential if a reasonable person in the relevant field would consider such information to be the Institution's confidential information given its content and the circumstances of the disclosure. Institution Confidential Information shall not include information to the extent that it: (i) is, or later becomes publicly known other than through a breach of this Agreement by the Company, its employees, or its agents; (ii) is lawfully made available to the Company, its employees or its agents, by a third party that Company reasonably believes owes no obligation of confidentiality to the Institution; or (iii) was already known to or is independently developed by the Company, its employees, or its agents. During the term of this Agreement and for a period of five (5) years after its expiration or earlier termination, the Company shall maintain the confidentiality of the institution Confidential Information and may not transfer or disclose Institution Confidential Information to any third party without the Institution's prior written consent other than as required by Applicable Law or as permitted pursuant to the terms of this Agreement.

5.2 Company Confidential Information. Company shall only disclose confidential information necessary for Institution's performance of the Study. "Company Confidential Information" shall mean and include all data and other information which are disclosed by the Company to Institution for the purposes of conducting Study or related to the Study Drug which is marked as "Confidential" at the time of disclosure, or (i) in the case of oral disclosures, identified at the time of such oral disclosure as confidential and reduced to writing and marked as "Confidential" within thirty (30) days of oral disclosure; (ii) if not marked, regarded as confidential if a reasonable person in the relevant field would consider such information to be the Company's confidential information given its content and the circumstances of the disclosure. Company Confidential Information shall not include information to the extent that it: (i) is, or later becomes publicly known other than through a breach of this Agreement by the Institution, its employees, or its agents, including the Principal Investigator; (ii) is lawfully made available to the Institution, its employees or its agents, including Principal Investigator, by a third party that Institution reasonably believes owes no obligation of confidentiality to the Company; or (iii) was already known to or is independently developed by the Institution, its employees, or its agents, including Principal Investigator without reference to or use of the Company Confidential Information. During the term of this Agreement and for a period of five (5) years after its expiration or earlier termination, the Institution shall maintain the confidentiality of the Company Confidential Information and may not transfer or disclose Company Confidential Information to any third party without the Company's prior written consent other than as required by Applicable Law or as permitted pursuant to the terms of this Agreement.

5.3 Permitted Uses and Disclosures of a Disclosing Party's Confidential Information. "Disclosing Party" as used herein means, with respect to Institution Confidential Information or Company Confidential Information, the Party who owns or otherwise controls such confidential information, and has disclosed such confidential information under this Agreement. A Disclosing Party's confidential information may be used by the Party receiving such confidential information ("Receiving Party") to the extent that it: (i) is disclosed for the purpose of performing the Study or exercising such Party's rights under this Agreement, provided that the Receiving Party has obligated its employees and agents to hold such Institution Confidential Information or Company Confidential Information in confidence at least to the same degree of care as the Receiving Party uses to protect its own confidential information hereunder; or (ii) is disclosed to medical professionals in order to provide reasonable and necessary medical care to a Study subject, provided that the Receiving Party advises such medical care provider(s) of the need to maintain the confidentiality of such Institution Confidential Information or Company Confidential Information.

5.4 Required Disclosures of Institution Confidential Information and Company Confidential Information. Notwithstanding any provisions of this Agreement, the Receiving Party may disclose Institution Confidential Information or Company Confidential Information which it is required by governmental order, subpoena or Applicable Law to disclose. The Receiving Party agrees to cooperate with any reasonable effort of the Disclosing Party to challenge a court-ordered, open records, or similar required disclosure; provided, however, that, with respect to an open records disclosure, the Receiving Party independently has determined that the information the Disclosing Party seeks to protect is exempted from disclosure under Applicable Law.

5.5 Return of Confidential Information. At any time and upon the Disclosing Party's advance written request, the Receiving Party shall return to the Disclosing Party promptly, or destroy, any and all Institution Confidential Information or Company Confidential Information and all copies thereof, furnished to the Receiving Party under this Agreement; provided, however, that the Receiving Party may retain one copy in a secure location for purposes of compliance with this Agreement and Applicable Law, subject to continuing confidentiality obligations. The Receiving Party shall not be required to delete or destroy any electronic back-up tapes or other electronic back-up files that have been created solely by the automatic or routine archiving and back-up procedures of the Receiving Party, to the extent created and retained in a manner consistent with its or their standard archiving and back-up procedures.

5.6 Accessibility of Institution Records. Institution, as an instrumentality of the State of California, is subject to certain state regulations and resolutions regarding access to Institution's records, including the requirement that Institution make available the terms and conditions of contracts. The actual contract agreement must be released upon request, although portions of the document may be withheld when redaction meets one of the legal exemptions under the California Public Records Act. As such, the general terms and conditions of this Agreement will be released to the public upon request. To the extent disclosure of other records, including the Protocol, terms of compensation and related documents, is requested, Institution will notify Company and work with Company to redact material which can be withheld from disclosure, to the extent permitted by law and at Company's request and expense. Furthermore, for the avoidance of doubt, Institution maintains a publicly accessible listing of all proposals and awards. The listing includes the name of the campus, sponsor, award amount, begin and end dates, principal investigator and co-investigator's name, project type, award instrument, indirect cost rate, account and fund number, department and academic discipline.

5.7 Use of Name. Neither party shall use the name, logo, mark or image of the other party in any publicity or advertising without the other party's written approval. California Education Code Section 92000 prohibits use of Institution's names to suggest that Institution endorses a product or service.

6. Publication

6.1 Right of Publication. Institution may freely publish and disseminate the results of the Study, or otherwise publish or submit for publication an article, manuscript, abstract, report, poster, presentation, or other material containing or dealing with results of the Study ("Publication"), only after coordinating the Publication in advance with the Company in writing, and provided that to the extent appropriate Institution shall include a credit to the Company, its research and investors.

6.2 Review Period of Publications. Institution shall send Company a copy of any proposed Publication sixty (60) days prior to submission for Publication ("Review Period"). Company may comment upon, but may not make any editorial changes to the proposed Publication, and any such comments shall be considered in good faith by the Institution. Upon Company's timely written request prior to submission to Publication, Institution shall delete any Company Confidential Information in the proposed Publication. At the Company's request, Institution shall delay Publication for an additional sixty (60) days in order to protect the potential patentability of an invention described therein.

6.3 Company's Right of Publication. For avoidance of doubt, it is clarified that Company may freely publish and disseminate the data generated in the performance of, and results of, the Study, or otherwise publish or submit for publication an article, manuscript, abstract, report, poster, presentation, or other material containing or dealing with results of the Study and will, as appropriate, seek Institution review of any publication or dissemination under this paragraph if Institution generated the data or results being published. Additionally, Institution will be provided credit, consistent with scientific custom, for its contributions.

6.4 Registration of Study. Institution shall register and report the results of the Study in accordance with the International Committee of Medical Journal Editors (ICMJE) clinical trial requirements for publication and as required under Applicable Law.

7. Indemnification, Subject Injury and Insurance

7.1 Institution Indemnification. To the extent permitted by law, Institution shall defend, indemnify and hold harmless Company, its directors, officers, agents and employees ("Company Indemnitees") from and against any and all claims, liabilities, expenses (including reasonable attorneys' fees), actions or demands that may be made or instituted against any of them by reason of injury (including death) to any person, or damage to property, arising out of or in connection with the Study ("Claims") except to the extent caused solely by the gross negligence or willful misconduct of Company. Company shall promptly notify Institution in writing after receipt by Company of any Claim subject to this Section.

7.2 Management of Indemnification. Institution shall have the right to manage the defense and settlement of any Claim, provided however, that the Institution shall not admit any liability or wrongdoing on the part of the Company or indemnitees, or settle any Claim which would involve such an admission, without the prior written consent of the Company, which consent will not be unreasonably withheld. The Company shall reasonably cooperate with the Institution regarding any such Claims, at the Institution's expense. Subject to the foregoing, Company may participate in any such Claims at its/his/her own cost and expense.

7.3 Subject Injury and Reimbursement for Subject Injury. Institution shall provide medical treatment to subjects injured as a result of their participation in the Study. Subjects will be advised in the informed consent that if they are injured as a direct result of participation in the Study, the University of California will provide any medical care they need to treat those injuries. The Company shall not be required to make any reimbursement in any event.

7.4 Insurance. The Institution shall have sufficient liability, professional indemnity and clinical trial insurance and other adequate forms of protection to satisfy all the obligations set forth in this Agreement, including without limitation with respect to Study subjects and any injury thereto. Institution shall secure and maintain in full force and effect through the performance of the Study (and following termination of the Study to cover any claims arising from the Study) self - insurance coverage for: (i) medical professional and/or medical malpractice liability; (ii) general liability; and (iii) workmen's compensation, each such insurance coverage in amounts appropriate to the conduct of Institution's and Principal Investigator's business activities and the services contemplated by the Study. The amount of such insurance coverage shall not be construed as creating a limit on any obligations assumed herein. The insurance policy shall include the Company as additional named insured. The insurance will be regarded as primary insurance and not contributory. Institution shall present the Company with appropriate insurance confirmation prior to the commencement of the Study.

7.5 No party hereto shall be responsible or liable with respect to any subject matter of this Agreement under any contract, negligence, strict liability or other theory for any indirect, incidental, special or consequential damages including but not limited to loss of revenues and loss of profits.

8. Term and Termination

8.1 Term. This Agreement shall take effect on the Effective Date and shall continue until the earlier of: (i) completion of the Study and submission to the Company of a final report summarizing the results of the Study pursuant to this Agreement; or (ii) until Study is sooner terminated or suspended as provided for in this Agreement and pursuant to the Protocol.

8.2 Termination. Either Party may terminate this Agreement: (i) upon thirty (30) days prior written notice to the other Party, in its sole discretion; or (ii) upon written notice to the other Party, if the terminating Party determines that termination of the Study is necessary for the safety of the Study subjects.

