XTL BIOPHARMACEUTICALS LTD
Form 20-F
March 23, 2007

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

FORM 20-F

(Mark One)
o REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2006

OR

o TRANSITIONAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

o SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from _____to _____.

Commission file number **000-51310**

XTL BIOPHARMACEUTICALS LTD.
(Exact name of registrant as specified in its charter)

Israel
(Jurisdiction of incorporation or organization)

750 Lexington Avenue, 20th Floor
New York, New York 10022
(Address of principal executive offices)

Securities registered or to be registered pursuant to Section 12(b) of the Act:
American Depositary Shares,
each representing ten Ordinary Shares, par value NIS 0.02
(Title of Class)

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

None.

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

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report.

4,333,047 American Depositary Shares	220,124,349 Ordinary Shares

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

Yes o No ý

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 o No ý

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

Yes ý No o

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 ý Non-accelerated filer £

Indicate by check mark which financial statement item the registrant has elected to follow.

Item 17 o Item 18 ý

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes o No ý

XTL BIOPHARMACEUTICALS LTD.
ANNUAL REPORT ON FORM 20-F

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This annual report on Form 20-F contains trademarks and trade names of XTL Biopharmaceuticals Ltd., including our name and logo.

SPECIAL CAUTIONARY NOTICE REGARDING FORWARD-LOOKING STATEMENTS

Certain matters discussed in this report, including matters discussed under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations," may constitute forward-looking statements for purposes of the Securities Act of 1933, as amended, or the Securities Act, and the Securities Exchange Act of 1934, as amended, or the Exchange Act, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from the future results, performance or achievements expressed or implied by such forward-looking statements. The words "expect," "anticipate," "intend," "plan," "believe," "seek," "estimate," and similar expressions are intended to identify such forward-looking statements. Our actual results may differ materially from the results anticipated in these forward-looking statements due to a variety of factors, including, without limitation, those discussed under "Item 3. Key Information-Risk Factors," "Item 4.- Information on the Company," "Item 5. Operating and Financial Review and Prospects," and elsewhere in this report, as well as factors which may be identified from time to time in our other filings with the Securities and Exchange Commission, or the SEC, or in the documents where such forward-looking statements appear. All written or oral forward-looking statements attributable to us are expressly qualified in their entirety by these cautionary statements.

The forward-looking statements contained in this report reflect our views and assumptions only as of the date this report is signed. Except as required by law, we assume no responsibility for updating any forward-looking statements.

PART I

Unless the context requires otherwise, references in this report to "XTL," "we," "us" and "our" refer to XTL Biopharmaceuticals Ltd. and our wholly-owned subsidiaries, XTL Biopharmaceuticals, Inc. and XTL Development, Inc. We have prepared our consolidated financial statements in United States, or US, dollars and in accordance with US generally accepted accounting principles, or US GAAP. All references herein to "dollars" or "$" are to US dollars, and all references to "Shekels" or "NIS" are to New Israeli Shekels.

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

Not applicable

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

Not applicable

ITEM 3. KEY INFORMATION

Selected Financial Data

The table below presents selected statement of operations and balance sheet data for the fiscal years ended and as of December 31, 2006, 2005, 2004, 2003 and 2002. We have derived the selected financial data for the fiscal years ended December 31, 2006, 2005, and 2004, and as of December 31, 2006 and 2005, from our audited consolidated financial statements, included elsewhere in this report and prepared in accordance with US GAAP. We have derived the selected financial data for fiscal years ended December 31, 2003 and 2002 and as of December 31, 2004, 2003 and 2002, from audited financial statements not appearing in this report, which have been prepared in accordance with US GAAP. You should read the selected financial data in conjunction with "Item 5. Operating and Financial Review and Prospects," "Item 8. Financial Information" and "Item 18. Financial Statements."

	Year Ended December 31,				
	2006	2005	2004	2003	2002
	(In thousands, except share and per share amounts)				
Statements of Operations Data:					
Revenues					
Reimbursed out-of-pocket expenses	$ --	$ 2,743	$ 3,269	$ --	$ --
License	454	454	185	--	--
	454	3,197	3,454	--	--
Cost of Revenues					
Reimbursed out-of-pocket expenses	--	2,743	3,269	--	--
License (with respect to royalties)	54	54	32	--	--
	54	2,797	3,301		
Gross Margin	400	400	153	--	--
Research and development					
Research and development costs	10,229	7,313	11,985	14,022	13,231
Less participations	--	--	--	3,229	75
	10,229	7,313	11,985	10,793	13,156
In-process research and development	--	1,783	--	--	--
General and administrative	5,576	5,457	4,134	3,105	3,638
Business development costs	641	227	810	664	916
Operating loss	(16,046)	(14,380)	(16,776)	(14,562)	(17,710)
Other income (expense)					
Financial and other income, net	1,141	443	352	352	597
Taxes on income	(227)	(78)	(49)	(78)	(27)
Loss for the period	$ (15,132)	$ (14,015)	$ (16,473)	$ (14,288)	$ (17,140)
Loss per ordinary share					
Basic and diluted	$ (0.08)	$ (0.08)	$ (0.12)	$ (0.13)	$ (0.15)
Weighted average shares outstanding	201,737,295	170,123,003	134,731,766	111,712,916	111,149,292

	As of December 31,				
	2006	2005	2004	2003	2002
	(In thousands)				
Balance Sheet Data:					

Cash, cash equivalents, bank deposits and trading and marketable securities	$ 25,347	$ 13,360	$ 22,924	$ 22,262	$ 35,706
Working capital	22,694	11,385	20,240	19,967	33,396
Total assets	26,900	15,151	25,624	24,853	38,423
Long-term obligations	738	1,493	2,489	1,244	1,017
Total shareholders' equity	22,760	11,252	19,602	20,608	34,830

Risk Factors

Before you invest in our ordinary shares or American Depositary Receipts representing American Depositary Shares, which we refer to in this report as ADRs, you should understand the high degree of risk involved. You should carefully consider the risks described below and other information in this report, including our financial statements and related notes included elsewhere in this report, before you decide to purchase our ordinary shares or ADRs. If any of the following risks actually occur, our business, financial condition and operating results could be adversely affected. As a result, the trading price of our ordinary shares or ADRs could decline and you could lose part or all of your investment.

Risks Related to Our Business

We have incurred substantial operating losses since our inception. We expect to continue to incur losses in the future and may never become profitable.

You should consider our prospects in light of the risks and difficulties frequently encountered by development stage companies. We have incurred operating losses since our inception and expect to continue to incur operating losses for the foreseeable future. As of December 31, 2006, we had an accumulated deficit of approximately $114.9 million. We have not yet commercialized any of our drug candidates or technologies and cannot be sure we will ever be able to do so. Even if we commercialize one or more of our drug candidates or technologies, we may not become profitable. Our ability to achieve profitability depends on a number of factors, including our ability to complete our development efforts, obtain regulatory approval for our drug candidates and technologies and successfully commercialize them.

If we are unable to successfully complete our clinical trial programs for our drug candidates, or if such clinical trials take longer to complete than we project, our ability to execute our current business strategy will be adversely affected.

Whether or not and how quickly we complete clinical trials is dependent in part upon the rate at which we are able to engage clinical trial sites and, thereafter, the rate of enrollment of patients. Patient enrollment is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the study and the existence of competitive clinical trials. If we experience delays in identifying and contracting with sites and/or in patient enrollment in our clinical trial programs, we may incur additional costs and delays in our development programs and may not be able to complete our clinical trials on a cost-effective basis.

If third parties on which we rely for clinical trials do not perform as contractually required or as we expect, we may not be able to obtain regulatory approval for or commercialize our products.

We depend on independent clinical investigators, contract research organizations and other third-party service providers to conduct the clinical trials of our drug candidates and technologies and expect to continue to do so. We rely heavily on these parties for successful execution of our clinical trials, but we do not control many aspects of their activities. Nonetheless, we are responsible for confirming that each of our clinical trials is conducted in accordance with the general investigational plan and protocol. Our reliance on these third parties that we do not control does not relieve us of our responsibility to comply with the regulations and standards of the US Food and Drug Administration, or the FDA, relating to good clinical practices. Third parties may not complete activities on schedule or may not conduct our clinical trials in accordance with regulatory requirements or the applicable trial's plans and protocols. The failure of these third parties to carry out their obligations could delay or prevent the development, approval and commercialization of our products or result in enforcement action against us.

If the clinical data related to our drug candidates and technologies do not confirm positive early clinical data or preclinical data, our corporate strategy and financial results will be adversely impacted.

All of our drug candidates and technologies are in preclinical or clinical stages. Specifically, a clinical trial with Bicifadine for neuropathic pain indications is pending commencement, XTL-2125 and XTL-6865 are currently in a Phase I clinical trial and one of our programs under development, DOS, has not yet been tested in humans. In order for our candidates to proceed to later stage clinical testing, they must show positive preclinical or clinical data. While Bicifadine, XTL-6865 and XTL-2125 have shown promising preclinical data and Bicifadine has shown promising clinical data in the treatment of acute pain prior to it being in-licensed to us, preliminary results of pre-clinical or clinical tests do not necessarily predict the final results, and promising results in pre-clinical or early clinical testing might not be obtained in later clinical trials. Drug candidates in the later stages of clinical development may fail to show the desired safety and efficacy traits despite having progressed through initial clinical testing. Any negative results from future tests may prevent us from proceeding to later stage clinical testing which would materially impact our corporate strategy and our financial results may be adversely impacted.

We have limited experience in conducting and managing clinical trials necessary to obtain regulatory approvals. If our drug candidates and technologies do not receive the necessary regulatory approvals, we will be unable to commercialize our products.

We have not received, and may never receive, regulatory approval for commercial sale for any of our products. We currently do not have any drug candidates or technologies pending approval with the FDA or with regulatory authorities of other countries. We will need to conduct significant additional research and human testing before we can apply for product approval with the FDA or with regulatory authorities of other countries. Pre-clinical testing and clinical development are long, expensive and uncertain processes. Satisfaction of regulatory requirements typically depends on the nature, complexity and novelty of the product and requires the expenditure of substantial resources. Regulators may not interpret data obtained from pre-clinical and clinical tests of our drug candidates and technologies the same way that we do, which could delay, limit or prevent our receipt of regulatory approval. It may take us many years to complete the testing of our drug candidates and technologies, and failure can occur at any stage of this process. Negative or inconclusive results or medical events during a clinical trial could cause us to delay or terminate our development efforts.

Clinical trials also have a high risk of failure. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in clinical trials, even after achieving promising results in earlier trials. If we experience delays in the testing or approval process or if we need to perform more or larger clinical trials than originally planned, our financial results and the commercial prospects for our drug candidates and technologies may be materially impaired. In addition, we have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approval in the US and abroad and, accordingly, may encounter unforeseen problems and delays in the approval process.

Even if regulatory approval is obtained, our products and their manufacture will be subject to continual review, and there can be no assurance that such approval will not be subsequently withdrawn or restricted. Changes in applicable legislation or regulatory policies, or discovery of problems with the products or their manufacture, may result in the imposition of regulatory restrictions, including withdrawal of the product from the market, or result in increased costs to us.

Because we license some of our proprietary technologies from third-parties, some of these third-parties could prevent us from licensing our drug candidates.

We do not own all of our drug candidates and technologies. We have licensed the patent rights to some of our drug candidates and/or the technologies on which they are based from others. Specifically, we have licensed Bicifadine

from Dov Pharmaceutical, Inc., or DOV, who in turn licensed it from Wyeth Pharmaceuticals, Inc., or Wyeth. In addition, we have licensed XTL-2125 from B&C Biopharm Co. Ltd., we have licensed the two human monoclonal antibodies comprising XTL-6865 from Stanford University and DRK-Blutspendedienst Baden-Wurttemberg, and we have licensed certain other Hepatitis C virus, or HCV, compounds from VivoQuest Inc., or VivoQuest. We have also licensed the Trimera technology that was used in the development of XTL-6865, XTL-2125 and HepeX-B from the Yeda Research and Development Company Ltd., which we refer to as Yeda. These license agreements require us to meet development or financing milestones and impose development and commercialization due diligence requirements on us. In addition, under these agreements, we must pay royalties on sales of products resulting from licensed drugs and technologies and pay the patent filing, prosecution and maintenance costs related to the licenses. While we have the right to defend patent rights related to our licensed drug candidates and technologies, we are not obligated to do so. In the event that we decide to defend our licensed patent rights, we will be obligated to cover all of the expenses associated with that effort. If we do not meet our obligations in a timely manner or if we otherwise breach the terms of our agreements, our licensors could terminate the agreements, and we would lose the rights to our drug candidates and technologies. For a further discussion on our license agreements, the patent rights related to those licenses, and the expiration dates of those patent rights, see “Item 4. Information on the Company - Business Overview - Intellectual Property and Patents” and “Item 4. Information on the Company - Business Overview - Licensing Agreements and Collaborations,” below. In addition, see “- Risks Related to Our Intellectual Property,” below regarding potential issues related to the use of patents owned by third-parties.

