UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2015

OR

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

Commission File Number 001-36830

CARBYLAN THERAPEUTICS, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**20-0915291**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
3181 Porter Drive, Palo Alto, California 94304	
(Address of principal executive offices)	

Registrant's telephone number, including area code: (650) 855-6777

Title of each class	**Name of exchange on which registered**
Common Stock, par value $0.001 per share	**The NASDAQ Stock Market LLC (The NASDAQ Global Market**

Securities registered pursuant to Section 12(g) of the Act: **None**

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

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the Registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit and post such files). YES ☒ NO ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definition of "large accelerated filer", "accelerated filer", and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒ (Do not check if a small reporting company)	Small reporting company	☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The NASDAQ Global Market on June 30, 2015, was $88,485,047.

The number of shares of Registrant's Common Stock outstanding as of March 15, 2016 was 26,332,494.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Part III of the Annual Report on Form 10-K is incorporated by reference to the registrant's definitive proxy statement for the registrant's 2016 Annual Meeting of Stockholders, which will be filed with the Securities and Exchange Commission not later than 120 days after the close of the registrant's fiscal year ended December 31, 2015.

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PART I

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. All statements other than statements of historical facts contained in this report are forward-looking statements. In some cases, you can identify forward- looking statements by terminology such as "may," "could," "will," "would," "should," "expect," "plan," "anticipate," "believe," "estimate," "intend," "predict," "seek," "contemplate," "potential" or "continue" or the negative of those terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- expectations regarding the timing, likelihood, nature and effects of our ongoing exploration of strategic alternatives and any consummation of a strategic transaction;
- the success, cost and timing of our product development activities and clinical trials and projections as to the timing of clinical studies and regulatory submissions;
- our ability to obtain and maintain regulatory approval of Hydros-TA, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or become available;
- the loss of key scientific or management personnel;
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act;
- the sufficiency of our capital resources;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and
- our expectations regarding our ability to obtain and adequately maintain sufficient intellectual property protection for our current or future product candidates.

These forward-looking statements relate to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance and achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things those listed under "Risk Factors" and elsewhere in this Annual Report on Form 10-K.

Any forward-looking statement in this Annual Report on Form 10-K reflects our current views with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future-growth. Given these uncertainties, you should not place undue reliance upon these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for certain drugs, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to certain uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise specifically stated, we obtained this industry, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

Forward-looking statements do not reflect the potential impact of any future in-licensing, collaborations, acquisitions, mergers, dispositions, joint ventures, or investments we may enter into or make. Except as required by law, we undertake no obligation to, and expressly disclaim any obligation to, revise or update the forward-looking statements made herein or the risk factors whether as a result of new information, future events or otherwise.

Unless the context requires otherwise, in this Annual Report on Form 10-K the terms “Carbylan”, “we,” “us,” “our” and “the Company” refer to Carbylan Therapeutics, Inc.

Carbylan ® and our logo are some of our trademarks used in this Annual Report on Form 10-K. We also use trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, these trademarks and tradenames referred to appear without the ® and ™ symbol, but, in the case of our trademark and tradenames, those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, to our trademarks or tradenames.

As of December 31, 2015, our common stock is traded on The NASDAQ Global Market ("NASDAQ") under the trading symbol "CBYL" In March 2016, the Company received notice from NASDAQ of potential delisting. For more information on the potential delisting of our common stock see "Item 1A: Risk Factors—Risks Related to Our Business."

Item 1. Business.

We are a clinical-stage specialty pharmaceutical company focused on the development and commercialization of novel and proprietary combination therapies that address significant unmet medical needs. Our initial focus is on the development of Hydros-TA, our proprietary, potentially best-in-class intra-articular (“IA”), injectable product candidate to treat pain associated with osteoarthritis (“OA”), of the knee. Current joint injection, or intra-articular, treatments for OA pain include corticosteroids, which provide short-term relief, and viscosupplements, which provide relief over the longer-term. In contrast, Hydros-TA utilizes our proprietary cross-linking technology to deliver both rapid pain relief with a low dose corticosteroid triamcinolone acetonide, or TA, and sustained pain relief from our novel hyaluronic acid viscosupplement.

In February 2016, we announced topline results of our COR1.1 trial, a Phase 3, multi-center, international, randomized, double-blind, three-arm trial that enrolled 560 patients with grade two and grade three OA of the knee, comparing treatment with Hydros-TA to treatment with Hydros and with TA, on a standalone basis. The primary endpoints of the trial were changes from baseline in the WOMAC A pain scores at week 2 for Hydros-TA versus Hydros and at week 26 for Hydros-TA versus TA, as well as a safety assessment of adverse events. Hydros-TA met the first of its two primary endpoints, demonstrating a statistically significant improvement from baseline in the WOMAC A pain score at week 2 versus Hydros. In addition, Hydros-TA maintained a significant reduction in pain from baseline over 26 weeks. However, patients in the TA arm continued to show an unexpected significant reduction in pain through 26 weeks. Given the comparable effectiveness at 26 weeks, COR1.1 did not meet its second primary endpoint. Hydros-TA was generally well tolerated with no treatment related serious adverse events, or SAEs, and adverse events, or AEs, were mostly mild and included arthralgia (knee pain) and swelling.

In March 2016, we engaged a financial and strategic advisor, Wedbush PacGrow, to advise us on strategic alternatives. Wedbush PacGrow will provide a range of advisory services aimed to enhance shareholder value. The alternatives to be considered will include the potential for an acquisition, merger, strategic partnership or other strategic transactions. We expect to devote substantial time and resources to exploring strategic alternatives, however, there can be no assurance that such activities will result in any agreements or transactions that will enhance shareholder value. Further, any strategic transaction that is completed ultimately may not deliver the anticipated benefits or enhance shareholder value.

We own the global development and commercialization rights to Hydros-TA, except in China, Taiwan, Hong Kong and Macau. We have three issued U.S. patents and ten issued non-U.S. patents, the earliest of which will expire in 2030, and 25 patent applications worldwide covering our Hydros platform technology, including claims directed to composition of matter, methods of use and product-by-process.

Osteoarthritis Overview

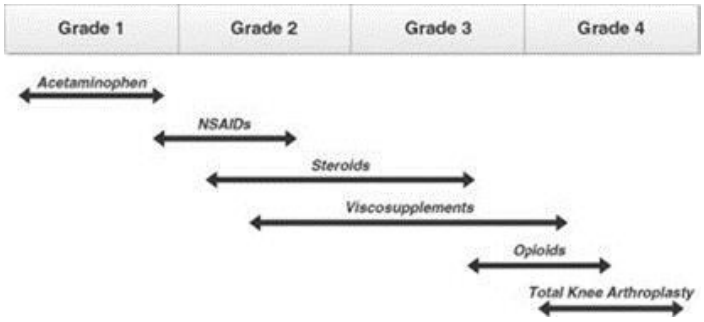
OA is a joint disorder involving the degradation of the IA cartilage, joint lining, ligaments and, ultimately, underlying bone. OA results in inflammation of the soft tissue and bony structures of the joint, which worsens over time and leads to progressive thinning of articular cartilage. Symptoms of this disease include pain, stiffness, swelling and limitation in the function of the joint. There is no known way to reverse the progression of OA and while there are a number of therapeutic options to treat the pain associated with OA, the disease typically continues to advance.

In the United States, there are over 27 million patients with OA, and approximately half of all adult patients will develop symptomatic OA of the knee. According to Millennium Research Group, in 2012, 1.65 million IA knee injections of hyaluronic acid, or HA, were administered. In the same year, worldwide sales of HA were approximately $1.76 billion, $726 million of which came from the United States.

Limitations of Current Treatments

OA severity is generally graded on a scale from one to four. When OA advances and oral or topical drug treatments are not sufficient to effectively address the associated pain, physicians often turn to IA treatments, such as corticosteroids, commonly known as steroids, and HA viscosupplements.