8.3 Termination for Material Breach. Either Party may terminate this Agreement upon written notice to the other Party if the other Party materially breaches this Agreement and the breaching Party fails to cure the breach within thirty (30) days after receipt of written notice of the breach from the other Party.

8.4 Early Termination Procedures. If this Agreement is terminated before completion of the Study, the Parties shall negotiate in good faith on the phase-out for Study subjects and subsequent treatment of Study subjects. In the event such early termination occurs, which is not due to a breach of this Agreement by Institution and/or Principal Investigator or their bankruptcy/insolvency, and/or is not terminated by Institution for convenience, Company shall reimburse the Institution for (i) obligations incurred in accordance with the Study budget that cannot be cancelled or mitigated by Institution using reasonable efforts; (ii) reasonable costs incurred in connection with the safe withdrawal of Study subjects; and (iii) any other post-termination expenses mutually agreed to by the Parties.

8.5 Return of Property. Within thirty (30) days following the expiration or earlier termination of this Agreement: (a) the Institution shall return to the Company, at Company's sole and reasonable expense (i) any remaining Study Supplies (except as required by Applicable Law); (ii) any equipment on loan or lease from the Company; and (iii) subject to the terms of Section 5 of this Agreement, any copies of Company Confidential Information provided by the Company that are in the possession of or are under the control of the Institution; (b) the Company shall return to the Institution, at Institution's sole and reasonable expense, subject to the terms of Section 5 of this Agreement, any copies of Institution Confidential Information provided by Institution that are in the possession of or are under the control of the Company.

8.6 Survival. The following provisions shall survive expiration or termination of this Agreement: Sections 1.2,1.3,1.4, 2.1, 3, 4, 5, 6, 7, 8.4, 8.5, 8.6 and 9.

8A. Warranties

It is understood that the Study Drug and any other materials provided are investigational in nature. COMPANY MAKES NO WARRANTIES, EXPRESS OR IMPLIED, INCLUDING AND WITHOUT LIMITATION ANY OF THE IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE AND NON-INFRINGEMENT, REGARDING THE STUDY DRUG. ADDITIONALLY, COMPANY MAKES NO REPRESENTATION OF ANY KIND, EXPRESS OR IMPLIED, REGARDING THE SAFETY OR EFFICACY OF THE STUDY DRUG.

9. Miscellaneous

9.1 Independent Contractor. All research performed by Institution, Principal Investigator and any Study Staff pursuant to this Agreement shall be performed as an independent contractor. The relationship between the Parties does not constitute a partnership, joint venture, or agency. Neither Party shall have the authority to bind the other Party without that other Party's express and written consent.

9.2 Remedies and Waiver. The remedies provided in this Agreement are not exclusive and the Party suffering from breach or default of this Agreement may pursue all other remedies, both legal and equitable. No express or implied waiver by a Party of any breach or default will be construed as a waiver of a future or subsequent breach or default. The failure or delay of any Party in exercising any of its rights under this Agreement will not constitute a waiver of any such right, and any single or partial exercise of any particular right by any Party will not exhaust the same or constitute a waiver of any other right provided in this Agreement.

9.3 Assignment. Neither Party may assign any of its rights or delegate any of its duties under this Agreement without the prior written consent of the other Party, except that Company may assign this Agreement to a third party in connection with a merger or sale of all or substantially all of its assets relating to the Study Drug, and Company may delegate its obligations or assign its rights under this Agreement to a contractor, provided that Company remains liable for the performance of all delegated obligations and written notice is provided to Institution. Any unauthorized attempted assignment shall be null and void and of no force or effect.

9.4 Governing Law. This Agreement is governed by the laws of the State of California without regard to its conflict of law provisions.

9.5 No Implied Right or License. No implied right or license is granted under this Agreement by either Party except those specifically set forth herein. Nothing contained in this Agreement shall impose an obligation of exclusivity on one Party to the other Party.

9.6 Severability. If any provision of this Agreement is held to be unenforceable for any reason, that unenforceability shall not affect the enforceability of any other provision of this Agreement. The Parties shall negotiate in good faith to substitute an enforceable provision with similar terms.

9.7 Entire Agreement. This Agreement, and any Exhibits thereto, constitutes the entire agreement between the Parties and supersedes all prior agreements and understandings relating to its subject matter. This Agreement, and any Exhibits thereto, may not be altered, modified or waived in whole or part except in writing signed by duly authorized representatives of both Parties. In the event of a conflict between the provisions of this Agreement and Exhibit A or other Study document, the provisions of this Agreement will govern.

9.8 Counterparts. This Agreement may be executed in counterparts, via facsimile or .pdf file and each of which shall be deemed to be an original, but all of which constitute one instrument.

9.9 Force Majeure. If either Party's performance of this Agreement or Study is prevented, restricted or delayed, either totally or in part, for reasons beyond the affected Party's reasonable control and is not due to the action or inaction of such Party, the affected Party will, upon giving notice to the other Party, be excused from such performance to the extent of such prevention, restriction or delay; provided, that the affected Party will use reasonable efforts to avoid or remove such causes of non-performance and will continue its performance whenever such causes are removed. For purposes of this Section, a lack of funds shall not be considered a cause beyond the reasonable control of the Parties.

9.10 Order of Precedence. The terms of this Agreement and the Protocol shall take precedence over other documentation, including but not limited to the Informed Consent in the interpretation and resolution of disputes concerning this Study. In the event that there is a conflict between the terms of the Protocol and the terms of this Agreement, the terms of this Agreement will govern with respect to legal contract terms, but the Protocol will govern with respect to the scientific/clinical conduct of the Study.

9.11 Notices. All notices required or permitted hereunder must be in writing, and will be deemed to be effective only when delivered personally or transmitted by email or facsimile, or sent by certified or registered mail, postage prepaid, return receipt requested, and addressed to the address set out above, with the following additional information:

To the Institution:

UCSD OCGA

Attn: Contract Officer

Torrey Pines Center North

9500 Gilman Drive #0934

La Jolla, CA 92093-0934

With a copy to the Principal Investigator:

Contact person:	Dr. Rohit Loomba
	Associate Professor of Clinical Medicine
Fax number:	(858) 534-0280
E-mail:	roloomba@ucsd.edu

To the Company:

Contact person:	Allen Baharaff, CEO
Fax number:	+972-3-693-8447
E-mail:	ab@galmedpharma.com

or at such other address, facsimile number or e-mail as a Party shall have given a written notice of pursuant hereto. Notices shall be deemed properly and effectively served two (or five if sent by airmail) working days after posting and on the first business day (at the receiving end) following transmission, if transmitted by hand, email or facsimile.

In witness whereof, the Parties have caused this Agreement to be executed by their duly authorized representatives.

COMPANY

By:	/s/ Allen Baharaff	By:	/s/ Maya Halpern
Print Name:	Allen Baharaff	Print Name:	Maya Halpern
Title:	CEO	Title:	CMO
Date:	2/8/2015	Date:	2/8/2015

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

By:	/s/ Rachel sievert
Print Name:	Rachel Sievert
Title:	Contract Officer
Date:	2/5/2015

WHILE NOT A PARTY TO THIS AGREEMENT I HAVE READ THE AGREEMENT AND ACKNOWLEDGE MY RESPONSIBILITIES AS THE PRINCIPAL INVESTIGATOR:

/s/ Rohit Loomba

Name: Dr. Rohit Loomba

Title: Principal Investigator

Enclosures: Exhibit A: Protocol

Exhibit B: Payment Schedule

Exhibit C: Budget

Exhibit A

[Protocol]

CLINICAL RESEARCH PROTOCOL
UNIVERSITY OF CALIFORNIA SAN DIEGO
DEPARMENT OF MEDICINE
DIVISION OF GASTROENTEROLOGY

DATE: February 4, 2015

CLINICAL PROTOCOL NO:
IND NO:

TITLE: **Aramchol versus placebo in the treatment of HIV-associated nonalcoholic fatty liver disease and lipodystrophy: A randomized, double-blinded, allocation-concealed, placebo-controlled clinical trial**

ABBREVIATED TITLE: Aramchol for HIV-associated nonalcoholic fatty liver disease and lipodystrophy

IDENTIFYING WORDS: Aramchol, HIV, Lipodystrophy, Nonalcoholic fatty liver disease, Obesity, Fatty Liver, Cirrhosis

PRINCIPAL INVESTIGATOR:
Rohit Loomba, MD, MHSc

ASSOCIATE INVESTIGATORS:
Ahilan Arulanandan, MD
Irine Vodkin, MD
Lisa Richards, NP
Claude Sirlin, MD

ESTIMATED DURATION OF STUDY: 16 WEEKS

NUMBER AND TYPE OF PATIENTS: Up to 50 patients with HIV, ages above 18 years, both male and female who have NAFLD.

SUBJECTS OF STUDY:	Number	Sex	Age Range
Patients	50	Male & Female	Above 18 years
Volunteers	None		

PROJECT USES IONIZING RADIATION: No
PROJECT USES “DURABLE POWER OF ATTORNEY”: No
OFF-SITE PROJECT: No
MULTI-INSTITUTIONAL PROJECT: No

Abstract

One in every three adult Americans is afflicted by nonalcoholic fatty liver disease (NAFLD). NAFLD represents a spectrum of diseases ranging from simple steatosis to nonalcoholic steatohepatitis (NASH), the progressive form of liver disease that can lead to cirrhosis and liver-related mortality in persons who drink little or no alcohol. NASH represents the more severe end of this spectrum and is characterized by steatosis, ballooning degeneration and lobular inflammation with or without fibrosis. NASH can progress to hepatocellular carcinoma and liver-related death. The etiology of NASH is not completely understood, but it is often associated with obesity, type 2 diabetes, hyperlipidemia and insulin resistance. Lipotoxicity, insulin resistance and oxidative stress appear to be central to the pathogenesis of NASH. Currently, there is no FDA approved treatment for NAFLD or NASH, although weight loss and exercise have demonstrated some benefit.