In addition, under the terms of our license agreement with Yeda, we are required to obtain their approval under the license in order to grant sub-licenses to collaborative partners to develop or commercialize XTL-6865, XTL-2125 and HepeX-B. The requirement of obtaining these approvals, and any conditions that Yeda may impose upon such approvals, could have the effect of delaying or impeding our ability to enter into agreements with collaborative partners or result in our having to accept terms and conditions that might not be favorable to us. For a discussion of further required approvals, see "- Risks Relating to Operations in Israel," below regarding potential restrictions from the Office of the Chief Scientist regarding the manufacture of XTL-6865, XTL-2125 and HepeX-B outside the State of Israel.

If we do not establish or maintain drug development and marketing arrangements with third parties, we may be unable to commercialize our drug candidates and technologies into products.

We are an emerging company and do not possess all of the capabilities to fully commercialize our drug candidates and technologies on our own. From time to time, we may need to contract with third parties to:

- assist us in developing, testing and obtaining regulatory approval for some of our compounds and technologies;
- manufacture our drug candidates; and
- market and distribute our products.

We can provide no assurance that we will be able to successfully enter into agreements with such third-parties on terms that are acceptable to us. If we are unable to successfully contract with third parties for these services when needed, or if existing arrangements for these services are terminated, whether or not through our actions, or if such third parties do not fully perform under these arrangements, we may have to delay, scale back or end one or more of our drug development programs or seek to develop or commercialize our drug candidates and technologies independently, which could result in delays. Further, such failure could result in the termination of license rights to one or more of our drug candidates and technologies. Moreover, if these development or marketing agreements take the form of a partnership or strategic alliance, such arrangements may provide our collaborators with significant discretion in determining the efforts and resources that they will apply to the development and commercialization of our products. Accordingly, to the extent that we rely on third parties to research, develop or commercialize our products, we are unable to control whether such products will be scientifically or commercially successful.

For example, in June 2004, we announced the completion of a license agreement with Cubist Pharmaceuticals, Inc., or Cubist, for the worldwide development and commercialization of HepeX-B. Under this agreement, we were responsible for certain clinical and product development activities of HepeX-B through August 2005, at the expense of Cubist. Thereafter, we transferred full responsibility for completing the development of HepeX-B to Cubist. In July 2006, Cubist announced that it has decided not to make any further investment in the HepeX-B program, while it evaluates its strategic options for HepeX-B, including the sub-licensing of the product. Accordingly, at this time there can be no assurance that the drug candidate will be further developed in the future, that any such development would be successful, or that we will receive any proceeds from the sales of HepeX-B.

If our products fail to achieve market acceptance, we will never record meaningful revenues.

Even if our products are approved for sale, they may not be commercially successful in the marketplace. Market acceptance of our product candidates will depend on a number of factors, including:

- perceptions by members of the health care community, including physicians, of the safety and efficacy of our products;

- the rates of adoption of our products by medical practitioners and the target populations for our products;
- the potential advantages that our products offer over existing treatment methods or other products that may be developed;
- the cost-effectiveness of our products relative to competing products;
- the availability of government or third-party payor reimbursement for our products;
- the side effects or unfavorable publicity concerning our products or similar products; and
- the effectiveness of our sales, marketing and distribution efforts.

Because we expect sales of our products to generate substantially all of our revenues in the long-term, the failure of our products to find market acceptance would harm our business and could require us to seek additional financing or other sources of revenue.

If the third parties upon whom we rely to manufacture our products do not successfully manufacture our products, our business will be harmed.

We do not currently have the ability to manufacture for ourselves the compounds that we need to conduct our clinical trials and, therefore, rely upon a limited number of manufacturers to supply our drug candidates. We have no experience in manufacturing compounds for clinical or commercial purposes and do not have any manufacturing facilities. We rely upon, and intend to continue to rely upon, third parties to manufacture our drug candidates for use in clinical trials and for future sales. In order to commercialize our products, such products will need to be manufactured in commercial quantities while adhering to all regulatory and other requirements, all at an acceptable cost. We may not be able to enter into future third-party contract manufacturing agreements on acceptable terms, if at all.

We expect to continue to rely on contract manufacturers and other third parties to produce sufficient quantities of our drug candidates for use in our clinical trials. See “Item 4. Information on the Company - Business Overview - Supply and Manufacturing,” below. We believe that our existing manufacturing arrangements with these parties will be adequate to satisfy our current clinical supply needs for XTL-2125 and XTL-6865, and that our agreement with DOV provides us with access to sufficient inventory to satisfy our current clinical supply needs for Bicifadine. If our contract manufacturers or other third parties, such as DOV, fail to deliver our product candidates for clinical use on a timely basis, with sufficient quality, and at commercially reasonable prices, and we fail to find replacement manufacturers, we may be required to delay or suspend clinical trials or otherwise discontinue development and production of our drug candidates.

Our contract manufacturers are required to produce our drug candidates in strict compliance with current good manufacturing practices, or cGMP, in order to meet acceptable standards for our clinical trials. If such standards change, the ability of contract manufacturers to produce our drug candidates on the schedule we require for our clinical trials may be affected. In addition, contract manufacturers may not perform their obligations under their agreements with us or may discontinue their business before the time required by us to successfully produce and market our drug candidates. Any difficulties or delays in our contractors’ manufacturing and supply of drug candidates could increase our costs, cause us to lose revenue or make us postpone or cancel clinical trials.

In addition, our contract manufacturers will be subject to ongoing periodic, unannounced inspections by the FDA and corresponding foreign governmental agencies to ensure strict compliance with, among other things, current good manufacturing practices, in addition to other governmental regulations and corresponding foreign standards. We will not have control over, other than by contract, third-party manufacturers’ compliance with these regulations and standards. No assurance can be given that our third-party manufacturers will comply with these regulations or other regulatory requirements now or in the future.

In the event that we are unable to obtain or retain third-party manufacturers, we will not be able to commercialize our products as planned. If third-party manufacturers fail to deliver the required quantities of our products on a timely basis and at commercially reasonable prices, our ability to develop and deliver products on a timely and competitive basis may be adversely impacted and our business, financial condition or results of operations will be materially harmed.

If our competitors develop and market products that are less expensive, more effective or safer than our products, our commercial opportunities may be reduced or eliminated.

The pharmaceutical industry is highly competitive. Our commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective or safer than our products. Other companies have drug candidates in various stages of pre-clinical or clinical development to treat diseases for which we are also seeking to discover and develop drug candidates. For a discussion of these competitors and their drug candidates, see “Item 4. Information on the Company - Business Overview - Competition,” below. Some of these potential competing drugs are further advanced in development than our drug candidates and may be commercialized earlier. Even if we are successful in developing safe, effective drugs, our products may not compete successfully with products produced by our competitors, who may be able to more effectively market their drugs.

Our competitors include pharmaceutical companies and biotechnology companies, as well as universities and public and private research institutions. In addition, companies that are active in different but related fields represent substantial competition for us. Many of our competitors have significantly greater capital resources, larger research and development staffs and facilities and greater experience in drug development, regulation, manufacturing and marketing than we do. These organizations also compete with us to recruit qualified personnel, attract partners for joint ventures or other collaborations, and license technologies that are competitive with ours. As a result, our competitors may be able to more easily develop products that could render our technologies or our drug candidates obsolete or noncompetitive.

If we lose our key personnel or are unable to attract and retain additional personnel, our business could be harmed.

As of February 28, 2007, we had 33 full-time employees. To successfully develop our drug candidates and technologies, we must be able to attract and retain highly skilled personnel. The retention of their services cannot be guaranteed. In particular, if we lose the services of Michael S. Weiss, our Chairman, or Ron Bentsur, our Chief Executive Officer, our ability to continue to execute on our business plan could be materially impaired. Our agreement with Mr. Weiss provides that he may terminate his agreement with us upon 30 days' prior written notice if he is not re-elected as Chairman of our Board, his fees for service as Chairman are reduced by more than 10%, we breach any material term of his agreement, or there is a change of control or reorganization of our company. Our agreement with Mr. Bentsur provides that he may terminate his agreement with us upon 30 days' prior written notice if he is no longer the highest ranking member of our company's management team, his annual base salary is reduced by more than 10% (except where we have made similar reductions in the base salary of senior management throughout our company), we breach any material term of his agreement, or there is a change of control or reorganization of our company. We do not maintain a key man life insurance policy covering either Mr. Weiss or Mr. Bentsur.

Any acquisitions we make may dilute your equity or require a significant amount of our available cash and may not be scientifically or commercially successful.

As part of our business strategy, we may effect acquisitions to obtain additional businesses, products, technologies, capabilities and personnel. If we make one or more significant acquisitions in which the consideration includes our ordinary shares or other securities, your equity in us may be significantly diluted. If we make one or more significant acquisitions in which the consideration includes cash, we may be required to use a substantial portion of our available cash.

Acquisitions also involve a number of operational risks, including:

- difficulty and expense of assimilating the operations, technology and personnel of the acquired business;
- our inability to retain the management, key personnel and other employees of the acquired business;
- our inability to maintain the acquired company's relationship with key third parties, such as alliance partners;
- exposure to legal claims for activities of the acquired business prior to the acquisition;
- the diversion of our management's attention from our core business; and
-

the potential impairment of substantial goodwill and write-off of in-process research and development costs, adversely affecting our reported results of operations.

In addition, the basis for completing the acquisition could prove to be unsuccessful as the drugs or processes involved could fail to be scientifically or commercially viable. In addition, we may be required to pay third parties substantial transaction fees, in the form of cash or ordinary shares, in connection with such transactions.

If any of these risks occur, it could have an adverse effect on both the business we acquire and our existing operations.

We face product liability risks and may not be able to obtain adequate insurance.

The use of our drug candidates and technologies in clinical trials, and the sale of any approved products, exposes us to liability claims. Although we are not aware of any historical or anticipated product liability claims against us, if we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to cease clinical trials of our drug candidates and technologies or limit commercialization of any approved products.

We believe that we have obtained sufficient product liability insurance coverage for our clinical trials. We intend to expand our insurance coverage to include the commercial sale of any approved products if marketing approval is obtained; however, insurance coverage is becoming increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost. We may not be able to obtain additional insurance coverage that will be adequate to cover product liability risks that may arise. Regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for a product;
- injury to our reputation;
- inability to continue to develop a drug candidate or technology;
- withdrawal of clinical trial volunteers; and
- loss of revenues.

Consequently, a product liability claim or product recall may result in material losses.

Risks Related to Our Financial Condition

If we are unable to obtain additional funds on terms favorable to us, or at all, we may not be able to continue our operations.

We expect to use, rather than generate, funds from operations for the foreseeable future. We currently have an average projected burn rate of approximately $1.2 million per month in 2007 (excluding a $7.5 million payment made to DOV in January 2007, pursuant to a license agreement). Based on our current business plan, we believe that we have sufficient resources to fund our operations for approximately the next 12 months; however, the actual amount of funds that we will need will be determined by many factors, some of which are beyond our control. These factors include:

- the progress of our development activities;
- the progress of our research activities;
- the number and scope of our development programs;
- our ability to establish and maintain current and new licensing or acquisition arrangements;
- our ability to achieve our milestones under our licensing arrangements;
- the costs involved in enforcing patent claims and other intellectual property rights; and

- the costs and timing of regulatory approvals.

We may seek additional capital through a combination of public and private equity offerings, debt financings and collaborative, strategic alliance and licensing arrangements. We have made no determination at this time as to the amount, method or timing of any such financing. Such additional financing may not be available when we need it. If we are unable to obtain additional funds on terms favorable to us or at all, we may be required to cease or reduce our operating activities or sell or license to third parties some or all of our technology. If we raise additional funds by selling ordinary shares or other securities, the ownership interests of our shareholders will be diluted. If we need to raise additional funds through the sale or license of our drug candidates or technology, we may be unable to do so on terms favorable to us.

We are likely to be subject to taxation in the US, which could significantly increase our tax liability in the US for which we may not be able to apply the net losses accumulated in Israel.

The residency of the Chairman of our Board of Directors and our Chief Executive Officer in the US, as well as other less significant contacts we have with the US could likely lead to a determination by the US Internal Revenue Service that we currently have a "permanent establishment" in the US, which began in 2005. As a result, any income attributable to such permanent establishment in the US would be subject to US corporate income tax. If this is the case, we may not be able to utilize any of the accumulated Israeli loss carryforwards reflected on our balance sheet as of December 31, 2006 since these losses were all accumulated under Israeli tax laws. However, we would be able to utilize losses attributable to the US permanent establishment to offset such US taxable income. As of December 31, 2006, we estimate that these U.S. net operating loss carryforwards are approximately $15.2 million. These losses can be carried forward twenty years to offset future US taxable income. US corporate tax rates are higher than those to which we are subject in the State of Israel, and if we are subject to US corporate tax, it would have a material adverse effect on our results of operations.

Risks Related to Our Intellectual Property

If we are unable to adequately protect our intellectual property, third parties may be able to use our technology, which could adversely affect our ability to compete in the market.