While steroid injections can provide rapid pain relief, clinical practice and medical literature suggest that they generally provide only short-term pain relief of two to four weeks post injection. On the other hand, while HA injections can often provide long-term pain relief of up to approximately six months, they do not generally begin to provide peak pain relief until five weeks post injection. The following graph sets out what we believe to be the standard treatment progression for the treatment of OA pain in the knee:



Despite the use of currently available treatments, many OA patients experience persistent and worsening pain. Joint replacement surgery, often referred to as total knee arthroplasty, or TKA, is generally the last option for the treatment of OA. Compared to other treatments, this invasive surgery is an expensive option, with an initial surgical procedure cost of approximately $33,000 to $40,000. With patients receiving TKAs more frequently at a younger age, surgery to replace a previously performed TKA, known as a revision surgery, is increasingly common. Revision surgeries are not only more costly, at approximately $74,000, they are also associated with significantly higher morbidity and failure rates than the initial TKA surgery. Due to the expense of surgery and the limitations of treatments administered to prevent such surgeries, there exists a need for an alternative treatment that could provide both rapid and sustained relief from OA pain and potentially delay the need for joint replacement surgery.

Our Solution — Hydros-TA

Hydros-TA is a combination IA product, designed to provide both rapid and sustained pain relief with a single 6 ml intra-articular injection comprised of 52 mg of bacterially derived HA and 10 mg of TA. Rapid relief may be provided from our low dose steroid component and sustained pain relief, up to six months, may be provided from our proprietary HA component. Hydros-TA is comprised of bacterially derived HA-based hydrogel particles suspended in a solution of hyaluronic acid. The hydrogel particles contain the steroid, TA, which is entrapped within these particles. The dose of TA used in Hydros-TA is 10 mg, which is one quarter of the dose of TA that is often given clinically for IA injections into the knee. We believe the incorporation of a low dose steroid into Hydros-TA provides a means of rapid pain relief currently missing from commercially-available HA. We believe that a clinically-proven and FDA-approved combination Hydros-TA product will provide a compelling alternative to sequential injections of steroids and viscosupplements.

Hydros-TA Clinical Program

COR1.1

Our first Phase 3 clinical trial of Hydros-TA, known as COR1.1, was a multi-center, international, randomized, double-blind, three-arm trial that enrolled 560 patients with grade two and grade three OA of the knee, comparing treatment with Hydros-TA to treatment with Hydros and with TA 10mg, on a standalone basis. We utilized the WOMAC NRS 3.1 Index in our COR1.1 trial (0-10 point scale). Our studies also utilize standardized criteria to define the number and percentage of defined positive “strict responders” (>50% and >20 mm improvements in WOMAC A (pain) or WOMAC C (function) scores, respectively, over baseline).

Our COR1.1 trial was conducted in 30 clinical centers across Canada, Europe, Australia, New Zealand, and the Caribbean with a total of 560 enrolled subjects that were treated and followed for six months with an optional 1 year safety follow-up. These subjects were randomized 1:1:1 to three study treatment arms: Hydros-TA, Hydros (the viscosupplement without steroid) and TA 10mg. The primary endpoints of the trial were changes from baseline in the WOMAC A pain scores at week 2 for Hydros-TA versus Hydros and at week 26 for Hydros-TA versus TA 10mg.Hydros-TA met the first of its two primary endpoints, demonstrating a statistically significant improvement from baseline in the WOMAC A pain score at week 2 versus Hydros. In addition, Hydros-TA maintained a significant reduction in pain from baseline over 26 weeks. However, patients in the TA arm continued to show an unexpected significant reduction in pain through 26 weeks. Given the comparable effectiveness at 26 weeks, COR1.1 did not meet its second primary endpoint. Hydros-TA was generally well tolerated with no treatment related serious adverse events, or SAEs, and adverse events, or AEs, were mostly mild and included arthralgia (knee pain) and swelling.

The following table represents the COR1.1 trial baseline scores for each of the treatment groups, as well as the WOMAC pain score least square mean reductions from baseline at 1, 2, 6, 13 and 26 week post injection. The estimated difference between the treatment groups is also represented.

Time Point	TA 10 mg n=185	Hydros n=189	Hydros-TA n=186	Extra Pain Reduction Hydros-TA vs. Hydros	Extra Pain Reduction Hydros-TA vs. TA 10mg
Baseline	7.1	7.3	7.1	N/A	N/A
1 week	-4.5	-3.3	-4.7	-1.4	-0.2
2 weeks	-4.5	-3.9	-4.6	-0.7	-0.1
6 weeks	-4.4	-4.1	-4.2	-0.1	0.2
13 weeks	-4.3	-4.1	-4.1	0.0	0.2
26 weeks	-4.0	-4.1	-3.9	0.2	0.1

COR1.0

Our Phase 2b clinical trial of Hydros-TA, known as COR1.0, was a prospective, multicenter, randomized, double-blind feasibility study to evaluate the safety and performance of Hydros-TA in subjects with OA of the knee. Our COR1.0 trial was conducted in eight clinical centers in Canada, Europe and the Caribbean with a total of 98 enrolled subjects that were treated and followed for six months thereafter. These subjects were randomized 1:1:1 to three study treatment arms: Hydros-TA, Hydros (the viscosupplement without steroid) and Synvisc-One (the U.S. market leading HA viscosupplement). In our primary endpoint, WOMAC pain score, pain reduction from baseline was observed in all treatment groups, however, Hydros-TA provided greater pain reduction compared to Synvisc-One at all study time points, as well as over the full study follow-up period of 26 weeks. Though we did not design our COR1.0 trial to enroll a sufficient number of patients to demonstrate statistical significance generally, the separation of pain reduction scores between Hydros-TA and Hydros was large enough to demonstrate statistical significance at the two week measurement point with the number of patients actually enrolled. Though statistical significance was not achieved at any other time point and in any other comparison of treatment arms, the separation between Hydros-TA and Synvisc-One represented approximately 10% of the baseline score, a numerical amount generally considered “clinically meaningful” and, we believe, not often seen in viscosupplementation trials with active comparators. For our secondary endpoints, WOMAC B (stiffness), WOMAC function, and responder rate, we saw a similar trend of improved outcomes with Hydros-TA compared to Synvisc-One. In addition, Hydros-TA was generally well-tolerated with fewer product-related adverse events reported than Synvisc-One.

The following table represents the COR1.0 trial baseline scores for each of the treatment groups, as well as the WOMAC pain score least square mean reductions from baseline over the full 26 week evaluation period, as well as at the 2, 6, 13 and 26 week time points post injection. The estimated difference between the treatment groups is also represented.

Time Point	Synvisc-One n=32	Hydros n=32	Hydros-TA n=34	Extra Pain Reduction Hydros vs. Synvisc-One	Extra Pain Reduction Hydros-TA vs. Hydros	Extra Pain Reduction Hydros-TA vs. Synvisc-One
Baseline	66.4	68.1	69.4	N/A	N/A	N/A
2 weeks	-28.5	-23.3	-35.6	5.2	-12.4	-7.2
6 weeks	-25.6	-32.4	-33.4	-6.7	-1.1	-7.8
13 weeks	-29.0	-33.9	-33.3	-4.9	0.6	-4.3
26 weeks	-28.9	-32.4	-35.2	-3.5	-2.8	-6.3
Overall	**-28.0**	**-30.5**	**-34.4**	**-2.5**	**-3.9**	**-6.4**

Future Development of Hydros-TA

We are required to successfully complete two Phase 3 clinical trials and one safety trial in order to satisfy the requirements for the demonstration of safety and efficacy of Hydros-TA in our initial indication for OA pain in the knee. In addition to the two Phase 3 clinical trials, we will need to collect safety data from an additional 400 to 450 patients, which will provide us with approximately 800 patients to make up our safety database. Since TA is an approved product in different pharmaceutical preparations, we may rely on the FDA's prior findings of safety and efficacy for TA and, thus, the Hydros-TA new drug application, or NDA, could benefit from being filed under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or the FDCA, by eliminating the need for certain pre-clinical safety studies of TA. Hydros is considered a new molecular entity, or NME, and we are required to complete full pre-clinical testing to assure its safety profile. However, since Hydros-TA is our product candidate, not Hydros alone, in order to obtain regulatory approval of Hydros-TA, Hydros will not have to undergo any clinical testing independent of the Hydros-TA studies. While we are considering potential strategic alternatives, we are also considering the potential for the future clinical development of Hydros-TA.