Among patients with human immunodeficiency virus (HIV) infection, liver disease is among the leading causes of death. Progression of liver disease in HIV is linked to metabolic derangements associated with hepatic steatosis. Till date there are no therapies for the treatment of HIV-associated NAFLD and this area remains understudied with paucity of clinical trials. Recent studies have shown that Aramchol, a fatty acid-bile acid conjugate, may improve serum alanine (ALT) and aspartate (AST) aminotransferase levels and liver fat content on magnetic resonance spectroscopy (MRS) in Israeli patients with primary NAFLD. Aramchol inhibits stearoyl coenzyme A desaturase 1 (SCD1) activity, a key enzyme in fatty acid synthesis. This inhibition may lead to increase in fatty acid oxidation and reduce hepatic steatosis. In addition, it activates cholesterol efflux by stimulating adenosine triphosphate-binding cassette transporter Al, a pan-cellular cholesterol export pump, and thereby, reducing hepatic steatosis and reducing atherosclerosis.

Aramchol has not been studied in HIV-associated NAFLD. In this study, we propose to treat 50 patients with HIV and NAFLD with either Aramchol or placebo for 16 weeks. After an initial evaluation for magnetic resonance imaging (MRI) liver fat distribution and dual energy x-ray absorptiometry (DEXA) whole body fat, patients will receive either 600 mg/day of Aramchol or placebo. Patients will be monitored at regular intervals for symptoms of liver disease, side effects of Aramchol and serum biochemical and metabolic indices. After 16 weeks, patients will have a repeat medical evaluation, liver MRI, and DEXA scan. Pre and post treatment MRI-derived liver fat content and total body fat via DEXA will be compared. The primary end point of successful therapy will be improvement in hepatic steatosis measured by MRI. Secondary end points will be improvement in total body fat, metabolic profile, and liver biochemistry.

Background

Nonalcoholic fatty liver disease is the most common cause of chronic liver disease in the United States and it affects almost 30% of adults in Western countries.[1-3] With climbing obesity rates and more sedentary patient populations, the prevalence of NAFLD is increasing worldwide and is becoming the predominant cause of chronic liver disease in parts of the world.[4] NAFLD represents a spectrum of diseases ranging from simple steatosis to nonalcoholic steatohepatitis (NASH), the progressive form of fatty liver disease that can lead to cirrhosis and liver-related mortality in persons who drink little or no alcohol. NASH represents the more severe end of this spectrum and is characterized by steatosis, ballooning degeneration and lobular inflammation with or without fibrosis.[5] Long-term risks of NASH include cirrhosis, hepatocellular carcinoma and end stage liver disease requiring liver transplantation.[6, 7]

The majority of patients with NAFLD are asymptomatic. Clinical history, laboratory and radiological investigations are useful in excluding other causes of liver disease but do not permit an accurate diagnosis of NAFLD[8]. The diagnosis is usually suspected in a patient with elevated serum alanine aminotransferase (ALT) who drinks no or minimal amounts of alcohol, who has evidence of increased fat in the liver by ultrasound, CT scan or MRI, and who tests negative for the common causes of chronic liver disease. Liver biopsy is the gold standard for the accurate diagnosis of NAFLD, but inherent risks of biopsy such as pain, bleeding, and bacteremia make interval biopsies impractical in the management of this disease.

Recently, innovative imaging tools have demonstrated potential to change how we study and monitor liver disease.[9, 10] An advanced magnetic resonance imaging based biomarker, the proton-density fat fraction (MRI-PDFF), has been validated as a precise and accurate method of quantifying liver fat in NAFLD.[11-15] This provides a unique opportunity to research the progression and treatment of NAFLD without invasive procedures.

A subset of patients with NAFLD that have not been extensively studied are those infected with human immunodeficiency virus (HIV). Among patients with HIV infection, liver disease is one of the leading causes of death.[16] Progression of liver disease in HIV is linked to metabolic derangements associated with hepatic steatosis. Till date there are no therapies for the treatment of HIV-associated NAFLD and this area remains understudied with paucity of clinical trials.

Medical Therapy for NAFLD in HIV patients:

Currently, there is no FDA approved treatment for NAFLD or NASH. Additionally, there have been no significant clinical trials for HIV patients with NAFLD and there are no approved treatment options. Current treatments for NAFLD are limited to weight loss and exercise, but this is often difficult to adhere to for many patients. Therapeutic agents are being investigated but the trials thus far including ursodeoxycholic acid, metformin, clofibrate, betaine, N-acetylcystine, atorvastatin, and orlistat have demonstrated very limited benefit. Pioglitazone has been shown to be somewhat beneficial reducing liver fat but weight gain due to increased adiposity is harmful in the long run. Additionally, none of these trials were for HIV-infected patients. Further therapies for NAFLD and NASH are still under investigation.

Aramchol:

Aramchol, also known as arachidyl amido cholanoic acid, is a fatty acid bile acid conjugate (FABAC) that was created by conjugating 2 natural components, cholic acid and arachidic acid, through a stable amide bond. Aramchol inhibits stearoyl coenzyme A desaturase 1 (SCD1), a key enzyme in fatty acid synthesis. SCD1 is an endoplasmic reticulum enzyme that catalyzes the rate-limiting step in the biosynthesis of monounsaturated fatty acids from saturated fatty acids. Inhibiting SCD1 decreases synthesis and increases beta-oxidation of fatty acids, causing decreased storage of fatty acids. SCD1 has been demonstrated to be tightly associated with control of lipid homeostasis and body weight regulation. Within in vitro models, Aramchol has demonstrated significant (70% to 83%) inhibition of the SCD1 activity.[17] Additionally, Aramchol increases cholesterol efflux by stimulating the adenosine triphosphate-binding cassette transporter A1. This has demonstrated an anti-atherogenic effect in animal models with increased fecal sterol output and decreased plasma cholesterol levels in mice.[18]

Aramchol and the liver:

The three proposed mechanisms of Aramchol's effects on liver fat are 1) reducing de novo fatty acid synthesis, 2) reducing SCD1 activity, and 3) increasing beta-oxidation of fatty acids.[19] In a 2003 study by Gilat,[20] Aramchol significantly reduced hepatic fat content in animals (rats, hamsters, and mice) with a high-fat diet model. These animals gained total weight although they had less fat deposition in their liver, measured histologically, which suggests a redistribution of fat deposition in the body. The authors hypothesized that redistribution of liver fat to adipose tissue was the most likely explanation, but the mechanism was unknown.

However, additional animal studies demonstrated that FABACs have specific metabolic effects as they increase cholesterol efflux from fibroblasts and may not affect the import of dietary fat.[21] In addition, preliminary data indicate that Aramchol may increase fatty acid catabolism in the liver by acting as a peroxisome proliferator-activated receptor agonist.[22, 23] These studies have proposed possible mechanisms of FABACs but further study of fatty acid and triglyceride synthesis vs. degradation in the liver are needed to identify the in vivo mechanisms of Aramchol.

Effect of Aramchol on NAFLD and total body fat:

A recent study by Safadi[24] demonstrated that Aramchol significantly reduced liver fat content, measured by magnetic resonance sprectroscopy (MRS), in 60 Israeli NAFLD patients after 12 weeks of 300mg Aramchol per day. Their trial gave patients either 100mg or 300mg of Aramchol or placebo (3 groups; n = 20/group) once daily for 12 weeks. Their primary finding was that liver fat content decreased by 12.57% (+/- 22.14% standard deviation) in the high dose Aramchol group. There were no serious or drug-related adverse events in the study and the authors proposed that Aramchol might be used for the treatment of fatty liver disease. Aramchol has not yet been studied in HIV-associated NAFLD.

Side effects of Aramchol:

Patient trials with Aramchol are limited to the Safadi study,[24] but the clinical trial demonstrated no significant adverse events in the 12-week treatment period for 58 patients that underwent the trial. The few adverse events were mild (abdominal pain, back pain, constipation) and did not cause anyone to drop out of the trial. There were no severe adverse effects. The previous studies on Aramchol were done in animal models.

Hypothesis

It is well known that MRI is superior to CT in qualitative and quantitative assessment of liver fat and may be a more robust measure of changes during therapy[25]. Using MRI to detect changes in liver fat content, we plan to test the following hypotheses via this randomized-controlled trial.

Hypothesis 1: Aramchol at 600 mg orally daily for 16 weeks is superior to placebo in improving liver fat content assessed by MRI in patients with HIV-associated NAFLD.

Hypothesis 2: Aramchol at 600 mg orally daily for 16 weeks is superior to placebo in improving total body fat content assessed by DEXA in patients with HIV-associated NAFLD.

Specific Aims

We plan to conduct a randomized, double-blinded, placebo-controlled clinical trial to examine the efficacy of Aramchol at 600 mg orally daily versus identical placebo given over 16 weeks to improve HIV-associated hepatic steatosis as measured by a validated and accurate magnetic resonance imaging (MRI)-based technique.

In this study, we propose to randomize up to 50 patients with HIV-associated NAFLD to either Aramchol or placebo for 16 weeks. We plan to enroll a total of 55 patients, expecting some drop outs prior to randomization. After an initial evaluation for insulin sensitivity, liver fat measurement by MRI, and total body fat content by DEXA, patients will be randomized to receive either Aramchol 600 mg or placebo orally for 16 weeks. Patients will be monitored at regular intervals for symptoms of liver disease, side effects of medication, and serum biochemical and metabolic indices. At the end of 16 weeks, patients will have a repeat medical evaluation, liver fat measurement, and total body fat content measurement.