Our commercial success will depend in part on our ability and the ability of our licensors to obtain and maintain patent protection on our drug products and technologies and successfully defend these patents and technologies against third-party challenges. As part of our business strategy, our policy is to actively file patent applications in the US and internationally to cover methods of use, new chemical compounds, pharmaceutical compositions and dosing of the compounds and composition and improvements in each of these. See “Item 4. Information on the Company - Business Overview - Intellectual Property and Patents,” below regarding our patent position with regard to our product candidates. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that before we commercialize any of our products, any related patent may expire or remain in existence for only a short period following commercialization, thus reducing any advantage of the patent.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date. Accordingly, the patents we use may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative technologies or design around our patented technologies. The patents we use may be challenged or invalidated or may fail to provide us with any competitive advantage. Moreover, in certain parts of the world, such as in China, western companies are adversely affected by poor enforcement of intellectual property rights. See “Item 4. Information on the Company - Business Overview - License Agreements and Collaborations,” below regarding our license of Ab65, a component of XTL-6865.

Generally, patent applications in the US are maintained in secrecy for a period of 18 months or more. Since publication of discoveries in the scientific or patent literature often lag behind actual discoveries, we are not certain that we were the first to make the inventions covered by each of our pending patent applications or that we were the first to file those patent applications. We cannot predict the breadth of claims allowed in biotechnology and pharmaceutical patents, or their enforceability. Third parties or competitors may challenge or circumvent our patents or patent applications, if issued. If our competitors prepare and file patent applications in the US that claim compounds or technology also claimed by us, we may choose to participate in interference proceedings declared by the United States Patent and Trademark Office to determine priority of invention, which could result in substantial cost, even if the eventual outcome is favorable to us. While we have the right to defend patent rights related to the licensed drug candidates and technologies, we are not obligated to do so. In the event that we decide to defend our

licensed patent rights, we will be obligated to cover all of the expenses associated with that effort.

We also rely on trade secrets to protect technology where we believe patent protection is not appropriate or obtainable. Trade secrets are difficult to protect. While we require our employees, collaborators and consultants to enter into confidentiality agreements, this may not be sufficient to adequately protect our trade secrets or other proprietary information. In addition, we share ownership and publication rights to data relating to some of our drug candidates and technologies with our research collaborators and scientific advisors. If we cannot maintain the confidentiality of this information, our ability to receive patent protection or protect our proprietary information will be at risk.

Specifically, we intend to apply for patent protection for each new monoclonal antibody produced. Such patents may include claims relating to novel human monoclonal antibodies directed at targets for which other human monoclonal antibodies already exist, or at targets which are protected by patents or patent applications filed by third parties. No assurance can be given that any such patent application by a third-party will not have priority over patent applications filed by us.

Several groups are attempting to produce and patent a chimeric mouse with human tissue. To the extent any patents issued to other parties claiming, in general, mouse-human chimeras, the risk increases that the potential products and processes of our or our future strategic partners may give rise to claims of patent infringement.

We plan to use the recombinant production of antibodies in Chinese Hamster Ovary cells, or CHO cells, in the development and production of some of our products. Patents relating to this method of antibody production are owned by third-parties. We are also aware that third parties have patent protection covering hepatitis C antigens and antibodies, which will be needed in order to commercialize XTL-6865. If we or our collaborative partners are unable to license such patent rights on commercially acceptable terms, the ability to develop, manufacture and sell these products could be impaired. Further, royalties payable to third parties may reduce the payments we will receive from our licensees or development partners.

We plan to pursue patent protection in the US and in certain foreign countries relating to our development and commercialization of Bicifadine. Bicifadine and its acid addition salts, including Bicifadine HCl, are disclosed in US Pat. Nos. 4,231,935, issued November 4, 1980, and 4,196,120, issued April 1, 1980, now expired. Currently, we are the exclusive licensee of one issued patent and multiple patent applications filed by DOV relating to Bicifadine. See "Item 4. Informationon the Company — Business Overview — Intellectual Property and Patents." However, we cannot guarantee the scope of protection of any issued patents, or that such patents will survive a validity or enforceability challenge, or that any pending patent applications will issue as patents.

Under the terms of the license agreements between DOV and Wyeth and between DOV and us relating to Bicifadine, Wyeth has retained limited rights in the Wyeth patent rights, certain DOV patent rights, and know-how to make and develop Bicifadine for the “treatment or amelioration of vasomotor symptoms caused by or occurring in relation to or in connection with menopause or other female hormonal fluctuations” (“the Wyeth Retained Field”). Under the terms of the DOV/Wyeth agreement, Wyeth can only develop Bicifadine for use in the Wyeth Retained Field in collaboration with DOV, and under the license agreement between DOV and XTL, DOV will not conduct research or development with Wyeth for the use of Bicifadine in the Wyeth Retained Field.

Certain of the Wyeth patent rights and DOV patent rights may claim overlapping subject matter which may result in the declaration of an interference proceeding before the United States Patent and Trademark Office (USPTO). If an interference is declared, Wyeth and DOV have agreed to meet and attempt to amicably resolve such interference with the goal of having a US patent issue to the assignee of the first inventor of the invention claimed by such conflicting claims. In the event of an interference, we cannot predict whether Wyeth and DOV will be able to reach agreement, or, if not, which party would prevail in such a proceeding.

In addition to patent protection, we may utilize certain regulatory marketing exclusivities for our drug candidates, including New Drug Product Exclusivity as provided by the Federal Food, Drug, and Cosmetic Act under section 505(c)(3)(E) and 505(j)(5)(F). Exclusivity provides the holder of an approved new drug application limited protection from new competition in the marketplace for the innovation represented by its approved drug product. This limited protection precludes approval of certain 505(b)(2) applications or certain abbreviated new drug applications (ANDAs) for prescribed periods of time. Some exclusivity provisions also provide protection from competition by delaying the submission of 505(b)(2) applications and ANDAs for certain periods of time. Exclusivity is available for new chemical entities (NCEs), which by definition are innovative, and for significant changes in already approved drug products, such as a new use.

We may also utilize orphan drug regulations to provide market exclusivity for certain of our drug candidates. The orphan drug regulations of the FDA provide incentives to pharmaceutical and biotechnology companies to develop and manufacture drugs for the treatment of rare diseases, currently defined as diseases that exist in fewer than 200,000 individuals in the US, or, diseases that affect more than 200,000 individuals in the US but that the sponsor does not realistically anticipate will generate a net profit. Under these provisions, a manufacturer of a designated orphan drug can seek tax benefits, and the holder of the first FDA approval of a designated orphan product will be granted a seven-year period of marketing exclusivity for such FDA-approved orphan product. We believe that certain of the indications for our drug candidates will be eligible for orphan drug designation. However, we cannot guarantee that any drug candidates will qualify, and, if any do qualify, that we will be the holder of the first FDA approval of such qualifying drug candidates.

If DOV declares bankruptcy, they may choose to repudiate their license agreement with Wyeth which could prevent us from pursuing the development of Bicifadine, and would have a material adverse impact on our financial condition.

In January 2007, we entered into a license agreement with DOV covering certain patent rights associated with the drug candidate Bicifadine. Some of the patent rights covered by that agreement are in turn under license to DOV by Wyeth. DOV is currently in default under certain of its corporate indebtedness. DOV is negotiating with the holders of that debt to restructure the obligations and payments due, but to date, to our knowledge, they have not reached an agreement. There is a possibility that DOV will be forced to declare bankruptcy whether or not they reach an agreement with the holders of their debt. If they do so, they can under the relevant bankruptcy laws refuse to abide by the terms of their license agreement with Wyeth and they can repudiate the agreement thereby putting their rights, and as a result our rights, to some of the patents covering Bicifadine in question. While we can and will take action in any DOV bankruptcy to protect our rights under our agreement with DOV, we cannot control any action of DOV with regard to their agreements with Wyeth. We have undertaken to enter into a standby license agreement with Wyeth which would become effective if DOV in any way repudiated their agreement with Wyeth. While we believe this will reduce the risk described above, there can be no assurance we will be able to successfully complete an agreement with Wyeth on terms satisfactory to us.

Litigation or third-party claims of intellectual property infringement could require us to spend substantial time and money defending such claims and adversely affect our ability to develop and commercialize our products.

Third parties may assert that we are using their proprietary technology without authorization. In addition, third parties may have or obtain patents in the future and claim that our products infringe their patents. If we are required to defend against patent suits brought by third parties, or if we sue third parties to protect our patent rights, we may be required to pay substantial litigation costs, and our management's attention may be diverted from operating our business. In addition, any legal action against our licensors or us that seeks damages or an injunction of our commercial activities relating to the affected products could subject us to monetary liability and require our licensors or us to obtain a license to continue to use the affected technologies. We cannot predict whether our licensors or we would prevail in any of these types of actions or that any required license would be made available on commercially acceptable terms, if at all.

In addition, there can be no assurance that our patents or patent applications or those licensed to us will not become involved in opposition or revocation proceedings instituted by third parties. If such proceedings were initiated against one or more of our patents, or those licensed to us, the defense of such rights could involve substantial costs and the outcome could not be predicted.

Competitors or potential competitors may have filed applications for, may have been granted patents for, or may obtain additional patents and proprietary rights that may relate to compounds or technologies competitive with ours. If patents are granted to other parties that contain claims having a scope that is interpreted to cover any of our products (including the manufacture thereof), there can be no assurance that we will be able to obtain licenses to such patents at reasonable cost, if at all, or be able to develop or obtain alternative technology.

In addition, we use or have used certain technology in our DOS program for the development of novel hepatitis C small molecule inhibitors that may or may not be covered by third party patents. In response to a request by a third party, we are currently evaluating certain patents to determine whether or not we may be required to enter into a license under such patents. In the event that we do not license the patent rights, and such third party makes a claim of patent infringement, we may be required to pay substantial litigation costs, and our management's attention may be diverted from operating our business. In addition, any legal action against us that seeks damages or an injunction relating to the affected activities could subject us to monetary liability and/or require us to discontinue the affected technologies or obtain a license to continue use thereof.

Risks Related to Our Ordinary Shares and ADRs

Our ADRs are traded in small volumes, limiting your ability to sell your ADRs that represent ordinary shares at a desirable price, if at all.

The trading volume of our ADRs has historically been low. Even if the trading volume of our ADRs increases, we can give no assurance that it will be maintained or will result in a desirable stock price. As a result of this low trading volume, it may be difficult to identify buyers to whom you can sell your ADRs and you may be unable to sell your ADRs at an established market price, at a price that is favorable to you, or at all. A low volume market also limits your ability to sell large blocks of our ADRs at a desirable or stable price at any one time. You should be prepared to own our ordinary shares and ADRs indefinitely.

Our stock price can be volatile, which increases the risk of litigation and may result in a significant decline in the value of your investment.

The trading price of the ADRs representing our ordinary shares is likely to be highly volatile and subject to wide fluctuations in price in response to various factors, many of which are beyond our control. These factors include:

- developments concerning our drug candidates;
- announcements of technological innovations by us or our competitors;
- introductions or announcements of new products by us or our competitors;
- announcements by us of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- changes in financial estimates by securities analysts;
- actual or anticipated variations in interim operating results;
- expiration or termination of licenses, research contracts or other collaboration agreements;
- conditions or trends in the regulatory climate and the biotechnology and pharmaceutical industries;
- changes in the market valuations of similar companies; and
- additions or departures of key personnel.

In addition, equity markets in general, and the market for biotechnology and life sciences companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of companies traded in those markets. These broad market and industry factors may materially affect the market price of our ordinary shares or ADRs, regardless of our development and operating performance. In the past, following periods of volatility in the market price of a company's securities, securities class-action litigation has often been instituted against that company. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management's attention and resources even if we prevail in the litigation, all of which could seriously harm our business.

Future issuances of our ordinary shares could depress the market for our ordinary shares and ADRs.

Future issuances of a substantial number of our ordinary shares, or the perception by the market that those issuances could occur, could cause the market price of our ordinary shares or ADRs to decline or could make it more difficult for us to raise funds through the sale of equity in the future. We believe that we have the cash necessary to fund our operations for the next 12 months; however, prior to the end of that period it will be necessary for us to return to the capital markets through the sale of ADRs or ordinary shares.

Also, if we make one or more significant acquisitions in which the consideration includes ordinary shares or other securities, your portion of shareholders' equity in us may be significantly diluted. For example, pursuant to a license agreement with DOV, XTL Development licensed the worldwide rights for Bicifadine, a serotonin and norepinephrine reuptake inhibitor. Under the agreement, XTL Development, upon achievement of certain milestones, will make payments of up to $126.5 million to DOV over the life of the license. We may elect to issue up to an additional $121.5

million in ordinary shares to DOV in lieu of cash for such milestone payments. In addition, XTL Development committed to pay a third party a transaction advisory fee in the form of stock appreciation rights in an amount equivalent to 3% of our fully diluted ordinary shares at the close of the transaction, which are locked up for one year after the close of the transaction, and an additional 7% of our fully diluted ordinary shares at the close of the transaction, which vest following the first to occur of successful Phase III clinical trial results or the acquisition of our company. Payment of the stock appreciation rights by us can be satisfied, at our discretion, in cash and/or by issuance of our ordinary shares. Pursuant to a license agreement with VivoQuest, Inc., or VivoQuest, a privately held biotechnology company based in the US, we licensed (in all fields of use) certain intellectual property and technology related to VivoQuest's HCV program. Pursuant to the license agreement, we may elect to issue up to an additional $34.6 million in ordinary shares to VivoQuest in lieu of cash upon achievement of certain milestones. In the future, we may enter into additional arrangements with other third-parties permitting us to issue ordinary shares in lieu of certain cash payments.