Coverage and Reimbursement

Viscosupplemention has become an important treatment option for patients with osteoarthritis of the knee. A number of viscosupplementation products are currently approved by the FDA for marketing in the United States with indications for use in OA of the knee. Each has demonstrated a statistically significant reduction in pain and improvement in function. In the United States, third-party payors (such as Medicare, Medicaid, and commercial health plans) provide coverage to individuals for medically necessary services. The Medicare program covers certain individuals who are disabled or aged 65 or older, two groups with a comparatively higher incidence of OA. The Medicare program is increasingly used as a model for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Since no uniform policy of coverage and reimbursement for medical products exists among third-party payors, we may be required to provide economic, scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

AAOS issued a guideline in 2008 in which it found that the benefits of viscosupplementation were inconclusive and was unable to recommend for or against their use. In May 2013, AAOS issued a revised guideline on treatment of OA of the knee that stated "we cannot recommend using hyaluronic acid for patients with symptomatic osteoarthritis of the knee". AAOS stated that its recommendation was strong and was based on high quality supporting evidence related to lack of efficacy, rather than potential harm. In developing its 2013 guidelines, AAOS considered a different and smaller group of studies than it had in 2008 and found statistically significant positive treatment effects with respect to pain, function and stiffness. However, in 2013, it went on to consider whether the improvements in pain and function were large enough to pass "minimum clinically important improvement" thresholds and the evidence it considered approached, but did not pass, these thresholds.

While some third-party payors continue to cover HA for the treatment of OA of the knee after the publication of the AAOS guidelines, a number of third-party payors, including Blue Cross Blue Shield, have reversed their coverage policies and no longer cover the use of HA for the treatment of OA of the knee. Several payors still continue to cover viscosupplementation for patients with OA of the knee and related pain that interferes with function after more conservative therapies have been attempted. The more conservative therapies that payors expect to precede viscosupplementation include NSAIDs and intra-articular injection of steroids. Evidence-based review by payors has generally found a lack of reliable evidence that any particular brand of viscosupplement is superior to others when used for medically necessary indications. As a result, some payors may disfavor new products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Many payors also limit repeat treatment to 6 month intervals.

Manufacturing

We have relied on contract manufacturing organizations, or CMOs, to manufacture both the active pharmaceutical ingredient and final drug product dosage form for Hydros-TA that has been used as clinical trial material. We have manufactured the two intermediate components used in the manufacture of the hydrogel for the initial clinical studies. These two components will be outsourced to CMOs for future clinical material and for commercial production. Our management team has extensive experience with the management of a virtual supply chain consisting of CMOs, contract packaging operations and third-party logistics providers. We currently anticipate continuing to use CMOs to manufacture clinical material for future clinical studies and for the initial commercial product.

The manufacture of sterile injectables is a complex and expensive process that is subject to a high degree of regulatory oversight. All of our CMOs are experienced commercial manufacturers and are qualified by us before we begin to work with them. The patented and proprietary Hydros chemistry involves mild processing conditions and routine unit operations. Extensive development work has been completed to optimize the operations for commercial manufacture. Hyaluronic acid and triamcinolone acetonide, the two key raw materials for Hydros-TA, are readily available from multiple sources commercially.

Intellectual Property

Patents and Patent Applications

We seek to protect our product candidates and our technology through a combination of patents, trade secrets, proprietary know-how, FDA exclusivity and contractual restrictions on disclosure. Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our drug candidates, manufacturing and process discoveries and other know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. As a normal course of business, we pursue composition-of-matter and method-of-use patents for our product candidates in key therapeutic areas. As of December 31, 2015, we have three issued U.S. patents and ten issued non-U.S. patents, the earliest of which will expire in 2030, and 25 patent applications worldwide covering our Hydros platform technology, including claims directed to composition of matter, methods of use and product-by-process.

We also rely on trade secrets and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Currently our Hydros platform is covered by three patent families: (1) those relating to modified hyaluronic acid polymer compositions and related methods; (2) those relating to in-situ gel forming compositions; and (3) those relating to stabilized compositions of hyaluronic acid. For the modified hyaluronic acid polymer compositions and related methods patent family which covers the Hydros and Hydros-TA products, we have two issued U.S. patents and four issued non-U.S. patents, all of which will expire in 2030. These patents consist of composition of matter claims, method claims and product-by-process claims. We have issued patents and patent applications that cover Hydros-TA in the United States and 15 countries internationally.

Trade Secrets and Proprietary Information

During the development of the Hydros and Hydros-TA formulations, we have established numerous trade secrets that relate to the raw materials, formulation, manufacturing process and quality control testing of the product. We seek to protect our proprietary information, including our trade secrets and proprietary know-how, by requiring our employees to execute confidentiality and invention assignment agreements upon the commencement of their employment. Consultants and other advisors are required to sign confidentiality and consulting agreements. These agreements generally provide that all confidential information developed or made known during the course of the relationship with us be kept confidential and not be disclosed to third parties except in specific circumstances. In the case of our employees, the agreements also typically provide that all inventions resulting from work performed for us, utilizing our property or relating to our business and conceived or completed during employment shall be our exclusive property to the extent permitted by law. Further, we require confidentiality agreements from entities that receive our confidential data or materials or that generate confidential information and materials for us.

Government Regulation and Product Approval

Government authorities in the United States at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing. Hydros and Hydros-TA and any other drug candidate that we develop must be approved by the FDA before they may be legally marketed in the United States and by the corresponding foreign regulatory agencies before they may be legally marketed in foreign countries.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act and implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state and local statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable requirements at any time during the product development process, approval process or after approval may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement of profits or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies in compliance with Good Laboratory Practices, or GLP, or other applicable regulations;
- submission to the FDA of an IND application, which must become effective before human clinical trials in the United States may begin;
- approval by an independent institutional review board, or IRB, for each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with laws and FDA regulations pertaining to the conduct of human clinical studies, collectively referred to as Good Clinical Practices, or GCP, to establish the safety and efficacy of the proposed drug for each intended use;
- development of the product under rigorous development and design controls as stipulated by governing regulations such as 21 CFR 210 and 211, known as current Good Manufacturing Practices, or cGMP.
- submission to the FDA of an NDA for a proposed new drug;
- satisfactory completion of a potential FDA inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA's cGMP requirements, to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the NDA;
- satisfactory completion of a potential review by an FDA advisory committee, if applicable; and
- FDA review and approval of the NDA prior to any commercial marketing, sale or shipment of the drug.

The lengthy process of seeking FDA approval and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources and approvals are inherently uncertain. Notwithstanding the expenditure of time and resources approval is never guaranteed and FDA my grant approval for less than the desired indications. Moreover, the time required to obtain approval, if any, may vary substantially based upon the type, complexity and novelty of the product or disease.

Before testing any compounds with potential therapeutic value in humans, a drug candidate typically undergoes nonclinical testing, also referred to as pre-clinical testing. Pre-clinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the characteristics and potential safety and activity of the drug candidate. The conduct of the pre-clinical tests must comply with federal regulations and requirements including GLP.

An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The IND sponsor must submit the results of pre-clinical tests, together with manufacturing information, analytical data, information about product chemistry, any available clinical data or literature and a proposed clinical protocol, among other things, to the FDA as part of the IND. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin.

A separate submission to an existing IND application must also be made for each successive clinical trial conducted during product The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such trial.

Clinical Studies

Clinical trials involve the administration of the drug candidate to healthy subjects or patients with the target disease under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety. Each protocol must be submitted to the FDA under the IND. Clinical trials must be conducted in accordance with the FDA's regulations. Further, each clinical trial must be reviewed and approved by an IRB at or servicing each institution at which the clinical trial will be conducted before the trial commences at that site. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the Informed Consent Form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until it is completed.

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

- Phase 1. The drug is initially introduced into healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. The drug may also be tested for early evidence of effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted only in patients having the specific disease.
- Phase 2. The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for a specific indication and to determine the dosage tolerance, optimal dosage and dosing schedule for patients having the specific disease.
- Phase 3. The drug is administered to an expanded patient population in adequate and well-controlled clinical trials, typically at geographically dispersed clinical trial sites, to generate sufficient data to statistically confirm the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product. Generally, at least two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA, though a single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances (for example, where the study is a large multicenter trial providing highly reliable and statistically persuasive evidence of an important clinical benefit and confirmation of the result in a second trial would be practically or ethically impossible).

Post-approval studies, also referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and may be required by the FDA as part of the approval process.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points, including prior to submission of an IND, at the end of Phase 2 and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice and for the sponsor and FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to study subjects.