Pre and post treatment liver fat by MRI, ALT/AST, HbAlc, CRP, insulin sensitivity, and DEXA for whole body fat will be compared. The primary end point of successful therapy will be improvement in liver fat by MRI. Secondary end points will be improvement in insulin sensitivity and liver biochemistry. As this is a pilot study, we would also like to look at changes in liver histology if funds permit, which would guide the design of future studies with Aramchol to examine histologic improvement in patients with NAFLD.

Primary objectives:

1. To examine the efficacy of aramchol 600 mg orally daily versus placebo in improving hepatic steatosis assessed by magnetic resonance imaging in patients with HIV-associated NAFLD

Secondary objectives:

1. To examine the efficacy of aramchol 600 mg orally daily versus placebo in improving total body fat content assessed by DEXA in patients with HIV-associated NAFLD

2. To examine the efficacy of aramchol 600 mg orally daily versus placebo in improving serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels in patients with HIV-associated NAFLD

Exploratory objectives:

1. To examine the efficacy of aramchol in improving imaging-based biomarkers associated with changes in NAFLD

Protocol

This is a randomized, double-blinded, placebo-controlled clinical trial to examine the efficacy of Aramchol at 600 mg orally daily versus identical placebo given over 16 weeks to improve HIV-associated hepatic steatosis as measured by a validated and accurate magnetic resonance imaging (MRI)-based technique. 50 subjects will be randomized, monitored at regular intervals for the 16 weeks, and will be invited to continue participating in the study for an additional 5 years of annual monitoring.

Inclusion criteria

1. Age at entry at least 18 years.

2. Serum alanine (ALT) or aspartate (AST) aminotransferase activities that are above the upper limits of normal. 19 or more in women and 30 or more in men.

    1. An MRI-determined fat fraction classification threshold (≥5%) will be used to confirm subjects. MR examinations will include four research sequences (three imaging sequences and one single-voxel spectroscopy sequence) that have been developed and refined by Dr. Sirlin, allowing for the measurement of liver fat fraction and newer candidate MR biomarkers for future NAFLD studies. MR examinations will last 20-30 minutes and will be performed without contrast agents. Subjects will be scanned at 1.5T. To assess sequence repeatability, two sequences per subject, block randomized, will be run three times. For MR elastography, MR imaging will be done which will include placing a vibrating paddle over the abdomen while images are obtained. A comprehensive screening questionnaire will be utilized prior to subjects having an MRI. Experienced research MR technologists will perform MR examinations under the supervision of Dr. Sirlin.

3. History of HIV documented by a previously positive HIV Elisa or PCR.

4. Written informed consent.

Exclusion criteria

1. Evidence of another form of liver disease.

    a. Hepatitis B as defined as presence of hepatitis B surface antigen (HBsAg).

    b. Hepatitis C as defined by presence of hepatitis C virus (HCV) RNA in serum.

    c. Autoimmune hepatitis as defined by anti-nuclear antibody (ANA) of 1:160 or greater and liver histology consistent with autoimmune hepatitis or previous response to immunosuppressive therapy.

    d. Autoimmune cholestatic liver disorders as defined by elevation of alkaline phosphatase and anti-mitochondrial antibody of greater than 1:80 or liver histology consistent with primary biliary cirrhosis or elevation of alkaline phosphatase and liver histology consistent with sclerosing cholangitis.

e. Wilson disease as defined by ceruloplasmin below the limits of normal and liver histology consistent with Wilson disease.

f. Alpha-1-antitrypsin deficiency as defined by alpha-1-antitrypsin level less than normal and liver histology consistent with alpha-1-antitrypsin deficiency.

g. Hemochromatosis as defined by presence of 3+ or 4+ stainable iron on liver biopsy and homozygosity for C282Y or compound heterozygosity for C282Y/H63D.

h. Drug-induced liver disease as defined on the basis of typical exposure and history.

i. Bile duct obstruction as shown by imaging studies.

2. History of excess alcohol ingestion, averaging more than 30 gm/day (3 drinks per day) in the previous 10 years, or history of alcohol intake averaging greater than 10 gm/day (1 drink per day or 7 drinks per week) in the previous one year.

3. Contraindications to MRI:

   a. The subject has any contraindication to MR imaging, such as patients with pacemakers, metallic cardiac valves, magnetic material such as surgical clips, implanted electronic infusion pumps or other conditions that would preclude proximity to a strong magnetic field.

   b. The subject has a history of extreme claustrophobia

   c. The subject cannot fit inside the MR scanner cavity

4. Decompensated liver disease, Child-Pugh score greater than or equal to 7 points

5. History of gastrointestinal bypass surgery or ingestion of drugs known to produce hepatic steatosis including corticosteroids, high-dose estrogens, methotrexate, tetracycline or amiodarone in the previous 6 months.

6. Recent use (within the last 90 days) of medications to treat hepatic steatosis such as pioglotazone (or medications in the same class) or vitamin E.

7. Use of Aramchol or agents in the same class.

8. Recent use (within the last 90 days) of insulin as an outpatient for management of diabetes.

9. HbAlc > 9 or uncontrolled diabetes.

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10. Significant systemic or major illnesses other than liver disease, including congestive heart failure, coronary artery disease, cerebrovascular disease, pulmonary disease with hypoxia, renal failure, organ transplantation, serious psychiatric disease, malignancy that, in the opinion of the investigator would preclude treatment with Aramchol and adequate follow up.

11. Active substance abuse, such as alcohol, inhaled or injection drugs within the previous one year.

12. Pregnancy or inability to practice adequate contraception in women of childbearing potential.

13. Evidence of hepatocellular carcinoma: alpha-fetoprotein levels greater than 200 ng/ml and/or liver mass on imaging study that is suggestive of liver cancer.

14. Advanced HIV defined as CD4 count of less than 100, and/or life expectancy of less than 2 years.

15. Any other condition, which, in the opinion of the investigators would impede competence or compliance or possibility hinder completion of the study.

Initial Evaluation

Patients will be initially screened in the UCSD NAFLD research center clinic with history, physical examination, review of outside medical records (including HIV status) and routine blood tests. Alcohol history will be assessed in the medical interview, and the lifetime alcohol consumption will be estimated by standardized questionnaires. All patients will be asked to stop any medication being used for their liver disease, including herbal medications and vitamins. Only those meeting all inclusion criteria and avoiding all exclusion criteria will be invited to participate in the study. After the initial visit, those who meet all eligibility criteria and have no exclusion criteria will undergo more thorough evaluation with liver MRI and DEXA scan for total body fat. Patients with MRI-PDFF > 5% will be invited to participate in the study.

Following an information session during which the primary consent document, a genetic sampling consent document and the UCSD HIPPA forms are reviewed, discussed and signed the following tests and procedures will be done shortly before starting therapy at the UCSD Medical Center, Hillcrest. If they have already been completed elsewhere as part of the patient's original diagnostic evaluation at the referring clinic they do not need to be repeated.

The following evaluation will be done shortly before starting therapy.

1. History and physical examination.

2. Blood tests. These include complete blood count (CBC with differential and platelet count), prothrombin time, alanine aminotransferase (ALT), aspartate aminotransferase (AST), direct and total serum bilirubin, alkaline phosphatase, albumin, total protein, fasting plasma glucose, hemoglobin Alc, , creatinine phosphokinase (CPK), sodium, chloride, potassium, bicarbonate, blood urea nitrogen, creatinine, uric acid, calcium, phosphorus, ferritin, antinuclear antibody, thyroid stimulating hormone (TSH), HBsAg, anti HBs, anti HAV, anti HCV, ceruloplasmin, alpha-1-antitrypsin, fasting insulin, C-reactive protein, Elisa HIV test, CD4 count, CK-18 level.

3. Routine urinalysis.

4. Chest x-ray and electrocardiogram will be done if they have not been done in the previous year.

5. Detailed metabolic characterization

    a. Oral glucose tolerance test (OGTT): after an overnight fast, subjects will be given 75 grams oral glucose solution. Plasma glucose, insulin levels, and free fatty acids will be obtained from blood samples drawn at 0 and 120 minutes after the oral glucose load [26].

    b. Lipid profiles. Levels of fasting triglyceride, total cholesterol, LDL cholesterol, HDL cholesterol, free fatty acid will be obtained after an overnight fast.

6. Estimation of body fat and fat distribution

    a. Body Mass Index (BMI): For each patient, weight (kg) and height (m) will be recorded with empty bowel and bladder. BMI is calculated by the formula: BMI = weight (kg)/height $(m)^2$.

    b. A trained investigator will measure waist/hip ratio at the same time as other measures are taken.

    c. DEXA scan for whole body fat

    d. Magnetic resonance imaging (MRI) of the liver: MRI is done to evaluate liver size and estimate liver fat content.

    e. MR Elastography (MRE) of the liver: MRE will be done to evaluate changes in liver stiffness before and after therapy if additional funding is available.

Treatment

After the initial evaluation, patients who continue to fulfill all inclusion criteria will be randomized to receive either Aramchol 600 mg/day (1 tablet) or placebo (1 tablet) orally for a total of 16 weeks. Medication diaries and a count of residual tablets will monitor patient compliance at scheduled visits. Patients will be interviewed and examined by an investigator and have blood draw at weeks 0, 4, 8, and 16 of treatment. In addition, an ARFI ultrasound imaging examination of the abdomen will be performed. At each visit particular attention will be paid to symptoms associated with the possible side effects of Aramchol and patients will complete a standardized symptom scale.

Labs to be checked during the treatment phase include:

i. Urinalysis will be done with extended blood tests.

ii. Routine blood tests (Fasting specimens): CD4 counts, Complete metabolic panel (CMP) and protime/INR. In addition, research blood will be taken for cytokine levels and changes in lipid biomarkers.

iii. Extended blood tests (Fasting specimens): Insulin, plasma glucose, lipid profile (cholesterol, triglyceride, LDL and HDL), free fatty acids (FFA), and creatinephosphokinase (CPK), and glycosylated hemoglobin (HbAlc). In addition, research blood will be taken for cytokine levels and changes in lipid biomarkers.

iv. Stool and urine sample will be collected for analysis of changes related to the study drug.