Our ordinary shares and ADRs trade on more than one market, and this may result in price variations.

Our ordinary shares are traded on the London Stock Exchange and the Tel Aviv Stock Exchange and ADRs representing our ordinary shares are quoted on the Nasdaq Global Market. Trading in our securities on these markets is made in different currencies and at different times, including as a result of different time zones, different trading days and different public holidays in the US, Israel and the United Kingdom. Consequently, the effective trading prices of our shares on these three markets may differ. Any decrease in the trading price of our shares on one of these markets could cause a decrease in the trading price of our shares on the other market.

Holders of our ordinary shares who are US residents may be required to pay additional income taxes.

There is a risk that we will be classified as a passive foreign investment company ("PFIC") for certain tax years. If we are classified as a PFIC, a US holder of our ordinary shares or ADRs representing our ordinary shares will be subject to special federal income tax rules that determine the amount of federal income tax imposed on income derived with respect to the PFIC shares. We will be a PFIC if either 75% or more of our gross income in a tax year is passive income or the average percentage of our assets (by value) that produce or are held for the production of passive income in a tax year is at least 50%. The risk that we will be classified as a PFIC arises because under applicable rules issued by the US Internal Revenue Service, ("IRS"), cash balances, even if held as working capital, are considered to be assets that produce passive income. Therefore, any determination of PFIC status will depend upon the sources of our income and the relative values of passive and non-passive assets, including goodwill. A determination as to a corporation's status as a PFIC must be made annually. We believe that we were likely not a PFIC for the taxable years ended December 31, 2004 and 2005. However, we believe that we were a PFIC for the taxable year ended December 31, 2006. Although such a determination is fundamentally factual in nature and generally cannot be made until the close of the applicable taxable year, based on our current operations, we believe that there is a significant likelihood that we will be classified as a PFIC in the 2007 taxable year and possibly in subsequent years.

In view of the complexity of the issues regarding our treatment as a PFIC, US shareholders are urged to consult their own tax advisors for guidance as to our status as a PFIC. For further discussion of tax consequences of being a PFIC, see US Federal Income Tax Considerations - Tax Consequences If We Are A Passive Foreign Investment Company," below.

Provisions of Israeli corporate law may delay, prevent or affect a potential acquisition of all or a significant portion of our shares or assets and therefore depress the price of our ordinary shares.

Israeli corporate law regulates acquisitions of shares through tender offers. It requires special approvals for transactions involving significant shareholders and regulates other matters that may be relevant to these types of transactions. The provisions of Israeli law may delay or prevent an acquisition, or make it less desirable to a potential acquirer and therefore depress the price of our shares. Further, Israeli tax considerations may make potential transactions undesirable to us or to some of our shareholders.

Israeli corporate law provides that an acquisition of shares in a public company must be made by means of a tender offer if, as a result of such acquisition, the purchaser would become a 25% or greater shareholder of the company. This rule does not apply if there is already another 25% or greater shareholder of the company. Similarly, Israeli corporate law provides that 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's shareholdings would entitle the purchaser to over 45% of the shares in the company, unless there is a shareholder with 45% or more of the shares in the company. These requirements do not apply if, in general, the acquisition (1) was made in a private placement that received the approval of the company's shareholders; (2) was from a 25% or greater shareholder of the company which resulted in the purchaser becoming a 25% or greater shareholder of the company, or (3) was from a 45% or greater shareholder of the company which resulted in the acquirer becoming a 45% or greater shareholder of the company. These rules do not apply if the

acquisition is made by way of a merger. Regulations promulgated under Israeli corporate law provide that these tender offer requirements do not apply to companies whose shares are listed for trading outside of Israel if, according to the law in the country in which the shares are traded, including the rules and regulations of the stock exchange or which the shares are traded, either:

- there is a limitation on acquisition of any level of control of the company; or
- the acquisition of any level of control requires the purchaser to do so by means of a tender offer to the public.

Finally, in general, Israeli tax law treats specified acquisitions less favorably than does US tax law. See “Item 10. Additional Information - Taxation - Israeli Tax Considerations,” below.

Our ADR holders are not shareholders and do not have shareholder rights.

The Bank of New York, as depositary, executes and delivers our ADRs on our behalf. Each ADR is a certificate evidencing a specific number of ADSs. Our ADR holders will not be treated as shareholders and do not have the rights of shareholders. The depositary will be the holder of the shares underlying our ADRs. Holders of our ADRs will have ADR holder rights. A deposit agreement among us, the depositary and our ADR holders, and the beneficial owners of ADRs, sets out ADR holder rights as well as the rights and obligations of the depositary. New York law governs the deposit agreement and the ADRs. Our shareholders have shareholder rights. Israeli law and our Articles of Association, or Articles, govern shareholder rights. Our ADR holders do not have the same voting rights as our shareholders. Shareholders are entitled to our notices of general meetings and to attend and vote at our general meetings of shareholders. At a general meeting, every shareholder present (in person or by proxy, attorney or representative) and entitled to vote has one vote on a show of hands. Every shareholder present (in person or by proxy, attorney or representative) and entitled to vote has one vote per fully paid ordinary share on a poll. This is subject to any other rights or restrictions which may be attached to any shares. Our ADR holders may instruct the depositary to vote the ordinary shares underlying their ADRs, but only if we ask the depositary to ask for their instructions. If we do not ask the depositary to ask for the instructions, our ADR holders are not entitled to receive our notices of general meeting or instruct the depositary how to vote. Our ADR holders will not be entitled to attend and vote at a general meeting unless they withdraw the ordinary shares from the depository. However, our ADR holders may not know about the meeting enough in advance to withdraw the ordinary shares. If we ask for our ADR holders' instructions, the depositary will notify our ADR holders of the upcoming vote and arrange to deliver our voting materials and form of notice to them. The depositary will try, as far as practical, subject to the provisions of the deposit agreement, to vote the shares as our ADR holders instruct. The depositary will not vote or attempt to exercise the right to vote other than in accordance with the instructions of the ADR holders. We cannot assure our ADR holders that they will receive the voting materials in time to ensure that they can instruct the depositary to vote their shares. In addition, there may be other circumstances in which our ADR holders may not be able to exercise voting rights.

Our ADR holders do not have the same rights to receive dividends or other distributions as our shareholders. Subject to any special rights or restrictions attached to a share, the directors may determine that a dividend will be payable on a share and fix the amount, the time for payment and the method for payment (although we have never declared or paid any cash dividends on our ordinary stock and we do not anticipate paying any cash dividends in the foreseeable future). Dividends may be paid on shares of one class but not another and at different rates for different classes. Dividends and other distributions payable to our shareholders with respect to our ordinary shares generally will be payable directly to them. Any dividends or distributions payable with respect to ordinary shares will be paid to the depositary, which has agreed to pay to our ADR holders the cash dividends or other distributions it or the custodian receives on shares or other deposited securities, after deducting its fees and expenses. Our ADR holders will receive these distributions in proportion to the number of shares their ADSs represent. In addition, there may be certain circumstances in which the depositary may not pay to our ADR holders amounts distributed by us as a dividend or distribution. See the risk factor "- There are circumstances where it may be unlawful or impractical to make distributions to the holders of our ADRs," below.

There are circumstances where it may be unlawful or impractical to make distributions to the holders of our ADRs.

The deposit agreement with the depositary allows the depositary to distribute foreign currency only to those ADR holders to whom it is possible to do so. If a distribution is payable by us in New Israeli Shekels or Pounds Sterling, the depositary will hold the foreign currency it cannot convert for the account of the ADR holders who have not been paid. It will not invest the foreign currency and it will not be liable for any interest. If the exchange rates fluctuate during a time when the depositary cannot convert the foreign currency, our ADR holders may lose some of the value of the distribution.

The depositary is not responsible if it decides that it is unlawful or impractical to make a distribution available to any ADR holders. This means that our ADR holders may not receive the distributions we make on our shares or any value for them if it is illegal or impractical for the depository to make such distributions available to them.

Risks Relating to Operations in Israel

Conditions in the Middle East and in Israel may harm our operations.

Certain of our research and development facilities and some of our suppliers are located in Israel. Political, economic and military conditions in Israel directly affect our operations. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its Arab neighbors, as well as incidents of civil unrest, military conflicts and terrorist actions. There has been a significant increase in violence since September 2000, which has continued with varying levels of severity through to the present. This state of hostility has caused security and economic problems for Israel. To date, we do not believe that the political and security situation has had a material adverse impact on our business, but we cannot give any assurance that this will continue to be the case. Any hostilities involving Israel or the interruption or curtailment of trade between Israel and its present trading partners could adversely affect our operations and could make it more difficult for us to raise capital.

Our commercial insurance does not cover losses that may occur as a result of events associated with the security situation in the Middle East. Although the Israeli government currently covers the reinstatement value of direct damages that are caused by terrorist attacks or acts of war, we cannot assure you that this government coverage will be maintained. 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 and could harm our results of operations.

Further, in the past, the State of Israel and Israeli companies have been subjected to an economic boycott. 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 results of operations may be adversely affected by inflation and foreign currency fluctuations.

We generate all of our revenues and hold most of our cash, cash equivalents, bank deposits and marketable securities in US dollars. While a substantial amount of our operating expenses are in US dollars (approximately 90% in 2006), we incur a portion of our expenses in New Israeli Shekels. In addition, we also pay for some of our services and supplies in the local currencies of our suppliers. As a result, we are exposed to the risk that the US dollar will be devalued against the New Israeli Shekel or other currencies, and as result our financial results could be harmed if we are unable to guard against currency fluctuations in Israel or other countries in which services and supplies are obtained in the future. Accordingly, we may in the future enter into currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rates of currencies. These measures, however, may not adequately protect us from the adverse effects of inflation in Israel. In addition, we are exposed to the risk that the rate of inflation in Israel will exceed the rate of devaluation of the New Israeli Shekel in relation to the dollar or that the timing of any devaluation may lag behind inflation in Israel.

The Office of the Chief Scientist may refuse to approve the manufacture of some of our product candidates outside the State of Israel.

We have in the past participated in programs offered by the Office of the Chief Scientist under the Industry, Trade and Labor Ministry of Israel that supports research and development activities. Through December 31, 2006, we have received $7.3 million in grants from the Office of the Chief Scientist for several projects, including XTL-6865, HepeX-B and XTL-2125. Israeli law requires that the manufacture of products developed with government grants be carried out in Israel, unless the Office of the Chief Scientist provides a special approval to the contrary. This approval, if provided, is generally conditioned on an increase in the total amount to be repaid to the Office of the Chief Scientist to between 120% and 300% of the amount of funds granted. While we believe that the Office of the Chief Scientist does not unreasonably withhold approval if the request is based upon commercially justified circumstances and any

payment obligations to the Office of the Chief Scientist are sufficiently assured, the matter is solely within its discretion. We cannot be sure that such approval, if requested, would be granted upon terms satisfactory to us or granted at all. Without such approval, we would be unable to manufacture any products developed by this research outside of Israel, which may greatly restrict any potential revenues from such products (see Item 5. “Operating and Financial Review and Prospects - Israeli Government Research and Development Grants” below).

We may not continue to be entitled to certain tax benefits from the Israeli government.

We are entitled to receive certain tax benefits as a result of the Approved Enterprise status of our existing facilities in Israel. The Law for the Encouragement of Capital Investment, 1959, as amended, provides that a proposed capital investment in eligible facilities may, upon application to the Investment Center of the Ministry of Industry and Trade of the State of Israel, permit a company to recognize taxable income attributable to the Approved Enterprise subject to company tax at the maximum rate of 25% rather than the usual rate in 2007 of 29% (2006 -- 31%). This usual rate is currently scheduled to decrease as follows: in 2008 - 27%, 2009 - 26%, 2010 and after - 25%. For further discussion of these tax benefits, see “Item 10. Additional Information - Taxation - Israeli Tax Considerations,” below. To date we have not received any such tax benefits because we have not generated any taxable income to date. To maintain our eligibility for these tax benefits, we must meet certain reporting requirements and certain conditions that we have either obligated ourselves to meet or that are included in the Certificate of Approval from the Investment Center of the Ministry of Industry and Trade of the State of Israel. If we cease to become entitled to tax benefits, we may be required to pay repay corporate tax at the normal rate on all or part of the taxable income that we may generate from the eligible facilities in the future. We may, in the foreseeable future, cease to be entitled to the aforesaid tax benefits, as we may not in the future be in compliance with the Certificate of Approval from the Investment Center of the Ministry of Industry and Trade of the State of Israel due to a reduction in research and development activity in Israel.

It may be difficult to enforce a US judgment against us, our officers or our directors or to assert US securities law claims in Israel.