Concurrent with clinical trials, companies may complete additional animal studies, develop additional information about the chemistry and physical characteristics of the drug and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

FDA Review and Approval Processes

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the pre-clinical and clinical studies, together with detailed information relating to the product's chemistry, pharmacology, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is subject to a substantial application user fee and the manufacturer and/or sponsor under an approved NDA are also subject to annual product and establishment user fees.

NDAs for most new drug products are based on two Phase 3 clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for modified formulations or new uses of previously FDA-approved products. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted." If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain pre-clinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review.

The FDA may request additional information before accepting an NDA for filing. In this event, the NDA must be resubmitted with the additional information and is subject to payment of additional user fees. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the Prescription Drug User Fee Act, or PDUFA, the FDA has agreed to certain goals for review of NDAs. For an NDA that does not contain a new molecular entity (NME), FDA endeavors to complete its review of a standard NDA and respond to the applicant within 10 months after submission of the NDA, and to complete its review and respond to a priority review NDA within six months after submission of the NDA. For an NDA that contains an NME, the FDA endeavors to complete its review and respond to the applicant within 12 months after submission of a standard NDA and within eight months after submission of a priority review NDA. The FDA does not always meet its PDUFA goal dates for review of standard or priority review NDAs. The review process and the PDUFA goal date may be extended by additional three month review periods whenever the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission at any time during the review cycle.

The FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes independent clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

During the drug approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without a REMS, if required, and the sponsor must agree to the REMS at the time of approval. A REMS may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate healthcare providers of the drug's risks, limitations on who may prescribe or dispense the drug, or other elements to assure safe use, such as special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. In addition, the REMS must include a timetable to periodically assess the strategy. The requirement for a REMS can materially affect the potential market and profitability of a drug

Before approving an NDA, the FDA may inspect the facilities at which the product is to be manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with FDA regulations regarding conduct of clinical trials. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will inform the applicant of the deficiencies and often will request additional testing or information.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a "complete response" letter, or CRL. The FDA will issue a CRL to indicate that the review cycle for an application is complete and that the application is not ready for approval. A CRL generally describes the specific deficiencies in the NDA identified by the FDA and outlines the additional steps that would need to be undertaken in order for FDA to reconsider the application. These could include additional clinical trials, additional manufacturing or product characterization, or further pre-clinical or pharmacokinetic studies. If a CRL is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. If, or when, the deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. Should the applicant disagree with the decision to issue the CRL, there are dispute resolution processes through which the applicant can appeal the approvability of the NDA within the FDA. These processes can be lengthy and do not ensure that the NDA will be re-reviewed in its current state or subsequently approved.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require post-approval surveillance to monitor the drug's safety or efficacy or post-approval studies, referred to as Phase 4 studies, which involve clinical trials designed to further assess a product's safety and effectiveness. The FDA has the authority to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Post-Approval Requirements

Any drug products for which we receive FDA approvals will be subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to drug listing and registration, record-keeping, adverse event reporting, reporting updated safety and efficacy information, sampling and distribution and product promotion and advertising. These promotion and advertising requirements include, among other things, standards and regulations regarding direct-to-consumer advertising, prohibitions against promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use") and rules for conducting industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. While physicians may prescribe for off-label uses, manufacturers may only promote their products for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Failure to comply with FDA requirements can have negative consequences, including adverse publicity, enforcement letters from the FDA, mandated corrective advertising or communications with doctors and civil or criminal penalties. In addition, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Manufacturers of our products are required to comply with applicable FDA manufacturing requirements contained in the FDA's cGMP regulations, and quality-control, drug manufacture, packaging and labeling procedures must continue to conform to cGMP regulations after approval. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are also required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced and announced inspections by the FDA and certain state agencies to assess compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Failure to comply with regulatory standards, the emergence of problems following initial marketing, or the discovery of previously unrecognized problems with a product after approval may result in restrictions on a product or the manufacturer or holder of an approved NDA. These restrictions may include suspension of a product until the FDA is assured that quality standards can be met, continuing oversight of manufacturing by the FDA under a consent decree of permanent injunction, which frequently includes the imposition of costs and continuing inspections over a period of many years, as well as possible withdrawal of product approvals or a request for product recalls. The FDA may also impose a REMS requirement on a drug already on the market if the FDA determines, based on new safety information, that a REMS is necessary to ensure that the drug's benefits outweigh its risks. In addition, regulatory authorities may take other enforcement action, including, among other things, warning letters, the seizure of products, refusal to approve pending applications or supplements to approved applications, civil penalties and criminal prosecution.

Changes to the manufacturing process generally require prior FDA approval before being implemented. Other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval. In addition, the distribution of prescription pharmaceuticals is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. A growing majority of states also impose certain drug pedigree requirements on the sale and distribution of prescription drugs.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. Many commercial health plans may also require prior authorization to monitor compliance with patient selection and other coverage criteria.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

In addition to uncertainties surrounding coverage policies, there are periodic changes to reimbursement. Third-party payors regularly update reimbursement amounts and also from time to time revise the methodologies used to determine reimbursement amounts. This includes annual updates to payments to physicians and hospitals where our product candidates will be used. Because injection of the viscosupplement is performed by the physician, usually in the office or outpatient clinic, payors generally reimburse the physician for both the IA injection pursuant to a fee schedule and for the viscosupplement on the basis of the average selling price of each viscosupplement product plus a percentage, the total of which, for Medicare patients, is approximately 106% of the average selling price of each viscosupplement product. As a result, these payment updates could directly impact the demand for our product candidates, if approved. An example of payment updates is the Medicare program's updates to hospital and physician payments, which are done on an annual basis using a prescribed statutory formula. In the past, when the application of the formula resulted in lower payment, Congress has passed interim legislation to prevent the reductions. Most recently, the Protecting Access to Medicare Act of 2014, signed into law in April 2014, provided for a 0.5% update from 2013 payment rates under the Medicare Physician Fee Schedule through 2014 and a 0% update from January 1 until April 1, 2015. If Congress fails to intervene to prevent the negative update factor in future years, the resulting decrease in payment may adversely affect our revenues and results of operations.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Reform

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reduce healthcare costs.

By way of example, in March 2010, the President signed one of the most significant healthcare reform measures in decades. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively known as the Affordable Care Act, substantially changes the way healthcare will be financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. The comprehensive $940 billion dollar overhaul is expected to extend coverage to approximately 32 million previously uninsured Americans. The Affordable Care Act contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse, which will impact existing government healthcare programs and will result in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program. Additionally, the Affordable Care Act:

- mandates a further shift in the burden of Medicaid payments to the states;
- increases the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%;
- addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- requires collection of rebates for drugs paid by Medicaid managed care organizations;
- requires manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50 percent point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and
- imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013, and will stay in effect through 2024 unless congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates if approved, or additional pricing pressure.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, our activities are potentially subject to regulation under various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

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

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

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

- the federal transparency laws, including the federal Physician Payment Sunshine Act, that requires drug manufacturers to disclose payments and other transfers of value provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

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

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

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities in the future could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the Affordable Care Act broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

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

We are also subject to the Foreign Corrupt Practices Act, or FCPA, which prohibits improper payments or offers of payments to foreign governments and their officials for the purpose of obtaining or retaining business. Safeguards we implement to discourage improper payments or offers of payments by our employees, consultants and others may be ineffective, and violations of the FCPA and similar laws may result in severe criminal or civil sanctions, or other liabilities or proceedings against us, any of which would likely harm our reputation, business, financial condition and result of operations.

U.S. Marketing Exclusivity

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Act, Congress established abbreviated FDA approval procedures for drugs that are shown to be equivalent to proprietary drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. In support of such applications, a generic manufacturer may rely on the pre-clinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must generally find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug. . . ." In certain situations, an applicant may obtain ANDA approval of a generic product with a strength or dosage form that differs from a referenced innovator drug pursuant to the filing and approval of an ANDA Suitability Petition. The FDA will approve the generic product as suitable for an ANDA application if it finds that the generic product does not raise new questions of safety and effectiveness as compared to the innovator product. A product is not eligible for ANDA approval if the FDA determines that it is not equivalent to the referenced innovator drug, if it is intended for a different use, or if it is not subject to an approved Suitability Petition. However, such a product might be approved under an NDA, with supportive data from clinical trials.