Post-Treatment Phase:

At the end of the study, patients will undergo the same evaluation as listed under the initial evaluation as above, following which treatment will be stopped. Repeat MRI of the liver and full body DEXA scan will also be performed at study conclusion. It is not possible to predict the outcome of this study, but if Aramchol appears to have a significant effect on liver fat by MRI and/or total body fat by DEXA, we will likely develop a follow-up protocol to assess long-term therapy with Aramchol in a large multicenter study to examine the efficacy in improving liver histology.

Annual follow up visits:

Patients will be offered annual follow up visits if they choose to attend. At the annual follow up visit, subjects will undergo a detailed history and physical examination. Standardized questionnaires Skinner Lifetime Drinking History in addition to the Alcohol Use Disorders Identification Tests (AUDIT) will be used. A urine pregnancy test will be performed for all women of childbearing age. Women who have had hysterectomies are excluded from pregnancy testing. If the pregnancy test is positive, the patient will not be enrolled in the study. The patient will undergo full body DEXA scan, magnetic resonance elastography, and a magnetic resonance imaging for liver stiffness calculation and hepatic fat fraction, respectively.

Table I. Study design

Week	0	4	8	16
Routine blood tests	X	X	X	X
Serum/plasma	X	X	X	X
Extended blood tests	X		X	X
StooI/urine/DNA	X		X	X
Physical	X		X	X
DEXA	X			X
OGTT	X			X
MRI-PDFF	X			X
MRE*	X			X
Aramchol VS placebo	600mg/d	600mg/d	600mg/d	Stop

*additional funding permitting

Assessment of Response and Statistical Analyses

The primary outcome of this study will be improvement in hepatic steatosis by liver MRI. Statistical analyses will compare liver fat improvement between the treatments versus placebo- arms. It is not possible to predict what the spontaneous or therapeutic response rate will be. Thus, we predict that the spontaneous improvement rate would be zero to less than 1%. The sample size is chosen to avoid exposure of a large number of patients to 16 weeks of therapy and extensive evaluation if the study medication has no effect, but also to avoid missing a reasonably significant beneficial effect. We will require a sample size of 22 patients in each arm to have a power 90% (or higher) with a p of 0.05. We expect that Aramchol therapy group would have at least 6% reduction in liver fat compared to baseline as compared to 1% or less improvement in the placebo group. These estimates are also based upon our recent trial using MRJ-PDFF as an accurate and reproducible marker of hepatic steatosis.[12] We expect to enroll up to 55 patients in this study and randomize at least 50 of them to either treatment or placebo arm for a full 16 weeks with follow up evaluations. Clinical trials of experimental medications have had variable dropout rates. Our pilot studies of metformin had less than 9% dropouts, and all remaining patients underwent follow up evaluation and liver biopsy. In the randomized-controlled trial of colesevelam versus placebo, we had a 10% drop rate. Therefore, we expect less than a 10% drop out. Dropouts would be considered non-responders based upon intention to treat analysis. A modified intention to treat analysis will be done in which we will exclude the patients who dropped out before getting the week 16 exit evaluation.

Secondary outcomes will be assessed comparing pre-treatment to 16-weeks outcomes on therapy using parametric or non-parametric tests as indicated. The major secondary outcomes to be evaluated are:

1. Total body fat via DEXA scan
2. Serum ALT and AST values.
3. Lipid profiles.

We will compare the changes in the mean difference in the MRI-PDFF determined fat fraction between the treatment arm and the placebo arm at the co-localized region of interest. A two-tailed t-test would be utilized to compare the differences between the two groups. A two-tailed p- value of less than 0.05 is considered statistically significant. We will also conduct segment-to-segment changes in liver fat before and after treatment. We may perform internal validation by comparing MRI-PDFF with magnetic resonance spectroscopy between the two treatment arms in selected cases.

Hazards and Discomforts

1. The risks and discomforts of frequent phlebotomy. To document changes in levels of biochemical markers of liver disease and to monitor the metabolic effects and toxicities of Aramchol, frequent blood sampling will be required. Patients will have between 15 to 20 venipunctures during the period of evaluation, therapy and follow up. Each venipuncture will remove 15 to 70 ml of blood. However, no more than 6 ml/kg will be drawn from any one person during a four-week period. Blood collection by venipuncture is associated with mild discomfort, and the possibility of localized bruising, phlebitis, or extravasation. The risk of infection or fainting is extremely small.

2. The risks and discomforts of HIV testing. Patients will sign a standard consent for HIV testing for this study.

3. The risks and discomforts of other tests.

a) MRI of abdomen and liver. Patients will undergo two MRI examinations of the liver during this study. Each session will be completed within 30 minutes. While serial MRI scanning is thought to be safe, the procedure may cause anxiety in some patients since current equipment used at the Clinical Center uses a closed tube. Patients will be offered sedatives such as Valium if they express worry about being in a closed space.

b) MRE of abdomen and liver. MRE is a type of MR imaging where the images indicate tissue stiffness. MRE imaging involves placing a vibrating paddle over the abdomen while images are being obtained. This is an FDA-approved procedure when used clinically, but is considered to be investigational in this study. These vibrations are generally well tolerated by patients, but the vibrating paddle could be uncomfortable to some subjects. If so, subjects will be instructed to tell the MR technologist if the vibrations become uncomfortable and the MRE part of the examination will be discontinued.

c) Oral glucose tolerance test (OGTT). There will be two OGTT's during this protocol, one at the beginning and one after 16 weeks of treatment with Aramchol. The purpose of this test is to assess insulin sensitivity, insulin secretion as well as free fatty acid metabolism. The patients will have an intravenous catheter placed in the arm and be given 75mg of glucose as an oral solution. Subjects occasionally complain of nausea and rarely may vomit and there is a small risk of rebound hypoglycemia. Repeat blood draw will be done at 2 hours. Total amount of blood that will be drawn for glucose and insulin measurements during this test will be 100 to 120 ml. No more than 6 ml/kg of blood will be drawn from any one person during a four-week period.

5. Risks and hazards of Aramchol:

Patient trials with Aramchol are limited to the Safadi study[24], but the clinical trial demonstrated no significant adverse events in the 12-week treatment period for 58 patients that underwent the trial. The few adverse events were mild (abdominal pain, back pain, constipation) and did not cause anyone to drop out of the trial. There were no severe adverse effects. The previous studies were done in animal models. Due to the paucity of clinical trials to evaluate side effects of Aramchol, we will encourage patients to notify staff of any adverse reactions and we will monitor patients via physical exams and laboratory testing at regular intervals to ensure patient safety.

Dosage modification and discontinuation of Aramchol:

Patients will be monitored for side effects and the toxicity will be ranked as Grades 1 to 4. We will use the common toxicity criteria (CTC), version 4.0, for scoring adverse events during therapy. Specific scoring of toxicity for the major safety parameters to be followed in this study is shown in Table II. The criteria for grading leukocytes, platelets, prothrombin time, partial thromboplastin time, bilirubin, ALT, and AST are modified slightly from the CTC version 4.0 because these factors are likely to be abnormal before therapy in patients with chronic liver disease. An adverse event is defined as any adverse change from the patient's baseline (pre-treatment) condition. These include current illness during the course of the study, regardless of the illness being considered unrelated to treatment.

Dose modification of Aramchol: If any grade 2 adverse events (anemia, elevated serum CPK, hypoglycemia, decrease in serum bicarbonate, elevation in liver transaminases, elevation in bilirubin, anorexia, nausea, diarrhea) occur and persist on repeat testing for one week, Aramchol will be reduced from 600 mg daily to 300 mg daily and the patient will be closely monitored. If the adverse event resolves and in retrospect is not believed to be due to Aramchol, the drug will be restarted at the dose of 600 mg daily. If the adverse event recurs or persists for 2 weeks despite this dose reduction, Aramchol will be stopped.

Discontinuation of Aramchol: In this study, discontinuation of Aramchol will be based upon the scoring of adverse events as shown in the table below. Factors that will lead to discontinuation of Aramchol include pregnancy, any one of the grade 3 or 4 adverse events or any adverse event, which, in the opinion of the investigator, places the patient at increased risk. Aramchol will not be restarted unless another cause for the abnormality or symptom is found.