Service of process upon us, since we are incorporated in Israel, and upon our directors and officers and our Israeli auditors, some of whom reside outside the US, may be difficult to obtain within the US. In addition, because substantially all of our assets and some of our directors and officers are located outside the US, any judgment obtained in the US against us or any of our directors and officers may not be collectible within the US. There is a doubt as to the enforceability of civil liabilities under the Securities Act or the Exchange Act pursuant to original actions instituted in Israel. Subject to particular time limitations and provided certain conditions are met, executory judgments of a US court for monetary damages in civil matters may be enforced by an Israeli court. For more information regarding the enforceability of civil liabilities against us, our directors and our executive officers, see “Item 10. Additional Information - Memorandum and Articles of Association - Enforceability of Civil Liabilities,” below.

ITEM 4. INFORMATION ON THE COMPANY

History and Development of XTL

We are a biopharmaceutical company engaged in the acquisition, development and commercialization of pharmaceutical products for the treatment of unmet medical needs, particularly the treatment of neuropathic pain and hepatitis C.

Our lead compound is Bicifadine, a serotonin and norepineprine reuptake inhibitor that we are developing for the treatment of neuropathic pain, a chronic condition resulting from damage to peripheral nerves. We in-licensed Bicifadine from DOV in January 2007, and we expect to initiate a late-stage clinical trial with Bicifadine in the second half of 2007.

We are also developing XTL-2125, a small molecule non-nucleoside, polymerase inhibitor for the treatment of patients with hepatitis C. XTL-2125 is presently in a Phase I clinical trial in patients with chronic hepatitis C, with clinical trial results expected in the second quarter of 2007. A second drug candidate in hepatitis C is XTL-6865, a combination of two monoclonal antibodies against the hepatitis C virus. XTL-6865 is currently in a Phase I clinical trial in patients with chronic hepatitis C, also known as HCV, with results expected shortly. Our third program in the hepatitis C area is the Diversity Oriented Synthesis, or DOS, program. This program is focused on the development of novel hepatitis C small molecule inhibitors. These compounds are presently in advanced stages of optimization. HepeX-B, a combination of two monoclonal antibodies against Hepatitis B, was licensed to Cubist Pharmaceuticals Inc., or Cubist, in June 2004. In July 2006, Cubist announced that it has decided not to make any further investment in the HepeX-B program, while it evaluates its strategic options for HepeX-B, including the possible sub-licensing of the product to a third party.

Our legal and commercial name is XTL Biopharmaceuticals Ltd. We were established as a private company limited by shares under the laws of the State of Israel on March 9, 1993, under the name Xenograft Technologies Ltd. We re-registered as a public company on June 7, 1993, in Israel, and changed our name to XTL Biopharmaceuticals Ltd. on July 3, 1995. We commenced operations to use and commercialize technology developed at the Weizmann Institute, in Rehovot, Israel. Until 1999, our therapeutic focus was on the development of human monoclonal antibodies to treat viral, autoimmune and oncological diseases. Our first therapeutic programs focused on antibodies against the hepatitis B virus, interferon - and the hepatitis C virus.

Our ordinary shares are traded on the London Stock Exchange under the symbol “XTL,” and on the Tel Aviv Stock Exchange under the symbol “XTL.” Our ADRs are quoted on the Nasdaq Global Market under the symbol “XTLB.” We operate under the laws of the State of Israel, under the Israeli Companies Act, the regulations of the United Kingdom Listing Authority, which governs our listing on the London Stock Exchange, and in the US, the Securities Act, the Exchange Act and the regulations of the Nasdaq Global Market.

Our principal offices are located at 750 Lexington Avenue, 20th Floor, New York, New York 10022, and our telephone number is 212-531-5960. The principal offices of XTL Biopharmaceuticals, Inc., our wholly-owned US subsidiary and agent for service of process in the US, are located at 750 Lexington Avenue, 20th Floor, New York, NY 10022, and its telephone number is 212-531-5960. Our primary internet address is www.xtlbio.com. None of the information on our website is incorporated by reference into this annual report.

On March 22, 2006, we completed a private placement of 46,666,670 ordinary shares (equivalent to 4,666,667 ADRs) at $0.60 per share ($6.00 per ADR), together with warrants for the purchase of an aggregate of 23,333,335 ordinary shares (equivalent to 2,333,333.5 ADRs) at an exercise price of $0.875 ($8.75 per ADR). Total proceeds to us from this private placement were approximately $24.4 million, net of offering expenses of approximately $3.6 million. The private placement closed on May 25, 2006. Since inception, we have raised net proceeds of approximately $128.7

million to fund our activities, including the net proceeds from our recent private placement.

For the years ended December 31, 2006, 2005, and 2004 our capital expenditures were $21,000, $38,000 and $180,000, respectively. Our capital expenditures were primarily associated with the purchase of lab equipment for our research and development activities. There were no material divestitures during the years ended December 31, 2006, 2005 and 2004.

In January 2007, XTL Development, Inc., or XTL Development, our wholly-owned subsidiary, signed an agreement with DOV to in-license the worldwide rights for Bicifadine, a serotonin and norepinephrine reuptake inhibitor. XTL Development intends to develop Bicifadine for the treatment of neuropathic pain - a chronic condition resulting from damage to peripheral nerves. In accordance with the terms of the license agreement, XTL Development made an initial up-front payment of $7.5 million in cash. In addition, XTL Development will make milestone payments of up to $126.5 million, in cash and/or in our ordinary shares over the life of the license, of which up to $115 million will be due upon or after regulatory approval of the product. XTL Development is also obligated to pay royalties to DOV on net sales of Bicifadine. In connection with the license agreement, XTL Development has committed to pay a transaction advisory fee in the form of our stock appreciation rights in an amount equivalent to 3% of our fully diluted ordinary shares at the close of the transaction, vesting to a third party one year after the close of the transaction, and 7% of our fully diluted ordinary shares at the close of the transaction, vesting following the first to occur of successful Phase III clinical trial results or the acquisition of our company. Payment of the stock appreciation rights can be satisfied, at our discretion, in cash and/or by issuance of our ordinary shares. See “Item 10. Additional Information -Material Contracts.”

Business Overview

Introduction

We are a biopharmaceutical company engaged in the acquisition, development and commercialization of pharmaceutical products for the treatment of unmet medical needs, in particular the treatment of neuropathic pain and hepatitis C.

Our lead compound is Bicifadine. We are developing Bicifadine for the treatment of neuropathic pain - a chronic condition resulting from damage to peripheral nerves. Bicifadine is a serotonin and norepinephrine reuptake inhibitor, or SNRI. Compared to the currently approved SNRI’s, Bicifadine has a unique ratio of serotonin versus norepinephrine reuptake inhibition, which is weighted toward norepinephrine reuptake inhibition, providing a strong scientific rationale for using Bicifadine for the treatment neuropathic pain indications. Prior to it being in-licensed to us, Bicifadine has been tested extensively in over 15 clinical trials involving over 3,000 patients, and has been shown to be safe and generally well tolerated. Bicifadine was evaluated in various pain indications, including two large, randomized clinical trials (n=750 and n=540) in patients suffering from acute (non-neuropathic) pain, where Bicifadine demonstrated statistically significant efficacy. We intend to initiate a late-stage clinical trial with Bicifadine in neuropathic pain in the second half of 2007.

We currently have three products/programs under development with respect to Hepatitis C:

- **XTL-2125** is being developed for the treatment of hepatitis C. XTL-2125 is a novel orally-available non-nucleoside HCV RNA polymerase inhibitor. XTL-2125 has demonstrated potent activity against the hepatitis C virus in several pre-clinical systems. Investigational new drug application, or IND, enabling, good laboratory practice, or GLP, studies demonstrated that XTL-2125 has favorable oral pharmacokinetics and a good safety profile in multiple animal species. In May 2006, we announced the initiation of a Phase I, placebo-controlled, dose escalation trial of XTL-2125 in chronic HCV patients. In January 2007, the Phase I clinical trial - as originally designed - was completed. As no dose limiting toxicities have been encountered, we decided to add up to two additional higher dose cohorts to the study. We expect to announce results from this study in the second quarter of 2007. The compound was in-licensed by us from B&C Biopharm Co., Ltd., a Korean drug development company.

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XTL-6865 is also being developed for the treatment of hepatitis C. XTL-6865 (formerly known as the HepeX-C program) is a combination of two fully human monoclonal antibodies (Ab68 and Ab65) against the hepatitis C virus E2 envelope protein. The antibodies comprising XTL-6865 are expected to "trap" the virus in the patient's serum and prevent the infection of healthy liver cells. A single antibody version of this product was tested in a pilot clinical program that included both Phase I and Phase II clinical trials. In April 2005, we submitted an IND to the FDA in order to commence a Phase Ia/Ib clinical trial for XTL-6865, the dual-antibody product. In September 2005, we announced the initiation of a Phase Ia clinical trial with XTL-6865 in patients with chronic hepatitis C. We expect results from this trial shortly.

- **DOS** is a pre-clinical program focused on the development of novel hepatitis C small molecule inhibitors. Compounds developed to date inhibit HCV replication in a pre-clinical cell-based assay with potencies comparable to clinical stage drugs. These compounds are presently in advanced stages of optimization.

In addition, HepeX-B, a combination of two monoclonal antibodies against hepatitis B, or HBV, was licensed to Cubist in June 2004. In July 2006, Cubist announced that it has decided not to make any further investment in the HepeX-B program, while it evaluates its strategic options for HepeX-B, including the possible sub-licensing of the product to a third party.

To date, we have not received approval for the sale of any of our drug candidates in any market and, therefore, have not generated any commercial revenues from the sales of our drug candidates. Moreover, preliminary results of our pre-clinical or clinical tests do not necessarily predict the final results, and acceptable results in early preclinical or clinical testing might not be obtained in later clinical trials. Drug candidates in the later stages of clinical development may fail to show the desired safety and efficacy traits despite having progressed through initial clinical testing. We have received license and reimbursed out of pocket expense revenue pursuant to our agreement with Cubist with respect to HepeX-B, although HepeX-B has not yet been commercialized and may never be commercialized.

Our Strategy

Under our current strategy, we plan to:

- develop Bicifadine for the treatment of neuropathic pain;
- continue the clinical development of XTL-2125 and XTL-6865;
- identify clinical candidates from our DOS program and advance them into clinical development; and
- seek to in-license or acquire additional candidates.

Products Under Development

Bicifadine

Market Opportunity

We intend to develop Bicifadine for the treatment of neuropathic pain - a chronic condition resulting from damage to peripheral nerves. According to Datamonitor, there are over 15 million people suffering from neuropathic pain in the United States alone. With limited treatment options available, neuropathic pain represents a significant unmet medical need. According to Datamonitor, the global market for neuropathic pain drugs is expected to grow from $1.7 billion in 2005 to $5.5 billion by 2015.

Scientific Background

Bicifadine is a serotonin and norepinephrine reuptake inhibitor. Other members of the SNRI class include Cymbalta® (approved for depression and neuropathic pain), and Effexor® (approved only for depression). Both Cymbalta and Effexor have been shown to be efficacious in neuropathic pain. Activity on norepinephrine reuptake is thought to be necessary for anti-depressants to be effective in neuropathic pain. Compared to the currently approved SNRI's, Bicifadine has a unique ratio of serotonin versus norepinephrine reuptake inhibition, which is weighted toward norepinephrine reuptake inhibition, providing a strong scientific rationale for using Bicifadine for the treatment neuropathic pain indications.

Clinical Data

Four Phase I clinical trials and 14 Phase II clinical trials involving more than 1,000 patients have been conducted with an immediate release, or IR, formulation of Bicifadine for the treatment of acute pain. In five exploratory double-blind, placebo-controlled Phase II clinical trials of the IR formulation, Bicifadine demonstrated a statistically significant reduction in pain versus placebo, in some cases with an outcome suggesting it might be comparable to or better than positive controls such as codeine. In addition to these trials with the IR formulation, eight Phase I clinical trials using the sustained release, or SR, formulation of Bicifadine have been conducted. SR is a formulation that generally permits less frequent daily dosing and improves tolerability. We intend to use the SR formulation in future clinical development and for commercial use of Bicifadine.

In two additional larger (n=750 and n=540) single-dose, double-blind, placebo-controlled clinical trials with Bicifadine in the treatment of moderate to severe post-surgical acute dental pain, Bicifadine produced a highly statistically significant, dose-related reduction in pain compared to placebo, and which was comparable to a positive control arm (codeine or Tramadol). Both trials demonstrated Bicifadine to be safe and generally well-tolerated without producing any serious adverse events.

In a Phase III double-blind, placebo-controlled, clinical trial (n=325) with Bicifadine in the treatment of moderate to severe acute pain following bunionectomy surgery, statistically significant increases in analgesia were measured as early as 30 minutes after administration and these effects were sustained for the balance of the eight-hour measurement period. In this study, Bicifadine was safe and generally well-tolerated. The complete assessment of the analgesic action of Bicifadine under repeat dosing conditions could not be fully elucidated due to the high level of “rescue” analgesic medication used in both the placebo and active drug groups.