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

Non-Patent Exclusivity

The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity, which is a drug that contains an active moiety that has not been approved by the FDA in any other NDA. An "active moiety" is defined as the molecule or ion responsible for the drug substance's physiological or pharmacologic action. In cases where such exclusivity has been granted, an ANDA or 505(b)(2) application referencing that drug may not be filed with the FDA until the expiration of five years after the approval date of the referenced drug, unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the approval date of the referenced drug. The FDCA also provides for a period of three years of exclusivity for a particular condition of approval, or change to a marketed product such as a new formulation for a previously approved product, if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. In cases where such exclusivity is granted, the FDA would be precluded from approving any ANDA or 505(b)(2) application for the protected modification until after that three-year exclusivity period has run. However, unlike NCE exclusivity, the FDA can accept an application and begin the review process during the exclusivity period.

A 505(b)(2) NDA applicant also may be eligible for its own regulatory exclusivity period, such as three-year exclusivity. The first approved 505(b)(2) applicant for a particular condition of approval, or change to a marketed product, such as a new extended release formulation for a previously approved product, may be granted three-year Hatch-Waxman exclusivity if one or more clinical studies, other than bioavailability or bioequivalence studies, was essential to the approval of the application and was conducted/sponsored by the applicant. Should this occur, the FDA would be precluded from making effective any other application for the same condition of use or for a change to the drug product that was granted exclusivity until after that three-year exclusivity period has run. Additional exclusivities may also apply to products approved through the 505(b)(2) pathway.

Hatch-Waxman Patent Certification and the 30-Month Stay

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Upon approval of the NDA, each of the patents listed by the NDA sponsor is published in the Orange Book. When an applicant files an application with the FDA seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the applicant is not seeking approval.

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

- no patent information on the drug product that is the subject of the application has been submitted to the FDA;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted.

If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) application will not be approved until all the listed patents claiming the referenced product have expired.

A certification that the listed patent is invalid, unenforceable or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted is known as a Paragraph IV certification. If the ANDA or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or 505(b)(2) application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) application until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, the date of a settlement order or consent decree entered by the court stating that the patent is invalid or not infringed, or a court finding that the patent is invalid or infringed.

Europe/Rest of World Government Regulation

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

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

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with the ICH GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. In the European Economic Area, or EEA (which is comprised of the 27 Member States of the European Union plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations: the Community MA, which is issued by the European Commission through the Centralized Procedure based on the opinion of the Committee for Medicinal Products for Human Use, a body of the European Medicines Agency, or the EMA, and which is valid throughout the entire territory of the EEA; and the National MA, which is issued by the competent authorities of the Member States of the EEA and only authorized marketing in that Member State's national territory and not the EEA as a whole.

The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. The National MA is for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member state, or RMS. If the RMS proposes to authorize the product, and the other Member States do not raise objections, the product is granted a national MA in all the Member States where the authorization was sought. Before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Executive Officers of the Registrant

Executive Officers and Key Employees	Age	Position(s)
David M. Renzi	58	President, Chief Executive Officer and Director
Marcee M. Maroney	46	Vice President, Clinical Affairs
David M. Gravett, Ph.D.	49	Vice President, Research & Development
Prem Ramiya, Ph.D.	55	Vice President, Pharmaceutical Development & Supply Chain
John B. McKune	40	Corporate Controller & Principal Accounting Officer

David M. Renzi has served as our president and chief executive officer and as a member of our board of directors since June 2013. From May 2009 to December 2012, Mr. Renzi served as president and chief executive officer of Neomend, a privately-held company that developed and commercialized sprayable surgical sealants and anti-adhesion products, which was acquired by C.R. Bard in December 2012. From January 2005 to December 2008, Mr. Renzi served as the vice president of sales and marketing and the chief commercial officer of SurgRx, a medical device company acquired by the Ethicon Endo-Surgery division of Johnson & Johnson, a medical company, in October 2008. From June 2000 to December 2004, Mr. Renzi served as vice president of sales and marketing and chief marketing officer at Cytyc Surgical Products (formerly Novacept), a medical device company. From 1983 to 1997, Mr. Renzi held various sales and marketing positions at Ethicon Endo-Surgery, a medical company, most recently as its regional director of sales and director of marketing. Mr. Renzi received his B.S. in Marketing from the Kelley School of Business at Indiana University.

Marcee Maroney has served as our vice president of clinical affairs since June 2008. Ms. Maroney joined us as vice president of marketing in February 2006. From April 2003 to February 2006, Ms. Maroney served as a group manager at Baxter Healthcare, a healthcare company. Ms. Maroney received a B.S. in Physiology and an M.S. in Immunology, both from San Jose State University.

David M. Gravett, Ph.D. has served as our vice president of research and development since October 2007. Dr. Gravett joined us as a senior chemist in March 2007. From 2004 to 2007, Dr. Gravett served as vice president of formulations and polymer chemistry at Angiotech Pharmaceuticals, a medical drug and device company. Dr. Gravett received his BSc and MSc in Chemistry at the University of Natal, South Africa and a Ph.D. in Physical Chemistry from the University of Toronto in Canada.

Prem Ramiya, Ph.D. has served as our vice president of pharmaceutical development and supply chain since July 2015. Dr. Ramiya has over 20 years of broad drug development experience and worked in both large pharma (Abbott Labs) and smaller biotech as well as for a contract manufacturer supplying drug substances to other biotech and pharma companies. Dr. Ramiya was most recently Vice President, Process Development and Manufacturing at Geron Corporation and led the CMC function in out-licensing Imetelstat Sodium, to Janssen, a division of Johnson and Johnson. Previous to that position he was at deCODE Genetics and lead the drug substance manufacturing site that manufactured Phase I/II clinical materials for other biotech and pharma companies. Dr. Ramiya received his B.Sc. and M.Sc. in Chemistry from MK University in India and his Ph.D. in Organic Chemistry from the Indian Institute of Science, Bangalore, India.

John B. McKune has served as our corporate controller and principal accounting officer since August 2015. From January 2014 to July 2015, Mr. McKune served as corporate controller for View, a privately-held manufacturer of dynamic glass. From April 2012 to August 2013, Mr. McKune served as controller of Conceptus, a publicly-traded medical device manufacturer, which was acquired by Bayer Healthcare in June 2013. From June 2008 to April 2012, Mr. McKune served in several positions for Solyndra, a privately-held company in the energy industry, most recently as its corporate controller. From May 2003 to June 2008, Mr. McKune was with PricewaterhouseCoopers, most recently as an audit manager, where his responsibilities included managing financial statement audits of public and private companies. Mr. McKune has been a California-licensed certified public accountant (CPA) since 2005 and received his B.S. in accounting from Brigham Young University.

General Information

Our main corporate website address is www.carbylan.com. We make available on this web site, free of charge, copies of our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and our proxy statements, and any amendments to those reports, as soon as reasonably practicable after filing such material electronically or otherwise furnishing it to the Securities and Exchange Commission, the SEC. All SEC filings are also available at the SEC's website at www.sec.gov. The contents of our web site are not intended to be incorporated by reference into this report or in any other report or document we file or furnish, and any references to our web site are intended to be textual references only.

Item 1A. Risk Factors.

Our business involves significant risks, some of which are described below. You should carefully consider these risks, as well as other information in this Annual Report on Form 10-K, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations." The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations, cash flows, the trading price of our common stock and our growth prospects. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements

Our strategic initiatives and process may not be successful.

In March 2016, we engaged a financial and strategic advisor, Wedbush PacGrow, to advise us on strategic alternatives. Wedbush PacGrow will provide a range of advisory services aimed to enhance shareholder value. The alternatives to be considered will include the potential for an acquisition, merger, strategic partnership or other strategic transactions. We expect to devote substantial time and resources to exploring strategic alternatives, however, there can be no assurance that such activities will result in any agreements or transactions that will enhance shareholder value. Further, any strategic transaction that is completed ultimately may not deliver the anticipated benefits or enhance shareholder value.

We have a limited operating history, have incurred significant losses since our inception and we will incur losses in the future. We have only one product candidate in clinical trials and no product sales, which, together with our limited operating history, makes it difficult to assess our future viability.