Table II. Scoring of toxicity for dose modification

Adverse events	1	2	3	4	5
Allergic reaction	Transient flushing or rash, drug fever <38 degrees C (<100.4 degrees F): intervention not indicated	Intervention or infusion interruption indicated: responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDS, narcotics): prophylactic medications indicated for <=24 hrs	Prolonged (e.g., not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae (e.g.. renal impairment, pulmonary infiltrates)	Life threatening consequences: urgent intervention indicate	Death
Anaphylaxis			Symptomatic	Life-threatening	Death

			bronchospasm, with or without urticaria; parenteral intervention indicated; allergy-related edema/angioedema; hypoten	consequences; urgent intervention indicated	
Anorexia	Loss of appetite without alteration in eating habits	Oral intake altered without significant weight loss or malnutrition; oral nutritional supplements indicated	Associated with significant weight loss or malnutrition (e.g., inadequate oral caloric and/or fluid intake); tube feeding or TPN indicated	Life-threatening consequences; urgent intervention indicated	Death
Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated	-	-
Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 - 6 stools per day over baseline; moderate increase in ostomy output compared to baseline	Increase of >=7 stools per day over baseline; incontinence; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	Death
Fatigue	Fatigue relieved by rest	Fatigue not relieved by rest; limiting instrumental ADL	Fatigue not relieved by rest, limiting self care ADL	-	-
Anemia	Hemoglobin (Hgb) <LLN - 10.0 g/dL: <LLN - 6.2 mmol/L; <LLN - 100 g/L	Hgb <10.0 - 8.0 g/dL: <6.2 - 4.9 mmol/L; <100-80g/	Hgb <8.0 - 6.5 g/dL; <4.9 - 4.0 mmol/L; <80 - 65 g/L; transfusion indicated	Life-threatening consequences; urgent intervention indicated	Death
Leukocytes (cell/mm3)	3300 to 9600	2500 to 3300	2000 to 2500	1000-2000	<1000
Platelet count per mm3	154,000 to 345,000	70,000 to 150.000	50,000 to 70,000	10,000 to 50.000	<10,000
Prothrombin time	11.8 to 14.7	14.8 to 16	16.1 to 18	>18	-

Activated partial thromboplastin time prolonged	23.4 to 34.5	35.6 to 42	42 to 50	>50	-
Alkaline phosphatase (U/L)	37-116	117-250	401 - 400	401-600	>600
ALT (U/L)	Baseline-<1.5 times baseline	>200 and > 1.5 X baseline	300-400 and > 2 x baseline	401-800 and > 3x baseline	>800
AST (U/L)	Baseline-<1.5 times baseline	>200 and >1.5 X baseline	300-400 and > 2 x baseline	401-800 and > 3x baseline	>800
Total Bilirubin (mg/dL)	0.1 to 1	1.1 to 1.5 and direct bilirubin >0.5	1.5 to 5 and direct bilirubin > 1	5.1 to 10	>10
Albumin (g/dL)	<LLN - 3 g/dL; <LLN - 30 g/L	<3 - 2 g/dL; <30 -20 g/L	<2 g/dL; <20 g/L	Life-threatening consequences; urgent intervention indicated	Death
CPK increased (U/L)	>ULN - 2.5 x ULN	>2.5 x ULN - 5 x ULN	>5 x ULN - 10 x ULN	>10 x ULN	-
Glucose (mg/dL)	<LLN - 55 mg/dL; <LLN - 3.0 mmol/L	<55 - 40 mg/dL; <3.0 - 2.2 mmol/L	<40 - 30 mg/dL; <2.2 -1.7 mmol/L	<30 mg/dL; <1.7 mmol/L; life threatening consequences; seizures	Death
Creatinine (mg/dL)	Creatinine level increase of >0.3 mg/dL; creatinine 1.5 - 2.0 x above baseline	Creatinine 2-3 x above baseline	Creatinine >3 x baseline or >4.0 mg/dL; hospitalization indicated	Life-threatening consequences; dialysis indicate	Death

Table II. Scoring of toxicity for dose modification. Scoring of toxicity from the CTC Version 4.0, with modifications for leukocytes, platelets, prothrombin time, partial thromboplastin time, ALT, AST and bilirubin. Normal ranges for values at UCSD center are used.

Radiation Safety

There are no radiation studies in this protocol.

Data and Safety Monitoring

The principal and research coordinator of this protocol will monitor data and safety regularly at weekly meetings. These meetings are separate from regular clinical rounds and consist of review of all study patients including flow sheets of major safety and efficacy measurements. The rationale for not using an outside data and safety monitoring committee is that this is a small, single center study using a medication that has been associated with few severe side effects. All measurements and tests are well established in clinical medicine. Yearly reports are made to the UCSD IRB regarding safety and efficacy.

Adverse Event Reporting

All serious adverse events will be reported to the UCSD IRB and Galmed Pharmaceuticals within 7 days. Unexpected and related fatal or life-threatening events will be reported within 48 hours and reports will be sent to the FDA, MEDWATCH program (telephone 1-800-FDA-1088; or via the Internet at **www.fda.gov/medwatch/index.html** and Galmed Pharmaceuticals.

Informed Consents

All consents will be stored in well-marked binders in locked file cabinets located in private offices at UCSD Medical center. Databases with identifying information will be secure as they will be password protected and encrypted. Staff will be trained in HIPPA guidelines and confidentiality issues.

Patient Privacy

All data and study forms will be in secured locations (locked room or cabinet) and access is limited to study personnel. Subject names are not used; instead a name code is assigned upon enrollment. Release of data to persons or organizations outside study personnel will require written consent of the subject.

MRI Findings:

Liver MRI (Fat fraction) sequence does not provide detailed information regarding other organs within the abdomen cavity and is mainly dedicated to the liver. However, if there are any unexpected findings on the liver MRI, we would utilize following protocol to safeguard patient interest. A trained radiologist will read all MRI images. All abnormal findings will be communicated to the PI by the radiologist. Dr. Loomba (PI) is a gastroenterologist and a transplant hepatologist at UCSD who routinely provides consultation and management recommendations to other services regarding abnormal imaging findings. He would clinically correlate the significance of any unexpected MRI findings. These findings will be discussed with the patient by the study investigator and a follow-up plan will be established and documented. If the patient desires, this information will be released to the referring physician or any provider or entity that the patient would like us to send the information. The PI would be available to discuss the findings with the patient or their health care providers and assist in providing adequate follow-up. These abnormal findings would be systematically recorded and reported at yearly renewals and in the final manuscript.

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Exhibit B

Payment Schedule

The Parties agree that this Payment Schedule includes all Study-related costs, as referenced in the Protocol. Institution's sole payee for all services under this Agreement is The Regents of the University of California.

Protocol Title:	Aramchol Versus Placebo for the Treatment of HIV-associated NAFLD
Principal Investigator:	Dr. Rohit Loomba

Payee Information:

Checks shall be made payable to "The Regents of the University of California" and sent to the following address:

The Regents of the University of California
University of California-San Diego
Cashier's Office, Mail Code 0009
9500 Gilman Drive
La Jolla, CA 92093-0009

Payment Terms:

- Initial Payment. Company will make a non-refundable start-up fee payment of US $170,343 within seven (7) days from the date of contract execution.

- Milestones. Company will pay Institution in accordance with the following milestones:

  20% due when first patient randomized
  20% due when 50% of patients randomized
  20% due when all patients randomized
  10% due when the last patient finishes treatment
  10% due when the final report is submitted to Galmed

  If a Study subject discontinues from the Study for any reason, Company will pay for all payment-eligible Study visits completed by Study subject in accordance with Exhibit C.

- Tax. Should Institution be liable to pay value added tax (or any similar tax) with respect to any amount payable to it by Company hereunder, Company shall pay Institution the sum of the value added tax imposed on the amount together with the payment thereof, provided that Institution supplies Company with appropriate documentation supporting such payment obligation. Company shall be entitled to withhold any amount due as tax or other compulsory payments that applies or that shall apply to any payment due hereunder, if and to the extent required to do so by law, unless Institution provides Company with the required tax certificates indicating either exemption from such tax withholding or the percent of tax to be withheld.

- Final Payment. Final payment will be based on all work completed in accordance with the Protocol, non-cancelable obligations, if any, and any mutually agreeable costs associated with the phase-out of Study subjects, if any, including any withheld amounts earned for Study subject visits. In the event that the scheduled payments made by Company exceed the amount due hereunder, Institution will promptly refund any such excess to Company.

- Payment Upon Termination: In the event this Agreement or Study is terminated prior to Institution's completion of the Study, which is not due to a breach of this Agreement by Institution and/or Principal Investigator or their bankruptcy/insolvency, and/or is not terminated by Institution for convenience, Company shall pay Institution for actual costs incurred in the performance of the Study up to the date of termination.

- Screen Failures. Company will pay Institution for screening potential Study subjects who are not enrolled in the Study at the rate designated in the Budget, per screened and non-enrolled subject. Institution agrees to use reasonable efforts to select appropriate potential Study subjects to screen.

- Unscheduled Visits. In accordance with the Protocol for those Study subjects who require a visit outside of the scheduled visits, Institution will be reimbursed at the rate designated in the Budget.

- Full Remuneration. Neither Institution, nor the Principal Investigator, shall be entitled to any additional compensation and/or remuneration other than as explicitly set forth in this Agreement, including any expenses incurred by any of them in the performance of their tasks pursuant to this Agreement.

Exhibit C

[Budget]

CERTAIN PORTIONS OF THIS EXHIBIT HAVE BEEN OMITTED AND ARE SUBJECT TO A CONFIDENTIAL TREATMENT REQUEST. COPIES OF THIS EXHIBIT CONTAINING THE OMITTED INFORMATION HAVE BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION. THE OMITTED PORTIONS OF THIS DOCUMENT ARE MARKED WITH A [***].

UCSD PROPOSAL BUDGET FORM

University of California - San Diego

Cumulative Budget

Cumulative Budget Period: **From** **9/1/14** **Through** **8/31/19**

UCSD# **TBD**

	Year 1	Year 2	Year 3	Year 4	Year 5	Cumulative
Salaries	[***]	[***]	[***]	[***]	[***]	[***]
Fringe Benefits	34,418	36,101	26,632	1,361	1,455	99,967
Tuition Remission	-	-	-	-	-	-
Consultant(s)	-	-	-	-	-	-
Patient Costs	98,000	98,000	49,000	-	-	245,000
Supplies and Materials	3,000	3,000	3,000	-	-	9,000
Travel	3,000	6,000	6,000	3,000	-	18,000
Subaward(s)	-	-	-	-	-	-
Other Expenses	23,007	19,055	19,629	6,512	2,513	70,716
Total Direct Costs	$ [***]	$ [***]	$ [***]	$ [***]	$ [***]	$ [***]
Total Indirect Costs	$ 63,061	$ 63,883	$ 43,079	$ 3,748	$ 1,980	$ 175,750
Total Costs Requested	$ [***]	$ [***]	$ [***]	$ [***]	$ [***]	$ [***]

Office of Contract and Grant Administration – 11/2018

Exhibit 11.1

GALMED PHARMACEUTICALS LTD.