Due to the highly competitive nature of the market for acute pain drugs, and the FDA requirement to complete two repeat-dosing clinical trials in two different acute pain indications, no further studies in acute pain are planned.

Bicifadine has been further evaluated in three Phase III trials in chronic lower back pain, or CLBP. The primary efficacy endpoint in these trials was the change in pain severity rating score between baseline and the end of dosing. In these trials, Bicifadine was safe and generally well tolerated, but did not show a statistically significant effect relative to placebo on the primary endpoint of the study at any of the doses tested.

We believe that the failure of Bicifadine in the CLBP trials was a result of the inherent heterogeneity of the studied patient population (i.e. the varying causes of CLBP pain), uncontrolled physical activities in what is largely an activity-dependent pain indication, and a high placebo response.

Development Status

We believe that by re-directing the development of Bicifadine away from the novel indications in acute and chronic pain toward a proven area of efficacy of SNRI’s in the treatment of neuropathic pain, Bicifadine could be successfully developed for neuropathic pain, possibly offering a differentiated efficacy and safety profile based on the drug’s emphasis on norepinephrine reuptake inhibition.

We intend to initiate a late-stage clinical trial with Bicifadine in neuropathic pain in the second half of 2007.

Products for the treatment of Hepatitis C

Market Opportunity

We are developing several products for the treatment of hepatitis C. Chronic hepatitis C is a serious life-threatening disease which affects around 170 to 200 million people worldwide, according to a Datamonitor report from April 2005. We estimate that between eight to 10 million of these people reside in the US, Europe and Japan. According to the BioSeeker Group, 20% to 30% of chronic hepatitis patients will eventually develop progressive liver disease that may lead to decomposition of the liver or hepatocellular carcinoma (liver cancer). According to the National Digestive Diseases Information Clearing House, each year 10,000 to 12,000 people die from HCV in the US alone. The Centers for Disease Control, or CDC, predicts, that by the end of this decade, the number of deaths due to HCV in the US will surpass the number of deaths due to AIDS.

According to the BioSeeker Group, the worldwide market for the treatment of chronic HCV in 2003 was estimated at $3 billion and consists entirely of Interferon-based treatments. Interferon alpha was first approved for use against chronic hepatitis C in 1991. At present, the optimal regimen appears to be a 24 or 48 week course of the combination of Pegylated-Interferon and Ribavirin. In studies done at the St. Louis University School of Medicine, a 24 week course of this combination therapy yields a sustained response rate of approximately 40% to 45% in patients with genotype 1 (the most prevalent genotype in the western world according to the CDC) and a better sustained response with a 48 week course.

XTL-2125

XTL-2125 is a novel non-nucleoside HCV RNA polymerase inhibitor that is being developed for the treatment of chronic hepatitis C. XTL-2125's ability to inhibit HCV replication was demonstrated in XTL's proprietary cell-based assay for HCV infectivity. In addition, XTL-2125 was orally active in XTL's proprietary Trimera mouse model. IND-enabling GLP studies demonstrated that XTL-2125 has a favorable oral pharmacokinetics and a good safety profile in multiple animal species.

In the fourth quarter of 2005, we filed an application with the Israel Ministry of Health to conduct Phase I human trials of XTL-2125 in chronic HCV patients. In May 2006, we announced the initiation of patient dosing in a Phase I clinical trial of XTL-2125 for the treatment of chronic HCV. The Phase I trial is a placebo controlled, randomized, dose escalating study, designed to evaluate the safety, tolerability and antiviral activity of single and multiple doses of XTL-2125. The study - as originally designed - was expected to enroll 48 patients into six cohorts comprised of eight patients each (of which two are placebo patients). Each patient was expected to receive a single dose, followed by a 14-day multi-dosing regimen commencing one week after the single dose administration. In January 2007, the Phase I clinical trial - as originally designed - was completed. As no dose limiting toxicities have been encountered, we have decided to add up to two additional higher dose cohorts to the study. We expect to announce results from this study in the second quarter of 2007.

XTL-6865

XTL-6865 is being developed for the treatment of hepatitis C. XTL-6865 is a combination of two fully human monoclonal antibodies (Ab68 and Ab65) against the hepatitis C virus E2 envelope protein. The antibodies comprising XTL-6865 are expected to "trap" the virus in the patient's serum and prevent the infection of healthy liver cells. A single antibody version of this product, then referred to as HepeX-C, was tested in a pilot clinical program that included both Phase I and Phase II clinical trials. In April 2005, we submitted an IND to the FDA in order to commence a Phase Ia/Ib clinical trial for XTL-6865, the dual-antibodies product. In September 2005, we announced the initiation of a Phase Ia clinical trial with XTL-6865 in patients with chronic hepatitis C.

The two antibodies comprising XTL-6865 were selected by screening a large panel of candidates based on their high level of activity against the virus in our proprietary HCV models. We believe that a combination of two antibodies that bind to different epitopes is essential to provide broad coverage of virus quasispecies, and to minimize the probability for escape from therapy. We have shown that the two antibodies chosen (Ab68 and Ab65) specifically bind and immunoprecipitate viral particles from infected patients' sera with different HCV genotypes. In addition, both antibodies reduced mean viral load in HCV-Trimera mice. We have also shown that incubation of an infectious human serum with Ab68 or Ab65 prevented the serum's ability to infect human liver cells and human liver tissue.

The original Phase Ia single-dose study was designed to evaluate the safety, tolerability, and virologic activity of escalating single doses of XTL-6865 in patients with chronic hepatitis C virus infection, and to assess the pharmacokinetics of XTL-6865 in the presence of viral infection. The original study was a single-administration, randomized, double blind, placebo-controlled, multi-center design. Doses were administered to groups of four patients each: 5 mg, 20 mg, 75 mg, 250 mg, 600 mg, 1200 mg, 2400 mg, and placebo. Within each group, three subjects received XTL-6865 and one subject will receive placebo. No patient was enrolled in more than one dose level. Concentrations of anti-E2 antibody and HCV RNA in the peripheral blood were periodically evaluated. In December 2006, we completed dosing all patients in the trial - as originally designed. In January 2007, we added one multiple dose cohort to the trial, which includes four patients: three of whom will receive five daily dosings of 1200mg, and one of whom will receive placebo. Results from the trial are expected shortly.

DOS

DOS is a pre-clinical program focused on the development of three families of novel hepatitis C small molecule inhibitors. Compounds in each family inhibited HCV replication in a pre-clinical cell-based assay with potencies comparable to clinical stage drugs. These compounds are presently in advanced stages of optimization.

We gained access to the DOS program through a license and asset purchase agreement with VivoQuest that was completed in September 2005. Under this agreement, we licensed lead HCV molecules, a proprietary compound library and medicinal chemistry technologies. The DOS small molecule chemistry technology developed at VivoQuest was used to create these molecules and is currently being used to produce optimized compounds for advanced pre-clinical and IND-enabling GLP safety studies. See “Item 10. Additional Information -Material Contracts.”

HepeX-B

HepeX-B, a combination of two monoclonal antibodies against hepatitis B, or HBV, was licensed to Cubist in June 2004. In December 2005, Cubist announced the positive results of a Phase IIb study with HepeX-B, based on which Cubist planned to meet with the FDA to discuss a proposed Phase III trial design. In July 2006, Cubist reported that the FDA direction on the regulatory pathway for approval creates both operational and economic challenges to it. The size of the safety population the FDA is looking for translates to an extremely lengthy development timeline, as there are only about 500 liver transplants due to hepatitis B in the US and Europe each year. In July 2006, Cubist announced that it had decided not to make any further investment in the HepeX-B program while it evaluates its strategic options for HepeX-B, including the potential sub-licensing of the product.

Proprietary Technology

Our proprietary Trimera technology, which was in-licensed from Yeda, is a method for introducing functional human cells or tissue into a mouse. The Trimera technology is a patented tool whereby murine immune systems are ablated by radiation, and bone marrow is transplanted from genetically immuno-deficient mice to re-enable red blood cell production. The result is the production of “radiation chimeras.” As these chimeras have no immune system, they are able to accept implanted human cells, without rejection, thereby creating a “Trimera.” The resulting mouse can be used to generate humanized monoclonal antibodies, or hMAbs and/or as an animal model of human disease. These models can be used for testing various approaches to treat human disease, including the development of new prophylactic and therapeutic products and were used to discover the HepeX-B product and to screen the activity of XTL-6865 and XTL-2125. We have no plans to use these models and technology in our other current or planned development activities.

Intellectual Property and Patents

General

Patents and other proprietary rights are very important to the development of our business. We will be able to protect our proprietary technologies from unauthorized use by third parties only to the extent that our proprietary rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. It is our intention to seek and maintain patent and trade secret protection for our drug candidates and our proprietary technologies. As part of our business strategy, our policy is to actively file patent applications in the US and internationally to cover methods of use, new chemical compounds, pharmaceutical compositions and dosing of the compounds and compositions and improvements in each of these. We also rely on trade secret information, technical know-how, innovation and agreements with third parties to continuously expand and protect our competitive position. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that before we commercialize any of our products, any related patent may expire or remain in existence for only a short period following commercialization, thus reducing any commercial advantage or financial value attributable to the patent.

Generally, patent applications in the US are maintained in secrecy for a period of 18 months or more. Since publication of discoveries in the scientific or patent literature often lag behind actual discoveries, we are not certain that we were the first to make the inventions covered by each of our pending patent applications or that we were the first to file those patent applications. The patent positions of biotechnology and pharmaceutical companies are highly uncertain and involve complex legal and factual questions. Therefore, we cannot predict the breadth of claims allowed in biotechnology and pharmaceutical patents, or their enforceability. To date, there has been no consistent policy regarding the breadth of claims allowed in biotechnology patents. Third parties or competitors may challenge or circumvent our patents or patent applications, if issued. Granted patents can be challenged and ruled invalid at any time, therefore the grant of a patent is not of itself sufficient to demonstrate our entitlement to a proprietary right. The disallowance of a claim or invalidation of a patent in any one territory can have adverse commercial consequences in

other territories.

If our competitors prepare and file patent applications in the US that claim technology also claimed by us, we may choose to participate in interference proceedings declared by the US Patent and Trademark Office to determine priority of invention, which could result in substantial cost, even if the eventual outcome is favorable to us. While we have the right to defend patent rights related to our licensed drug candidates and technologies, we are not obligated to do so. In the event that we decide to defend our licensed patent rights, we will be obligated to cover all of the expenses associated with that effort.

If a patent is issued to a third party containing one or more preclusive or conflicting claims, and those claims are ultimately determined to be valid and enforceable, we may be required to obtain a license under such patent or to develop or obtain alternative technology. In the event of a litigation involving a third party claim, an adverse outcome in the litigation could subject us to significant liabilities to such third party, require us to seek a license for the disputed rights from such third party, and/or require us to cease use of the technology. Further, our breach of an existing license or failure to obtain a license to technology required to commercialize our products may seriously harm our business. We also may need to commence litigation to enforce any patents issued to us or to determine the scope, validity and/or enforceability of third-party proprietary rights. Litigation would involve substantial costs.

Bicifadine

There are currently eight patent families filed by DOV relating to Bicifadine: (i) methods and compositions containing Bicifadine for the treatment and prevention of hyperthermia; (ii) solid compositions containing the polymorph Form B of Bicifadine as characterized by certain infrared peaks and a distinct x-ray powder diffraction (XPRD) profile, and methods of treating pain in mammals using the same; (iii) methods and compositions employing a therapeutically effective amount of Bicifadine for preventing and treating a condition or symptom of acute pain, chronic pain, and/or a neuropathic disorder in mammalian subjects; (iv) methods and compositions containing Bicifadine HCl to prevent or treat neuropathic disorders in mammals, including, but not limited to, diabetic neuropathy; (v) methods and compositions containing Bicifadine for the prevention and treatment of lower urinary tract disorders; (vi) methods of making Bicifadine; (vii) methods and compositions for preventing or treating chronic pain comprising Bicifadine in combination with a non-steroidal anti-inflammatory drug (NSAID).

Of these eight patent families, there is one issued patent, U.S. Patent No. 7,094,799, generally directed to solid compositions containing the polymorph Form B of Bicifadine and “substantially free” of polymorph Form A. Pending patent applications filed by DOV in 2006 include:

- A patent application directed to sustained release formulations of Bicifadine.
- A patent application directed to the use of Bicifadine for treating a disability or reducing a functional impairment associated with acute pain, chronic pain, and/or neuropathic disorders.
- A patent application directed to the use of Bicifadine for preventing and treating neuropathic disorders, including, but not limited to, diabetic neuropathy, diabetic peripheral neuropathy, and neuropathy associated with alcoholism, sciatica, multiple sclerosis, spinal cord injury, chronic low back pain, HIV, cancer, etc.

In addition, there is one issued patent to Wyeth directed to a method of treating an addictive, compulsive disorder caused by alcohol or cocaine abuse using Bicifadine HCl. There are also three pending US applications filed by Wyeth in 2005 directed to methods for treating neuropathic disorders or conditions. At least one of these patent applications covers the use of Bicifadine in the treatment of neuropathic pain.