We are a clinical-stage specialty pharmaceutical company with a limited operating history. Pharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have focused substantially all of our efforts on our research and development activities on our lead product candidate, Hydros-TA. To date, we have not commercialized any products or generated any revenue from product sales. We are not profitable and have incurred losses in each year since our inception in 2004, and we do not know whether or when we will become profitable. We have only a limited operating history upon which to evaluate our business and prospects. We continue to incur significant research, development and other expenses related to our ongoing operations. Our net losses for the years ended December 31, 2015 and 2014 were $24.8 million and $13.4 million, respectively. As of December 31, 2015, we had an accumulated deficit of $72.6 million. To date, we have financed our operations primarily through the sale of equity securities and debt facilities. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity and/or debt financings and strategic collaborations. It will be several years, if ever, before Hydros-TA is ready for commercialization.

Our history of net losses and our expectation of future losses, together with our limited operating history, may make it difficult to evaluate our current business and predict our future performance. In addition, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

If we do not successfully consummate a strategic transaction, we will require substantial additional funding and may need to curtail operations if we have insufficient capital.

To date, we have not generated any revenue from product sales, and we do not know when, or if, we will generate any revenue from product sales. While we are exploring a range of alternatives to enhance stockholder value, including the potential for an acquisition, merger, strategic partnership or other strategic transactions, our operating plan may change or ability to consummate a transaction may be delayed.

Based upon our current operating plan, we believe that our existing cash and cash equivalents, will enable us to fund our operating expenses and capital requirements for at least the next 12 months. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. However, if our current operating plans change we may require substantial additional funding to operate.

Our future capital requirements will depend on many factors, including:

- our ability to identify and consummate a strategic transaction for the company;
- the timing and nature of any strategic transactions that we undertake, including, but not limited to potential joint developments or partnerships,
- whether, as a result of our strategic and financial review with Wedbush PacGrow we enter into a partnership or business combination;
- the time and cost necessary to obtain regulatory approvals for Hydros-TA and the costs of post-marketing studies that could be required by regulatory authorities;
- our ability to successfully commercialize Hydros-TA;
- our ability to establish and maintain collaboration partnerships, in-license/out-license or other similar arrangements and the financial terms of such agreements;
- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of Hydros-TA or any other future product candidates; and
- the cost incurred in responding to disruptive actions by activist stockholders.

Until such time, if ever, as we can generate substantial revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, government or other third-party funding and licensing or collaboration arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through government or other third-party funding, marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to curtail our operations.

Risks Related to Our Business

Our business to date has been almost entirely dependent on the success of Hydros-TA, and there is no guarantee that continued development of Hydros-TA or pursuit of strategic alternatives will be successful.

To date, we have invested substantially all of our efforts and financial resources in the research and development of Hydros-TA, which is our only product candidate in clinical trials. Hydros-TA is a new approach to treating osteoarthritis, or OA, pain in the knee by using a combination therapy treatment.

In February 2016, we announced topline results of our COR1.1 trial, a Phase 3, multi-center, international, randomized, double-blind, three-arm trial that enrolled 560 patients with grade two and grade three OA of the knee, comparing treatment with Hydros-TA to treatment with Hydros and with TA, on a standalone basis. The primary endpoints of the trial were changes from baseline in the WOMAC A pain scores at week 2 for Hydros-TA versus Hydros and at week 26 for Hydros-TA versus TA, as well as a safety assessment of adverse events. Hydros-TA met the first of its two primary endpoints, demonstrating a statistically significant improvement from baseline in the WOMAC A pain score at week 2 versus Hydros. In addition, Hydros-TA maintained a significant reduction in pain from baseline over 26 weeks. However, patients in the TA arm continued to show an unexpected significant reduction in pain through 26 weeks. Given the comparable effectiveness at 26 weeks, COR1.1 did not meet its second primary endpoint. Hydros-TA was generally well tolerated with no treatment related serious adverse events, or SAEs, and adverse events, or AEs, were mostly mild and included arthralgia (knee pain) and swelling.

In March 2016, we engaged a financial and strategic advisor, Wedbush PacGrow, to advise us on strategic alternatives. Wedbush PacGrow will provide a range of advisory services aimed to enhance shareholder value. The alternatives to be considered will include the potential for an acquisition, merger, strategic partnership or other strategic transactions. There can be no assurance that our process to identify and evaluate potential strategic alternatives will result in any definitive offer to acquire our company or any of its assets, or if made what the terms thereof will be or that any transaction will be approved or consummated. If any definitive offer to acquire our company or assets is received, there can be no assurance that a definitive agreement will be executed or that, if a definitive agreement is executed, the transaction will be consummated. In addition, there can be no assurance that any transaction, involving our company and/or assets, that is consummated would enhance shareholder value. There also can be no assurance that we will conduct drug development activities in the future.

If we fail to continue to meet all applicable NASDAQ Global Market requirements and NASDAQ determines to delist our common stock, the delisting could adversely affect the market liquidity of our common stock and the market price of our common stock could decrease.

Our common stock is listed on The NASDAQ Global Market. In order to maintain our listing, we must meet minimum financial and other requirements, including requirements for a minimum amount of capital, a minimum price per share and continued business operations so that we are not characterized as a "public shell company." On March 16, 2016, we received a deficiency letter from the Listing Qualifications Department of The NASDAQ Stock Market notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below the minimum $1.00 per share requirement for continued inclusion on The NASDAQ Global Market pursuant to NASDAQ Listing Rule 5450(a)(1). We have an initial period of 180 calendar days, or until September 12, 2016, to regain compliance with this listing rule. If, at any time before September 12, 2016, the bid price for our common stock closes at $1.00 or more for a minimum of 10 consecutive business days as required under Listing Rule 5810(c)(3)(A), NASDAQ will provide written notification to us that it is in compliance with the listing rule. We intend to actively monitor the bid price for our common stock between now and September 12, 2016, and will consider available options, including a reverse stock split, to resolve the deficiency and regain compliance with the listing rule. If we are unable to comply with NASDAQ's listing standards, NASDAQ may determine to delist our common stock from The NASDAQ Global Market. If our common stock is delisted for any reason, it could reduce the value of our common stock and its liquidity.

Our product candidates may cause undesirable side effects or have other properties that could delay our clinical trials, or delay or prevent regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following regulatory approval if any. If any of our product candidates receives marketing approval and we or others later identify undesirable side effects caused by the product candidate, the ability to market such product candidate could be compromised.

Undesirable side effects caused by a product candidate could cause us or regulatory authorities to interrupt, delay or halt clinical trials of the product candidate, result in the delay or denial of regulatory approval by the FDA or limit the commercial profile of an approved label. Some examples of drug-related side effects experienced by patients treated with Hydros-TA include injection site pain, arthralgia and injection site warmth. In the event that trials conducted by us of Hydros-TA or of future product candidates reveal an unacceptable severity and prevalence of these or other side effects, such trials could be suspended or terminated and the FDA could order us to cease further development of or deny approval of Hydros-TA, or any future product candidate, for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

In addition, in the event that Hydros-TA or any future product candidates receive regulatory approval and we or others later identify undesirable side effects caused by the product, a number of potentially significant negative consequences could occur, including:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or our collaboration partners, may be required to recall the product;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof, including the imposition of a Risk Evaluation and Mitigation Strategies, or REMS, plan that may require creation of a Medication Guide outlining the risks of such side effects for distribution to patients, as well as elements to assure safe use of the product, such as a patient registry and training and certification of prescribers;
- we, or our collaboration partners, may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us or a collaboration partner from achieving or maintaining market acceptance of a particular product candidate, if approved, and could result in the loss of significant revenue to us, which would materially and adversely affect our results of operations and business.

Even if we initiate and complete any necessary preclinical studies and clinical trials for any product candidates we may choose to develop, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate or the approval may be for a more narrow indication than we expect.

Even if we initiate any necessary preclinical studies and clinical trials for any product candidates we may choose to develop, we cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA advisory committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Regulatory agencies also may approve a treatment candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our treatment candidates.

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

Even if we obtain regulatory approval in a jurisdiction, regulatory authorities may still impose significant restrictions on the indicated uses or marketing of our product candidates, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. For example, the holder of an approved Biologic License Application, or BLA, is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. The holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with good manufacturing practices, or GMP, and adherence to commitments made in the BLA. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of any of our product candidates, a regulatory agency may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending BLA or supplements to a BLA submitted by us;
- seize product; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenues.