CODE OF BUSINESS CONDUCT AND ETHICS

Introduction

Purpose and Scope

The Board of Directors (the "Board") of Galmed Pharmaceuticals Ltd. (together with its subsidiaries, the "Company") established this Code of Business Conduct and Ethics (this "Code") to put in place a system to aid the Company's employees, officers and directors (the "Covered Persons") in making ethical and legal decisions when conducting the Company's business and performing their day-to-day duties and to ensure that the Company becomes aware of and takes prompt action against any questionable behavior. Ethical behavior is required and expected of every Covered Person. Among other things, this Code is designed and intended to:

- Promote honest and ethical conduct, including fair dealing and the ethical handling of actual or apparent conflicts of interest between personal and professional relationships;
- Promote full, fair, accurate, timely and understandable disclosure in reports and documents the Company files with, or submits or furnishes to, the U.S. Securities and Exchange Commission and other applicable governmental authorities, and in its other public communications;
- Promote compliance with applicable governmental laws, rules and regulations;
- Ensure the protection of the Company's assets, including its intellectual property, and legitimate business interests;
- Deter wrongdoing;
- Promote the prompt internal reporting of violations of this Code to the appropriate person at the Company as identified herein; and
- Promote accountability for adherence to this Code.

The Board or a committee of the Board is responsible for administering this Code. The Board has delegated day-to-day responsibility for administering and interpreting this Code to the Company's General Counsel to act as the Company's Compliance Officer (the "Compliance Officer") under this Code.

The Company expects each Covered Person to exercise reasonable judgment when conducting the Company's business. The Company encourages each Covered Person to refer to this Code frequently to ensure that he or she is acting within both the letter and the spirit of this Code. The Company also understands that this Code will not contain the answer to every situation you may encounter or every concern you may have about conducting the Company's business ethically and legally. In these situations, or if you otherwise have questions or concerns about this Code, the Company encourages each Covered Person to speak with his or her supervisor (if applicable) or, if you are uncomfortable doing that, with the Compliance Officer under this Code.

If a law conflicts with a policy in this Code, you must comply with the law; however, if you have any questions about any such conflict, you should ask your supervisor or the Compliance Officer how to handle the situation.

Contents of this Code

This Code has two sections which follow this Introduction. The first section, "Standards of Conduct", contains the actual guidelines that each Covered Person is expected to adhere to in the conduct of the Company's business. The second section, "Compliance Procedures", contains specific information about how this Code functions, including who administers this Code, who can provide guidance under this Code and how violations may be reported, investigated and punished. This second section also contains a discussion about waivers of and amendments to this Code.

A Note About Other Obligations

Each Covered Person generally has other legal and contractual obligations to the Company. This Code is not intended to reduce or limit the other obligations that you may have to the Company. Instead, the standards in this Code should be viewed as the minimum standards that the Company expects from each Covered Person in the conduct of the Company's business.

Standards of Conduct

Conflicts of Interest

The Company recognizes and respects the right of Covered Persons to engage in outside activities which they may deem proper and desirable, provided that these activities do not impair or interfere with the performance of their duties to the Company or their ability to act in the Company's best interests. In most, if not all, cases this will mean that Covered Persons must avoid situations that present a potential, apparent or actual conflict between their personal interests and the Company's interests.

A "conflict of interest" occurs when a Covered Person's personal interest interferes with the Company's interests. Conflicts of interest may arise in many situations. For example, conflicts of interest can arise when a Covered Person takes an action or has an outside interest, responsibility or obligation that may make it difficult for him or her to perform the responsibilities of his or her position objectively and/or effectively in the Company's best interests. Conflicts of interest may also occur when a Covered Person or his or her immediate family member receives some personal benefit (whether improper or not) as a result of the Covered Person's position with the Company. Each individual's situation is different and in evaluating his or her own situation, a Covered Person will have to consider many factors.

Loans to, or guarantees of obligations of, Covered Persons or their family members may create conflicts of interest. It is almost always a conflict of interest for a Covered Person to work or provide services simultaneously for a competitor, customer or supplier. If you are unsure whether working or providing services simultaneously for a competitor, customer or supplier creates a conflict of interest, please consult with the Compliance Officer.

Any material transaction or relationship that reasonably could be expected to give rise to a conflict of interest should be reported promptly to the Compliance Officer. The Compliance Officer may notify the Board or a committee thereof as he or she deems appropriate.

The provisions of this Code in no way derogate from the provisions of any applicable laws. Directors and officers of the Company owe a duty of loyalty to the Company and they should familiarize themselves with the nature and extent of this duty, as well as with the disclosure requirements under applicable law which apply to them and with the process of approving transactions between them and the Company or in which they have a personal interest. The requirements and provisions of applicable law, including, without limitation, the Israeli Companies Law, on these matters are separate and are not part of this Code.

Compliance with Laws, Rules and Regulations

The Company seeks to conduct its business in compliance with applicable laws, rules and regulations in the jurisdictions in which the Company conducts business. No Covered Person shall engage in any unlawful activity in conducting the Company's business or in performing his or her day-to-day company duties, nor shall any Covered Person instruct others to do so.

To maintain the Company's valuable reputation, compliance with our quality processes and safety requirements is essential. In the context of ethics, quality requires that our products and services will be designed and manufactured to meet our obligations to customers in the future. All inspection and testing documents must be handled in accordance with all applicable regulations.

Licensure and Certification

Covered Persons and other healthcare professionals and facilities retained by the Company in positions which require professional licenses, certifications or other credentials are responsible for maintaining the current status of their licenses, certifications and credentials and shall comply at all times with governmental requirements applicable to them . To ensure compliance, the Company may require evidence of the individual or facility having a current license or credential status.

The Company does not allow any Covered Person or other healthcare professional or facility to work or provide services without valid, current licenses or credentials, or to otherwise provide services unless fully authorized to do so by law.

Protection and Proper Use of the Company's Assets

Loss, theft and misuse of the Company's assets has a direct impact on the Company's business and its profitability. Covered Persons are expected to protect the Company's tangible and intangible assets, including, without limitation, its owned and licensed intellectual property, that are entrusted to them and to protect the Company's assets in general. Covered Persons are also expected to take steps to ensure that the Company's assets are used only for legitimate business purposes and in compliance with all applicable laws.

Corporate Opportunities

Covered Persons owe a duty to the Company to advance its legitimate business interests when the opportunity to do so arises. Each Covered Person is prohibited from:

- diverting to himself or herself or to others any opportunities that are discovered through the use of the Company's assets, property or information or as a result of his or her position with the Company, unless such opportunity has first been presented to, and rejected by, the Company;
- using the Company's assets, property or information or his or her position for improper personal gain; and
- competing with the Company.

Confidentiality

Confidential Information generated and gathered in the Company's business plays a vital role in its business, prospects and ability to compete. "Confidential Information" includes all non-public information that might be of use to competitors or harmful to the Company or its customers if disclosed. Covered Persons may not disclose or distribute the Company's Confidential Information, except when disclosure is authorized by the Company or required by applicable law, rule or regulation or pursuant to an applicable legal proceeding. Covered Persons shall use Confidential Information solely for legitimate company purposes. Covered Persons must return all of the Company's Confidential Information and proprietary information in their possession to the Company when they cease to be employed or engaged by or to otherwise serve the Company. To the extent more restrictive than the foregoing, the confidentiality provisions contained herein shall in no way derogate from the provisions and obligations of any Covered Person contained in any restrictive covenant or confidentiality agreement to which such Covered Person is a party.

Competition and Fair Dealing

Competing vigorously, yet lawfully, with competitors and establishing advantageous, but fair, business relationships with customers and suppliers is a part of the foundation for long-term success. However, unlawful and unethical conduct, which may lead to short-term gains, may damage a company's reputation and long-term business prospects. Accordingly, it is the Company's policy that Covered Persons must endeavor to deal ethically and lawfully with the Company's customers, clinical trial participants, suppliers, competitors and employees in all business dealings on the Company's behalf. Stealing proprietary information, possessing trade secret information that was obtained without the owner's consent, or inducing such disclosures by past or present employees of other companies is prohibited. No Covered Person should take unfair advantage of another person in business dealings on the Company's behalf through the abuse of privileged or confidential information or through improper manipulation, concealment or misrepresentation of material facts or otherwise.

Accuracy of Records

The integrity, reliability and accuracy in all material respects of the Company's books, records and financial statements is fundamental to the Company's continued and future business success. No Covered Person may cause the Company to enter into a transaction with the intent to document or record it in a deceptive or unlawful manner. In addition, no Covered Person may create any false or artificial documentation or book entry for any transaction entered into by the Company. Similarly, Covered Persons who have responsibility for accounting and financial reporting matters have a responsibility to accurately record all funds, assets and transactions on the Company's books and records.

Covered Persons are prohibited from directly or indirectly taking any action to fraudulently influence, coerce, manipulate or mislead the Company's independent auditors for the purpose of rendering the financial statements of the Company misleading.

Quality of Public Disclosures

The Company is committed to providing its shareholders with complete and accurate information about its financial condition and results of operations as required by the securities laws of the United States. It is the Company's policy that the reports and documents it files with or submits to the U.S. Securities and Exchange Commission, and its earnings releases and similar public communications made by the Company, include fair, timely and understandable disclosure. Covered Persons who are responsible for these filings and disclosures, including the Company's principal executive, financial and accounting officers, must use reasonable judgment and perform their responsibilities honestly, ethically and objectively to ensure that this disclosure policy is fulfilled. The Company's senior management are primarily responsible for monitoring the Company's public disclosure.