Under the license agreement with DOV, we have exclusive worldwide rights to the above patents and patent applications for all therapeutic uses, with the exception of the Wyeth Retained Field. Under the terms of the DOV/Wyeth agreement, Wyeth can only develop Bicifadine for use in the Wyeth Retained Field in collaboration with DOV, and under the license agreement between DOV and XTL Development, DOV will not conduct research or development with Wyeth for the use of Bicifadine in the Wyeth Retained Field. See “Item 3. Key Information-Risk Factors-Risks Related to Our Intellectual Property.”

XTL-2125

One patent family presently covers XTL-2125. It covers the structure of the compound, and its use for the treatment of chronic HCV patients. The patent application covers the unique structure of the molecules and their use as a pharmaceutical composition for the treatment of HCV. This patent family, if issued, will expire in 2023. Based on the provisions of the Patent Term Extension Act, we currently believe that we would qualify for certain patent term extensions. The patent application covering XTL-2125 is exclusively licensed to us by B&C Biopharm Co., Ltd.

XTL-6865

XTL-6865 is a combination of two human monoclonal antibodies against HCV, Ab68 and Ab65. Three patent families presently cover XTL-6865, including the two human monoclonal antibodies comprising XTL-6865 and its use to treat HCV infection. The patents cover both the treatment of chronic HCV patients with the antibodies and the prevention of liver re-infection in liver transplant recipients. One family concerns one antibody comprising XTL-6865, Ab68. Two families concern the second antibody comprising XTL-6865, Ab65.

The patent and patent applications covering Ab68 are exclusively licensed to us from the DRK-Blutspendedienst Baden-Wurttemberg (Ulm University, Ulm, Germany).

The patent and patent applications covering Ab65 are exclusively licensed to us from Stanford University, California in all territories outside China, and in China, it is co-exclusively licensed to us and Applied Immunogenetics.

Currently, XTL-6865 and its use to treat hepatitis C infection is covered by one issued US patent that will expire in 2019. Additional patent applications, if issued, will expire between 2018 and 2021. Based on the provisions of the Patent Term Extension Act, we currently believe that we would qualify for certain patent term extensions. We believe that we will have sufficient time to commercially utilize the inventions directed to the treatment and prevention of hepatitis C infection.

DOS

The lead molecules that are included in the VivoQuest license are covered by two issued patents and four patent applications. The patent applications describe both the structure of the compounds and their use for treating HCV infection. The two issued VivoQuest patents will expire in 2023. Additional patent applications, if issued, will expire in 2023, 2024 and 2025. Based on the provisions of the Patent Term Extension Act, we currently believe that we would qualify for certain patent term extensions.

We believe that we will have sufficient time to commercially utilize the inventions from our small molecule development program directed to the treatment and prevention of hepatitis C infection.

Other Intellectual Property Rights

We depend upon trademarks, trade secrets, know-how and continuing technological advances to develop and maintain our competitive position. To maintain the confidentiality of trade secrets and proprietary information, we require our employees, scientific advisors, consultants and collaborators, upon commencement of a relationship with us, to execute confidentiality agreements and, in the case of parties other than our research and development collaborators, to agree to assign their inventions to us. These agreements are designed to protect our proprietary information and to grant us ownership of technologies that are developed in connection with their relationship with us. These agreements may not, however, provide protection for our trade secrets in the event of unauthorized disclosure of such information.

In addition to patent protection, we may utilize orphan drug regulations to provide market exclusivity for certain of our drug candidates. The orphan drug regulations of the FDA provide incentives to pharmaceutical and biotechnology companies to develop and manufacture drugs for the treatment of rare diseases, currently defined as diseases that exist in fewer than 200,000 individuals in the US, or, diseases that affect more than 200,000 individuals in the US but that the sponsor does not realistically anticipate will generate a net profit. Under these provisions, a manufacturer of a designated orphan drug can seek tax benefits, and the holder of the first FDA approval of a designated orphan product will be granted a seven-year period of marketing exclusivity for such FDA-approved orphan product. While we believe that certain of the indications for our drug candidates will be eligible for orphan drug designation, we cannot assure you that our drugs will obtain such orphan drug designation or that we will be the first to receive FDA approval

for such drugs so as to be eligible for market exclusivity protection.

Licensing Agreements and Collaborations

We have formed strategic alliances with a number of companies for the manufacture and commercialization of our products. Our current key strategic alliances are discussed below. See “Item 5. Operating and Financial Review and Prospects - Obligations and Commitments” which describes contingent milestone payments we have undertaken to make to certain licensors over the life of the licenses described below.

Bicifadine License

In January 2007, XTL Development signed an agreement with DOV to in-license the worldwide rights for Bicifadine, a serotonin and norepinephrine reuptake inhibitor. XTL Development intends to develop Bicifadine for the treatment of neuropathic pain - a chronic condition resulting from damage to peripheral nerves. In accordance with the terms of the license agreement, XTL Development made an initial up-front payment of $7.5 million in cash. In addition, XTL Development will make milestone payments of up to $126.5 million, in cash and/or in our ordinary shares over the life of the license, of which up to $115 million will be due upon or after regulatory approval of the product and the remaining $11.5 million will be due prior to regulatory approval of the product. XTL Development is also obligated to pay DOV royalties on net sales of the product.

XTL-2125 License

XTL-2125 has been licensed from B&C since February 2003. Under the terms of the agreement, we have exclusive worldwide rights to XTL-2125, with the exception of Asia, which is shared between the two companies, and Korea, for which B&C retains exclusive rights. Under the terms of the agreement, we are obligated to make certain milestone payments in addition to royalties on product sales. To date we have made $1.5 million in license and milestone payments to B&C, and we have agreed to make additional contingent milestone payments of up to approximately $13.0 million over the life of the license, of which $8.0 million will be due upon or following regulatory approval of the drug. The license terminates upon the expiration of the last of the licensed patents. Notwithstanding the above, we may terminate this agreement upon specified notice to B&C.

XTL-6865 License

XTL-6865 is a combination of two human monoclonal antibodies against HCV, Ab68 and Ab65.

In April 2000, we licensed Ab68 under an exclusive worldwide license from the DRK-Blutspendedienst Baden-Wurttemberg (Ulm University, Germany, or Ulm). Under the terms of this agreement, we are obligated to pay Ulm a specified royalty rate on sales of product incorporating Ab68. We can deduct certain payments that are made to third parties from these royalties, subject to a minimum royalty rate. We are also obligated to pay Ulm a specified percentage of any milestone payments we may receive from any sublicensee to whom we may grant a license or sublicense of Ab68 or technology related to the production of Ab68. We can deduct certain of these payments that are made to third parties from the percentage of milestone payments owed to Ulm, subject to a minimum milestone payment amount. Either party may terminate the agreement, by written notice, upon or after the winding up or insolvency of the other party, or upon or after commitment of a material breach by the other party that cannot be cured, or if curable, has not been cured, within 60 days after receipt of notice. In the absence of such termination, the agreement shall expire upon the expiration of the patent family granted under the agreement. To date we have made $150,000 in license and milestone payments to Ulm.

In September 2003, we licensed Ab65 from Stanford University under an exclusive worldwide license agreement, excluding China. In China, we have co-exclusive rights with Applied Immunogenetics LLC. Under the terms of this agreement, we must use commercially reasonable efforts to commercialize and market Ab65. We are obligated to make royalty payments to Stanford University on sales of product incorporating Ab65, and we are also obligated to

make milestone payments upon the occurrence of certain specified events. To date we have made $202,000 in license and milestone payments to Stanford University, and we have undertaken to make contingent milestone payments of up to approximately $200,000 over the life of the license, all of which will be due upon or following regulatory approval of the drug. The license terminates upon the later of the expiration of last of the licensed patents or at the time of our last royalty payment. Notwithstanding the above, we may terminate this agreement upon specified notice to Stanford University. In addition, should we fail to meet certain developmental milestones for Ab65, our rights to the use of Ab65 become non-exclusive upon notice to that effect to us by Stanford University.

In addition, under an agreement entered into in September 2003, we are obligated to make royalty payments on sales of product incorporating Ab65 to Applied Immunogenetics LLC, a company that previously held non-exclusive rights to Ab65 and returned them to Stanford University, enabling us to gain exclusive rights to Ab65 from Stanford University. Our agreement with Applied Immunogenetics LLC expires on the expiration or termination of our exclusive agreement with Stanford University, as described above. To date we have made $183,000 in license and milestone payments to Applied Immunogenetics LLC. There are no additional contingent milestone payments.

Cubist License

We have entered into a licensing agreement with Cubist dated June 2, 2004, as amended, under which we granted to Cubist an exclusive, worldwide license (with the right to sub-license) to commercialize HepeX-B and any other product containing a hMAb or humanized monoclonal antibody or fragment directed at the hepatitis B virus owned or controlled by us. In August 2005, we transferred full responsibility for completing the development of HepeX-B to Cubist. Cubist will be responsible for completing the development and for registration and commercialization of the product worldwide. Nevertheless, during the term of this agreement, we have an ongoing obligation to transfer to Cubist all information Cubist may reasonably require and to provide Cubist with reasonable access to pertinent employees of ours that have experience with or information related to HepeX-B. We are also required to file, prosecute and maintain the relevant patents at our sole expense.

Cubist has the right to sub-license HepeX-B. The sub-licensee fees we will receive in such cases will vary according to the territory, the subject of the sub-license, the patent protection of HepeX-B in that territory, total costs of HepeX-B development, third party license payments, indemnification obligations and local competition.

In December 2005, Cubist announced the positive results of a Phase IIb study with HepeX-B, based on which Cubist planned to meet with the FDA to discuss a proposed Phase III trial design. In July 2006, Cubist reported that the FDA direction on the regulatory pathway for approval creates both operational and economic challenges to it. The size of the safety population the FDA is looking for translates to an extremely lengthy development timeline, as there are only about 500 liver transplants due to hepatitis B in the US and Europe each year. As of the date hereof, Cubist has decided not to make any further investment in the HepeX-B program while Cubist evaluates strategic options for HepeX-B.

The agreement expires on the later of the last valid patent claim covering HepeX-B to expire or 10 years after the first commercial sale of HepeX-B on a country-by-country basis.

VivoQuest License

In August 2005, we entered into a license agreement with VivoQuest covering a proprietary compound library, including certain HCV compounds. Under the terms of the license agreement, we have exclusive worldwide rights to VivoQuest’s intellectual property and technology in all fields of use. To date we have made approximately $0.9 million in license payments to VivoQuest under the license agreement. The license agreement also provides for additional milestone payments triggered by certain regulatory and sales targets. These additional milestone payments total $34.6 million, $25.0 million of which will be due upon or following regulatory approval or actual product sales, and are payable in cash or ordinary shares at our election. In addition, the license agreement requires that we make royalty payments to VivoQuest on product sales.

Yeda License

In April of 1993, we entered into a research and license agreement with Yeda, which we refer to as the Yeda Agreement, under which Yeda granted us an exclusive worldwide license to use the Trimera patent portfolio and to exclusively use the information derived from the performance of certain research for the purposes specified in the agreement. Subject to earlier termination in accordance with the Yeda Agreement, the term of the license with respect to any licensed product made and/or sold or to any other licensed activity conducted in any country where a licensed patent covers such product or other licensed activity is until the date on which the last licensed patent in that country expires or until 12 years from the first commercial sale of the product (or first receipts to us from such other licensed activity) in such country, whichever is the longer period and in any other country until 12 years from the first commercial sale of such product (or first receipts to us from such other licensed activity) in that country. Similar provisions fix the term of the license with respect to licensed activities not attributable to any particular country.

Under the agreement, any assignment or sublicense of the license granted by Yeda requires Yeda's prior written consent.

The Yeda Agreement has undergone a number of amendments, one of the end results of which is that we shall pay to Yeda the following royalties in connection with the license: a royalty of 3% of all net sales received by us; 25% of amounts received by us on net sales of third parties (less certain royalties payable by us to third parties), but no more than 3% and no less than 1.5% of such net sales; and a royalty ranging between 20% to 40% on any receipts to us other than our net sales or receipts on net sales made by third parties. Furthermore, such amendments have also changed the termination provisions relating to Yeda’s entitlement to terminate the agreement if we do not pay Yeda a certain minimum amount of annual royalties of $100,000 or $200,000, depending on the year. We may terminate the agreement with Yeda with six months advance notice in which event our rights in any technology licensed by Yeda to us shall terminate and all rights in any technology derived from research and development activities performed by us in connection with the technology licensed by Yeda to us shall vest in Yeda.

In the agreement between Yeda, us and Cubist, whereby Yeda gave its consent relating to the grant of the license by us to Cubist under the terms of the HepeX-B collaboration, Yeda received the right to receive at least 1.5% of net sales of HepeX-B by Cubist sub-licensees, regardless of the amount received by us from Cubist in respect of such sales.