The terms of our loan and security agreement may restrict our ability to engage in certain transactions.

In October 2011, we entered into a loan and security agreement with Silicon Valley Bank, or SVB. Pursuant to the terms of the loan and security agreement subject to certain exceptions, we cannot engage in certain transactions, unless certain conditions are met or we receive the prior approval of SVB. Such transactions include:

- disposing of our business or certain assets;
- changing our business, management, ownership or business locations;
- incurring additional debt or liens or making payments on other debt;
- making certain investments and declaring dividends;
- acquiring or merging with another entity;
- engaging in transactions with affiliates; or
- encumbering intellectual property.

If SVB does not provide its consent to such actions we could be prohibited from engaging in transactions that could be beneficial to our business and our stockholders unless we were to repay the loans, which may not be desirable or possible. The loan and security agreement is collateralized by a pledge of substantially all of our assets, except for intellectual property. If we were to default under the loan and security agreement, including for an inability to repay amounts as they become due, and were unable to obtain a waiver for such a default, SVB would have a right to accelerate our obligation to repay the entire loan and foreclose on these assets in order to satisfy our obligations under the loan and security agreement. In addition, SVB would also have the right to place a hold on our accounts maintained at SVB and refuse to fund any then unfunded commitments under the loan and security agreement. Any such action on the part of SVB against us could have a materially adverse impact on our business, financial condition and results of operations.

We face substantial competition and our competitors may discover, develop or commercialize products faster or more successfully than us.

The pharmaceutical, biotechnology and specialty pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. In addition, the competition in the OA pain market is intense. We have competitors in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions. In addition, we expect that injectable therapies such as Hydros-TA will continue to be used primarily after oral medications no longer provide adequate pain relief.

It is possible that our competitors will be able to leverage their large market share (for example, Sanofi S.A., the developer of Synvisc-One, holds more than 50% of the viscosupplement market as of 2012) to set prices at a level below that which is profitable for us. Our competitors may also be able to develop and market drugs or other treatments that are less expensive and more effective than Hydros-TA, or that will render Hydros-TA obsolete. It is also possible that our competitors will commercialize competing drugs or treatments before we can commercialize Hydros-TA. We also anticipate that we will face increased competition in the future as new companies enter into our target markets.

In addition to competitors in the viscosupplement market, as a result of the 2013 clinical practice guidelines released by the American Association of Orthopedic Surgeons, or AAOS, clinicians have been searching for alternatives to hyaluronic acid, or HA. To the extent additional alternative therapies are developed and receive positive support from AAOS, other professional medical societies and governmental agencies, these therapies would compete with Hydros-TA, if approved. For additional information regarding the AAOS guidelines, see the risk factor below "—Third-party payor coverage and reimbursement status of newly-approved products is uncertain and such coverage for viscosupplementation may be hampered by recommendations from AAOS. Failure to obtain or maintain adequate coverage and reimbursement for Hydros-TA, if approved, could limit our ability to market Hydros-TA and decrease our ability to generate revenue."

Many of our competitors have materially greater name recognition and financial, manufacturing, marketing, research and drug development resources than we do, as well as a significant share of the existing market for OA pain treatments. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Large pharmaceutical companies in particular have extensive expertise in pre-clinical and clinical testing and in obtaining regulatory approvals for drugs. In addition, academic institutions, government agencies and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaboration partnerships or licensing relationships with our competitors.

If engage in business outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If we decide to engage in business outside the United States, including entering into contractual agreements with third-parties, we expect that we will be subject to additional risks related to entering into these international business markets and relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- differing United States and foreign drug import and export rules;
- reduced protection for intellectual property rights in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems, and different competitive drugs;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;

- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- potential liability resulting from development work conducted by these distributors; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

Risks Related to our Reliance on Third Parties

We rely on third parties to conduct, supervise and monitor our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize Hydros-TA.

We do not have the ability to independently conduct clinical trials. We currently, and will continue to, rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct any of our clinical trials of Hydros-TA. The third parties with whom we contract for execution of the clinical trials we are conducting play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, these third parties are not our employees, and except for contractual duties and obligations, we control only certain aspects of their activities and have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely, and will continue to rely, on third parties to conduct our clinical trials, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with current GCPs for clinical studies. GCPs are regulations and guidelines enforced by the FDA through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our third-party contractors fail to comply with applicable regulatory requirements, including GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. There can be no assurance that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and increase cost.

We rely completely on third parties, and in some cases a single third-party, to manufacture our clinical drug supplies, and we intend to rely on third parties to produce commercial supplies of any approved product candidate. Our business would be harmed if those third parties fail to maintain approval from the FDA, fail to provide us with sufficient quantities of drug product or fail to do so at acceptable quality levels or prices.

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture our clinical drug supplies for use in the conduct of our clinical studies of Hydros-TA, and we lack the resources and the capability to manufacture Hydros-TA on a clinical or commercial scale. The facilities used by our contract manufacturers to manufacture any drug products must be approved by the FDA pursuant to inspections that will be conducted after an NDA is submitted to the FDA. We do not control the manufacturing process of Hydros-TA, and we are completely dependent on our contract manufacturing partners for compliance with the regulatory requirements, known as cGMPs, for manufacture of both active drug substances and finished drug products.

If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA withdraws approval of these facilities for the manufacture of Hydros-TA, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market Hydros-TA, if approved.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce Hydros-TA for our clinical studies. There are a limited number of suppliers for raw materials that we use to manufacture our drugs, and there may be a need to identify alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce Hydros-TA for our clinical studies, and, if approved, ultimately for commercial sale. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Although we generally do not begin a clinical study unless we believe we have on hand, or will be able to manufacture, a sufficient supply of Hydros-TA to complete such study, any significant delay or discontinuity in the supply of Hydros-TA, or the raw material components thereof, for an ongoing clinical study due to the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing and potential regulatory approval of Hydros-TA, which could harm our business and results of operations.

We may not realize the benefit of our existing collaboration partnership, may fail to form additional collaboration partnerships in the future and may not realize the benefits of such collaborations.

Our license agreement with Shanghai Jingfeng Pharmaceutical Co., Ltd., or Jingfeng, provides Jingfeng with the exclusive right and license to develop and commercialize Hydros-TA, or any improvements or modifications to Hydros-TA, for use in China, Taiwan, Hong Kong and Macau. Pursuant to the terms of the license agreement, Jingfeng is responsible for the manufacture and supply of Hydros-TA and the management and funding of all development activities, regulatory submissions and regulatory approvals for Hydros-TA within the applicable territory. Our ability to realize any of the approximately $6.5 million in remaining milestone payments pursuant to the terms of the license agreement is therefore outside of our control and as a result we can make no guaranty or assurance that all or a portion of such payments will be made. We may form additional collaboration partnerships, create joint ventures or enter into licensing arrangements with third parties with respect to our programs that we believe will complement or augment our existing business. We have historically engaged, and intend to continue to engage, in partnering discussions with a range of pharmaceutical and biotechnology companies and could enter into new collaboration partnerships at any time. We face significant competition in seeking appropriate collaboration partners, and the negotiation process to secure appropriate terms is time-consuming and complex. Any delays in identifying suitable collaboration partners and entering into agreements to develop Hydros-TA could also delay the commercialization of Hydros-TA, which may reduce its competitiveness even if it reaches the market. Moreover, we may not be successful in our efforts to establish such a collaboration partnership for any future product candidates and programs on terms that are acceptable to us, or at all. This may be because such future product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort, our research and development pipeline may be viewed as insufficient and/or third parties may not view such product candidates and programs as having sufficient potential for commercialization, including the likelihood of an adequate safety and efficacy profile.

Even if we are successful in entering into a collaboration partnership or license arrangement, there is no guarantee that the collaboration partnership will be successful. Collaborations may pose a number of risks, including:

- collaborators often have significant discretion in determining the efforts and resources that they will apply to the collaboration, and may not commit sufficient resources to the development, marketing or commercialization of the product or products that are subject to the collaboration;
- collaborators may not perform their obligations as expected;
- any such collaboration may significantly limit our share of potential future profits from the associated program, and may require us to relinquish potentially valuable rights to product candidates, potential products or proprietary technologies or grant licenses on terms that are not favorable to us;
- collaborators may cease to devote resources to the development or commercialization of Hydros-TA or future product candidates if the collaborators view such product candidates as competitive with their own products or product candidates;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the course of development, might cause delays or termination of the development or commercialization of product candidates, and might result in legal proceedings, which would be time-consuming, distracting and expensive;
- collaborators may be impacted by changes in their strategic focus or available funding, or business combinations involving them, which could cause them to divert resources away from the collaboration;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- the collaborations may not result in us achieving revenues to justify such transactions; and
- collaborations may be terminated and, if terminated, may result in a need for us to raise additional capital to pursue further development or commercialization of the applicable product candidate.