Insider Trading

In the course of a Covered Person's service for or employment with the Company, such Covered Person is likely to use or have access to information about the Company that is not generally available to the public. Because of such relationship with the Company, Covered Persons have certain responsibilities under the U.S. federal securities laws with respect to inside information. The Company has set forth in its Policy Statement on Inside Information and Insider Trading (the "Insider Trading Policy") its policies regarding the protection of "inside information" and trading and "tipping" (each as defined in the Insider Trading Policy), as well as the expected standards of conduct of the Company's directors, "management insiders", "financial insiders", "systems insiders", or "other insiders" (each as defined in the Insider Trading Policy) with respect to these highly sensitive matters. The Company's Insider Trading Policy is not a part of this Code. However, any Covered Person who is uncertain about the legal rules involving a purchase or sale of any Company securities or any securities in companies with which he or she is familiar by virtue of his or her work for the Company or whether the Insider Trading Policy applies to him or her, should consult with the Company's General Counsel and review the same, a copy of which may be obtained from the Company's General Counsel.

Bribes, Kickbacks and Other Improper Payments

The Company does not permit or condone bribes, kickbacks or other improper payments, transfers or receipts. No Covered Person should offer, give, solicit or receive any money or other item of value for the purpose of obtaining, retaining or directing business or bestowing or receiving any kind of favored treatment. In particular, the U.S. Foreign Corrupt Practices Act of 1977 (the "FCPA") prohibits any U.S. individual or business from authorizing, offering or paying money or anything of value, directly or indirectly, to any foreign official or employee, political party, or candidate for public office for the purpose of obtaining or maintaining business or for any other business advantage. The Company strictly prohibits making illegal payments to government officials, employees, parties or candidates for office of any country. Violation of applicable law, including, without limitation, the FCPA, could subject the Company and the Covered Persons to serious fines and criminal penalties.

Discrimination and Harassment

The diversity of the Company's employees and consultants is a tremendous asset. We are firmly committed to providing equal opportunity in all aspects of employment and service and will not tolerate any illegal discrimination or harassment or any kind.

Health and Safety

The Company strives to provide each Covered Person with a safe and healthful work environment. Each Covered Person has responsibility for maintaining a safe and healthy workplace for all Covered Persons by following safety and health rules and practices and reporting accidents, injuries and unsafe equipment, practices or conditions.

Violence and threatening behavior are not permitted. Covered Persons should report to work in a condition to perform their duties, free from the influence of illegal drugs or alcohol. The use of illegal drugs in the workplace will not be tolerated.

Compliance Procedures

The Compliance Procedures contained herein provide, among other things, an enforcement mechanism that is intended to ensure prompt and consistent enforcement of this Code, protection for persons reporting questionable behavior, clear and objective standards for compliance and a fair process by which to determine violations.

Communication of Code

All Covered Persons will be supplied with a copy of this Code upon beginning service at the Company and will be asked to review and sign an acknowledgment regarding this Code on a periodic basis. Updates of this Code will be provided from time to time. A copy of this Code is also available to all Covered Persons by requesting one from the Compliance Officer or by accessing the Company's website at http://www.galmedpharma.com/

Monitoring Compliance and Disciplinary Action

The Company's management, under the supervision of the Board or a committee thereof or, in the case of accounting, internal accounting controls, auditing or securities law matters, the Audit Committee of the Board (the "Audit Committee"), shall take reasonable steps from time to time to (i) monitor compliance with this Code and (ii) when appropriate, impose and enforce appropriate disciplinary measures for violations of this Code.

Disciplinary measures for violations of this Code will be determined in the Company's sole discretion and may include, but are not limited to, counseling, oral or written reprimands, warnings, probation or suspension with or without pay, demotions, reductions in salary, termination of employment or service, and restitution.

The Company's management shall periodically report to the Board or a committee thereof on these compliance efforts including, without limitation, periodic reporting of alleged violations of this Code and the actions taken with respect to any such violation.

Reporting Concerns/Receiving Advice

Communication Channels

Be Proactive. Reporting of questionable behavior is protected and encouraged, and fosters an atmosphere of self-awareness and prudent conduct. Every Covered Person is expected to act proactively by asking questions, seeking guidance and reporting suspected violations of this Code and other policies and procedures of the Company, as well as any violation or suspected violation of applicable law, rule or regulation arising in the conduct of the Company's business or occurring on the Company's property. **If any Covered Person believes that actions have taken place, may be taking place, or may be about to take place that violate or would violate this Code or any law, rule or regulation applicable to the Company, he or she must bring the matter to the attention of the Company**.

Seeking Guidance. The best starting point for a Covered Person seeking advice on ethics-related issues or reporting potential violations of this Code will usually be his or her supervisor, but may be the Compliance Officer. However, if the conduct in question involves his or her supervisor, if the Covered Person has reported the conduct in question to his or her supervisor and does not believe that he or she has dealt with it properly, or if the Covered Person does not feel that he or she can discuss the matter with his or her supervisor, the Covered Person may raise the matter with the Compliance Officer.

Communication Alternatives. Any Covered Person may communicate any concerns or questions, including any potential violations of this Code, any Company policy or procedure or applicable law, rule or regulation, with the Compliance Officer by any of the following methods:

- **In writing (which may be done anonymously as set forth below under "Reporting; Anonymity; Retaliation"), addressed to the Compliance Officer, by mail to c/o: Galmed Pharmaceuticals Ltd., 8 Shaul Ha'melech Blvd., Amot Mishpat Bldg., Tel Aviv, Israel 64733. or**

- **By e-mail to: ethics@galmedpharma.com**

Reporting Accounting and Similar Concerns. Any concerns or questions regarding any potential violations of this Code, any company policy or procedure or applicable law, rules or regulations that specifically involves accounting, internal accounting controls, auditing or related or similar matters should be directed to both the Compliance Officer and the Audit Committee or a designee of the Audit Committee in the same manners as set forth above.

Cooperation. Covered Persons are expected to cooperate with the Company in any investigation of a potential violation of this Code, any other Company policy or procedure, or any applicable law, rule or regulation.

Misuse of Reporting Channels. Covered Persons must not use these reporting channels in bad faith or in a false or frivolous manner. Furthermore, Covered Persons should not use the off-site voicemail account to report grievances that do not involve this Code or other ethics-related issues.

Reporting; Anonymity; Retaliation

When reporting suspected violations of this Code, the Company prefers that Covered Persons identify themselves to facilitate the Company's ability to take appropriate steps to address the report, including conducting any appropriate investigation. However, the Company also recognizes that some people may feel more comfortable reporting a suspected violation anonymously.

If a Covered Person wishes to remain anonymous, he or she may do so, and the Company will use reasonable efforts to protect the confidentiality of the reporting person subject to applicable law, rule or regulation or to any applicable legal proceedings. In the event the report is made anonymously, however, the Company may not have sufficient information to look into or otherwise investigate or evaluate the allegations. Accordingly, persons who make reports anonymously should provide as much detail as is reasonably necessary to permit the Company to evaluate the matter(s) set forth in the anonymous report and, if appropriate, commence and conduct an appropriate investigation.

No Retaliation

The Company expressly forbids any retaliation against any Covered Person who, acting in good faith on the basis of a reasonable belief, reports suspected misconduct. Specifically, the Company will not discharge, demote, suspend, threaten, harass or in any other manner discriminate against, such a Covered Person in the terms and conditions of his or her employment or service. Any person who participates in any such retaliation will be subject to disciplinary action, including termination.

Waivers and Amendments

No waiver of any provision of this Code for the benefit of a director or an executive officer (which includes without limitation, for purposes of this Code, the Company's principal executive, financial and accounting officers) shall be effective unless (i) approved by the Board and (ii) such waiver and the reason(s) for such waiver are promptly disclosed to the Company's shareholders in accordance with applicable U.S. securities laws and/or the rules and regulations of the exchange or system on which the Company's shares are traded or quoted, as the case may be. This disclosure requirement is intended to provide our shareholders with the comfort that waivers are not granted except where they are truly necessary and warranted, and that they are limited and qualified so as to protect the Company and its shareholders to the greatest extent possible.

Any waivers of this Code for other Covered Persons may be made by the Compliance Officer, the Board or, if permitted, a committee thereof.

All amendments to this Code must be approved by the Board or a committee thereof and, if applicable, must be promptly disclosed to the Company's shareholders in accordance with applicable U.S. securities laws and/or the rules and regulations of the exchange or system on which the Company's shares are traded or quoted, as the case may be.

ADOPTED BY THE BOARD OF DIRECTORS: March 30, 2015

Exhibit 12.1

CERTIFICATION

I, Allen Baharaff, certify that:

1. I have reviewed this Annual Report on Form 20-F of Galmed Pharmaceuticals Ltd.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;

4. The Company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and

5. The Company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's board of directors (or persons performing the equivalent 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.

By: /s/ Allen Baharaff
Allen Baharaff
President and Chief Executive Officer

Date: March 31, 2015

Exhibit 12.2

CERTIFICATION

I, Josh Blacher, certify that:

1. I have reviewed this Annual Report on Form 20-F of Galmed Pharmaceuticals Ltd.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the Company as of, and for, the periods presented in this report;

4. The Company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the period covered by the annual report that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and

5. The Company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the audit committee of the Company's board of directors (or persons performing the equivalent 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.

By: /s/ Josh Blacher
Josh Blacher
Chief Financial Officer

Date: March 31, 2015

Exhibit 13.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Galmed Pharmaceuticals Ltd. (the "Company") on Form 20-F for the period ending December 31, 2014, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned hereby certify that to the best of our knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operation of the Company.

By: /s/ Allen Baharaff
Allen Baharaff
President and Chief Executive Officer

By: /s/ Josh Blacher
Josh Blacher
Chief Financial Officer

Date: March 31, 2015

The certification set forth above is being furnished as an exhibit solely pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 and is not being filed as part of the Annual Report on Form 20-F for the period ended December 31, 2014, or as a separate disclosure document of the Company or the certifying officers.