Competition

Competition in the pharmaceutical and biotechnology industries is intense. Our competitors include pharmaceutical companies and biotechnology companies, as well as universities and public and private research institutions. In addition, companies that are active in different but related fields represent substantial competition for us. Many of our competitors have significantly greater capital resources, larger research and development staffs and facilities and greater experience in drug development, regulation, manufacturing and marketing than we do. These organizations also compete with us to recruit qualified personnel, attract partners for joint ventures or other collaborations, and license technologies that are competitive with ours. To compete successfully in this industry we must identify novel and unique drugs or methods of treatment and then complete the development of those drugs as treatments in advance of our competitors.

The drugs that we are attempting to develop will have to compete with existing therapies. In addition, a large number of companies are pursuing the development of pharmaceuticals that target the same diseases and conditions that we are targeting. Other companies have products or drug candidates in various stages of pre-clinical or clinical development to treat diseases for which we are also seeking to discover and develop drug candidates. Some of these potential competing drugs are further advanced in development than our drug candidates and may be commercialized earlier.

Competing Products for Treatment of Neuropathic Pain

Three oral drugs have been approved by the FDA for the treatment of neuropathic pain: Gabapentin (developed by Pfizer Inc.) which is approved for the treatment of post herpetic neuralgia; Pregabalin (developed by Pfizer Inc.) which is approved for post herpetic neuralgia and diabetic neuropathic pain; and Cymbalta (developed by Eli Lilly and Company) which is approved for diabetic neuropathic pain.

Several other drugs are in late-stage clinical trials for the treatment of neuropathic pain: milnacipran (developed by Cypress Bioscience Inc.) is presently is Phase III clinical trials for the treatment of fibromyalgia, and desvenlafaxin (developed by Wyeth Pharmaceuticals Inc.) is presently in Phase III clinical trials for the treatment of neuropathic pain. Wyeth has also filed a new drug application, or NDA, with the FDA, seeking approval of desvenlafaxin in depression.

Several additional companies are developing drugs for neuropathic pain including: Vernalis plc, Endo Pharmaceuticals Inc., GlaxoSmithKline plc, Avanir Pharmaceuticals, and UCB.

Competing Products for Treatment of Chronic Hepatitis C

We believe that a certain number of the drugs that are currently under development will become available in the future for the treatment of hepatitis C.

At present, the only approved therapies for treatment of chronic HCV are Interferon-based. There are multiple drugs presently under development for the treatment of HCV, most of which are in the pre-clinical or early stage of clinical development. These compounds are being developed by both established pharmaceutical companies, as well as by biotech companies. Examples of such companies are: Anadys Pharmaceuticals, Inc., F. Hoffman-LaRoche & Co., Intercell AG, Schering-Plough Corporation, Gilead Sciences, Inc., Idenix Pharmaceuticals, Inc., InterMune, Inc.,

Vertex Pharmaceuticals Incorporated and Viropharma Incorporated. Many of these companies and organizations, either alone or with their collaborative partners, have substantially greater financial, technical and human resources than we do. In addition, our competitors also include smaller private companies such as Pharmasset, Ltd.

Supply and Manufacturing

We currently have no manufacturing capabilities and do not intend to establish any such capabilities.

Bicifadine

As part of our license agreement with DOV, we have the right to purchase certain inventories of Bicifadine that have been produced for DOV. We believe that the present Bicifadine inventories owned by DOV will be adequate to satisfy our current clinical supply needs. For further late stage trials, we intend to utilize DOV's existing Bicifadine inventory so long as it meets the relevant specifications and quality control requirements. In the event that the inventory does not meet the proper specifications, or if DOV should fail to provide us with adequate supplies of the inventory, then we will contract with a manufacturer to supply us with our additional clinical needs. For commercial supply of Bicifadine, we intend to contract with the drug's existing manufacturers or other drug manufacturers to produce drug supply in sufficient quantity for launch and commercialization. See "Item 3. Key Information-Risk Factors-Risks Related to Our Intellectual Property."

XTL-2125

In 2003, we entered into a contract manufacturing agreement with an Israeli-based manufacturer for the supply of XTL-2125. We believe that this contract manufacturer will be adequate to satisfy our current clinical supply needs.

XTL-6865

In 2000, we entered into a contract manufacturing agreement with a US-based manufacturer for the supply of the HepeX-C drug product, the single antibody version of XTL-6865, and subsequently under a master agreement for the supply of XTL-6865, the dual-MAb product. We believe that this contract manufacturer will be adequate to satisfy our current clinical supply needs.

HepeX-B

In July 2006, Cubist announced that it has decided not to make any further investment in the HepeX-B program, while it evaluates its strategic options for HepeX-B, including the sub-licensing of the product.

Future supply of the HepeX-B clinical material will be manufactured by a contract manufacturer to be selected by our partner Cubist or its sub-licensor, should it sub-license HepeX-B to a third-party.

DOS

For planned pre-clinical and clinical supply of the HCV compounds licensed from VivoQuest, we intend to enter into a contract with a manufacturer to produce our pre-clinical and clinical supply needs.

General

At the time of commercial sale, to the extent possible and commercially practicable, we plan to engage a back-up supplier for each of our product candidates. Until such time, we expect that we will rely on a single contract manufacturer to produce each of our product candidates under cGMP regulations. Our third-party manufacturers have a limited numbers of facilities in which our product candidates can be produced and will have limited experience in manufacturing our product candidates in quantities sufficient for conducting clinical trials or for commercialization. Our third-party manufacturers will have other clients and may have other priorities that could affect our contractor's ability to perform the work satisfactorily and/or on a timely basis. Both of these occurrences would be beyond our

control. We anticipate that we will similarly rely on contract manufacturers for our future proprietary product candidates.

We expect to similarly rely on contract manufacturing relationships for any products that we may in-license or acquire in the future. However, there can be no assurance that we will be able to successfully contract with such manufacturers on terms acceptable to us, or at all.

Contract manufacturers are subject to ongoing periodic inspections by the FDA, the US Drug Enforcement Agency and corresponding state agencies to ensure strict compliance with cGMP and other state and federal regulations. Our contractor in Israel faces similar inspections from Israeli regulatory agencies and from the FDA. We do not have control over third-party manufacturers' compliance with these regulations and standards, other than through contractual obligations.

If we need to change manufacturers, the FDA and corresponding foreign regulatory agencies must approve these new manufacturers in advance, which will involve testing and additional inspections to ensure compliance with FDA regulations and standards and may require significant lead times and delay. Furthermore, switching manufacturers may be difficult because the number of potential manufacturers is limited. It may be difficult or impossible for us to find a replacement manufacturer quickly or on terms acceptable to us, or at all.

Government and Industry Regulation

Numerous governmental authorities, principally the FDA and corresponding state and foreign regulatory agencies, impose substantial regulations upon the clinical development, manufacture and marketing of our drug candidates and technologies, as well as our ongoing research and development activities. None of our drug candidates have been approved for sale in any market in which we have marketing rights. Before marketing in the US, any drug that we develop must undergo rigorous pre-clinical testing and clinical trials and an extensive regulatory approval process implemented by the FDA, under the Federal Food, Drug and Cosmetic Act of 1938, as amended. The FDA regulates, among other things, the pre-clinical and clinical testing, safety, efficacy, approval, manufacturing, record keeping, adverse event reporting, packaging, labeling, storage, advertising, promotion, export, sale and distribution of biopharmaceutical products.

The regulatory review and approval process is lengthy, expensive and uncertain. We are required to submit extensive pre-clinical and clinical data and supporting information to the FDA for each indication or use to establish a drug candidate's safety and efficacy before we can secure FDA approval. The approval process takes many years, requires the expenditure of substantial resources and may involve ongoing requirements for post-marketing studies or surveillance. Before commencing clinical trials in humans, we must submit an IND to the FDA containing, among other things, pre-clinical data, chemistry, manufacturing and control information, and an investigative plan. Our submission of an IND may not result in FDA authorization to commence a clinical trial.

The FDA may permit expedited development, evaluation, and marketing of new therapies intended to treat persons with serious or life-threatening conditions for which there is an unmet medical need under its fast track drug development programs. A sponsor can apply for fast track designation at the time of submission of an IND, or at any time prior to receiving marketing approval of the NDA. To receive fast track designation, an applicant must demonstrate that the drug:

- is intended to treat a serious or life-threatening condition;
- is intended to treat a serious aspect of the condition; and
- has the potential to address unmet medical needs, and this potential is being evaluated in the planned drug development program.

Clinical testing must meet requirements for institutional review board oversight, informed consent and good clinical practices, and must be conducted pursuant to an IND, unless exempted.

For purposes of NDA approval, clinical trials are typically conducted in the following sequential phases:

- *Phase I*: The drug is administered to a small group of humans, either healthy volunteers or patients, to test for safety, dosage tolerance, absorption, metabolism, excretion, and clinical pharmacology.
- *Phase II*: Studies are conducted on a larger number of patients to assess the efficacy of the product, to ascertain dose tolerance and the optimal dose range, and to gather additional data relating to safety and potential adverse events.

- *Phase III*: Studies establish safety and efficacy in an expanded patient population.

- *Phase IV*: The FDA may require Phase IV post-marketing studies to find out more about the drug's long-term risks, benefits, and optimal use, or to test the drug in different populations, such as children.

The length of time necessary to complete clinical trials varies significantly and may be difficult to predict. Clinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals. Additional factors that can cause delay or termination of our clinical trials, or that may increase the costs of these trials, include:

- slow patient enrollment due to the nature of the clinical trial plan, the proximity of patients to clinical sites, the eligibility criteria for participation in the study or other factors;
- inadequately trained or insufficient personnel at the study site to assist in overseeing and monitoring clinical trials or delays in approvals from a study site's review board;
- longer treatment time required to demonstrate efficacy or determine the appropriate product dose;
- insufficient supply of the drug candidates;
- adverse medical events or side effects in treated patients; and
- ineffectiveness of the drug candidates.

In addition, the FDA may place a clinical trial on hold or terminate it if it concludes that subjects are being exposed to an unacceptable health risk. Any drug is likely to produce some toxicity or undesirable side effects when administered at sufficiently high doses and/or for a sufficiently long period of time. Unacceptable toxicity or side effects may occur at any dose level at any time in the course of studies designed to identify unacceptable effects of a drug candidate, known as toxicological studies, or clinical trials of drug candidates. The appearance of any unacceptable toxicity or side effect could cause us or regulatory authorities to interrupt, limit, delay or abort the development of any of our drug candidates and could ultimately prevent approval by the FDA or foreign regulatory authorities for any or all targeted indications.

Before receiving FDA approval to market a product, we must demonstrate that the product is safe and effective for its intended use by submitting to the FDA an NDA containing the pre-clinical and clinical data that have been accumulated, together with chemistry and manufacturing and controls specifications and information, and proposed labeling, among other things. The FDA may refuse to accept an NDA for filing if certain content criteria are not met and, even after accepting an NDA, the FDA may often require additional information, including clinical data, before approval of marketing a product.

As part of the approval process, the FDA must inspect and approve each manufacturing facility. Among the conditions of approval is the requirement that a manufacturer's quality control and manufacturing procedures conform to cGMP. Manufacturers must expend time, money and effort to ensure compliance with cGMP, and the FDA conducts periodic inspections to certify compliance. It may be difficult for our manufacturers or us to comply with the applicable cGMP and other FDA regulatory requirements. If we or our contract manufacturers fail to comply, then the FDA will not allow us to market products that have been affected by the failure.

If the FDA grants approval, the approval will be limited to those disease states, conditions and patient populations for which the product is safe and effective, as demonstrated through clinical studies. Further, a product may be marketed only in those dosage forms and for those indications approved in the NDA. Certain changes to an approved NDA, including, with certain exceptions, any changes to labeling, require approval of a supplemental application before the drug may be marketed as changed. Any products that we manufacture or distribute pursuant to FDA approvals are subject to continuing regulation by the FDA, including compliance with cGMP and the reporting of adverse experiences with the drugs. The nature of marketing claims that the FDA will permit us to make in the labeling and

advertising of our products will be limited to those specified in an FDA approval, and the advertising of our products will be subject to comprehensive regulation by the FDA. Claims exceeding those that are approved will constitute a violation of the Federal Food, Drug, and Cosmetic Act. Violations of the Federal Food, Drug, and Cosmetic Act or regulatory requirements at any time during the product development process, approval process, or after approval may result in agency enforcement actions, including withdrawal of approval, recall, seizure of products, injunctions, fines and/or civil or criminal penalties. Any agency enforcement action could have a material adverse effect on our business.

Should we wish to market our products outside the US, we must receive marketing authorization from the appropriate foreign regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing and reimbursement vary widely from country to country. At present, companies are typically required to apply for foreign marketing authorizations at a national level. However, within the EU, registration procedures are available to companies wishing to market a product in more than one EU member state. Typically, if the regulatory authority is satisfied that a company has presented adequate evidence of safety, quality and efficacy, then the regulatory authority will grant a marketing authorization. This foreign regulatory approval process, however, involves risks similar or identical to the risks associated with FDA approval discussed above, and therefore we cannot guarantee that we will be able to obtain the appropriate marketing authorization for any product in any particular country. Our current development strategy calls for us to seek marketing authorization for our drug candidates outside the United States.