Our business involves the use of hazardous materials and we and third-parties with whom we contract must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

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

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data from completed or ongoing clinical trials for Hydros-TA could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of Hydros-TA or future product candidates could be delayed.

Risks Related to Government Regulation

The regulatory approval processes of the FDA are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for Hydros-TA, our business will be substantially harmed.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States. We are not permitted to market any drug product in the United States until we receive marketing approval from the FDA. We have not submitted an application or obtained marketing approval for Hydros-TA anywhere in the world. Obtaining regulatory approval of a new drug application, or NDA, can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable United States regulatory requirements may subject us to administrative or judicially imposed sanctions or other actions, including:

- warning letters;
- civil and criminal penalties;
- injunctions;
- withdrawal of regulatory approval of products;
- product seizure or detention;
- product recalls;
- total or partial suspension of production; and
- refusal to approve pending NDAs or supplements to approved NDAs.

Prior to obtaining approval to commercialize a drug candidate in the United States or abroad, we or our collaboration partners must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA, that such drug candidates are safe and effective for their intended uses.. The number of nonclinical studies and clinical trials that will be required for FDA approval varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate and, as such, we may be required to perform additional clinical trials. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our drug candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering drug candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials and result in the FDA or other regulatory authorities denying approval of a drug candidate for any or all targeted indications.

Regulatory approval of an NDA is not guaranteed and the time required to obtain approval is unpredictable, typically takes many years following the commencement of clinical studies, and depends upon numerous factors. The FDA has substantial discretion in the approval process and we may encounter matters with the FDA that require us to expend additional time and resources and which may delay or prevent the approval of Hydros-TA. For example, the FDA may require us to conduct additional studies or trials for Hydros-TA either prior to or post-approval, such as additional drug-drug interaction studies or safety or efficacy studies or trials, or it may object to elements of our clinical development program such as the number of subjects in our current clinical trials from the United States. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of Hydros-TA's clinical development, which may cause delays in the approval or result in a decision not to approve an application for regulatory approval. Despite the time and expense exerted, failure can occur at any stage. An NDA for Hydros-TA could fail to receive FDA approval for many reasons, including but not limited to the following:

- the FDA may disagree with the design or implementation of our clinical studies;
- the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which approval is sought;
- the FDA may disagree with the interpretation of data from pre-clinical studies or clinical studies;
- the data collected from clinical studies of Hydros-TA may not be sufficient to support the submission of a NDA or to obtain FDA approval;
- we may be unable to demonstrate to the FDA that Hydros-TA's risk-benefit ratio for its proposed indication is acceptable;
- the FDA may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers responsible for clinical and commercial supplies; and
- the approval policies or regulations of the FDA may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical studies, may result in our failure and/or that of a collaboration partner to obtain regulatory approval to market Hydros-TA, which would significantly harm our business, results of operations, and prospects. Additionally, if the FDA requires that we conduct additional clinical studies or delays or refuses approval to market Hydros-TA, our business and results of operations may be harmed.

In addition, even if we were to obtain approval, the FDA may approve Hydros-TA for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve Hydros-TA with a label that does not include the labeling claims necessary or desirable for successful commercialization. Any of the foregoing scenarios could materially harm the commercial prospects for Hydros-TA.

We and our contract manufacturers are subject to significant regulation with respect to manufacturing Hydros-TA. The manufacturing facilities on which we rely may not continue to meet regulatory requirements or may not be able to meet supply demands.

All entities involved in the preparation of product candidates for clinical studies or commercial sale, including our existing contract manufacturers for Hydros-TA, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. We or our contract manufacturers must supply all necessary documentation in support of an NDA on a timely basis and must adhere to cGMP regulations enforced by the FDA. Some of our contract manufacturers have never produced a commercially approved pharmaceutical product and therefore have not obtained the requisite regulatory authority approvals to do so. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of Hydros-TA. In addition, the FDA may, at any time, inspect a manufacturing facility involved with the preparation of Hydros-TA or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the product candidates manufactured at these facilities may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel.

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

If a third-party manufacturer with whom we contract fails to maintain regulatory compliance, the FDA may impose regulatory sanctions including, among other things, refusal to approve Hydros-TA or withdrawal of approval for Hydros-TA if previously approved. In addition, we may be subject to fines, unanticipated compliance expenses, recall or seizure, total or partial suspension of production and/or enforcement actions, including injunctions and criminal or civil prosecution. These possible sanctions would adversely affect our financial results and financial condition.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through a supplemental NDA, which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

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

If approved Hydros-TA may cause or contribute to adverse medical events that we are required to report to regulatory agencies, and if we fail to do so, we could be subject to sanctions that could materially harm our business.

Some participants in clinical studies of Hydros-TA have reported adverse effects after being treated with Hydros-TA, including injection site pain, arthralgia, meniscal lesion and cyst aspiration. If we are successful in commercializing Hydros-TA, FDA regulations require that we report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we fail to comply with our reporting obligations, the FDA could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products.

If we fail to comply or are found to have failed to comply with FDA and other regulations related to the promotion of Hydros-TA for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other government agencies. If we receive marketing approval for Hydros-TA, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. We intend to implement compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of Hydros-TA for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses. Over the past several years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various federal and state laws and regulations, including claims asserting antitrust violations, violations of the Food, Drug and Cosmetic Act, the False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. Many of these investigations originate as "qui tam" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim, or caused a false claim to be submitted, to the government for payment. The person bringing a qui tam suit is entitled to a share of any recovery or settlement. Qui tam suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a qui tam suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

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

In the United States, there have been and continue to be a number of legislative initiatives that could significantly change the statutory provisions governing the regulatory clearance or approval, manufacture, and marketing of regulated products or the coverage and reimbursement thereof. In addition, FDA regulations and guidance are often revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of Hydros-TA. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;
- changes to manufacturing methods;
- recall, replacement, or discontinuance of one or more of our products; and
- additional record keeping.

Each of these would likely entail substantial time and cost and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any future products would harm our business, financial condition and results of operations.

In addition, the full impact of recent healthcare reform and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model. In the United States, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act was enacted in 2010 with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers.

Further, third-party payors regularly update payments to physicians and hospitals where our product candidates will be used. Because viscosupplement injection is performed by the physician, usually in the office or outpatient clinic, payors generally reimburse the physician for both the IA injection and for the viscosupplement. As a result, these payment updates could directly impact the demand for our product candidates, if approved.

It is likely that federal and state legislatures within the United States will continue to consider changes to existing healthcare legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect the demand for any drug products for which we may obtain regulatory approval, our ability to set a price that we believe is fair for our products, our ability to obtain coverage and reimbursement approval for a product, our ability to generate revenues and achieve or maintain profitability, and the level of taxes that we are required to pay.

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

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

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act and its implementing regulations, which imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information;
- the federal physician sunshine requirements under the Affordable Care Act require manufacturers of drugs, devices, biologics, and medical supplies to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers, state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

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

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

Risks Related to Intellectual Property

We may become subject to claims alleging infringement of third parties' patents or proprietary rights and/or claims seeking to invalidate our patents, which would be costly, time consuming and, if successfully asserted against us, delay or prevent the development and commercialization of Hydros-TA or any future product candidates.

Our commercial success depends in part on avoiding infringement and misappropriation of the patents and proprietary rights of third parties. There have been many lawsuits and other proceedings asserting infringement or misappropriation of patents and other intellectual property rights in the pharmaceutical and biotechnology industries, including patent infringement lawsuits, interferences, oppositions and reexamination proceedings before the U.S. Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. As the pharmaceutical and biotechnology industries expand and more patents are issued in this area, the risk increases that Hydros-TA and any future product candidates may be subject to claims of infringement of the patent rights of third parties.

There can be no assurance that we will not be subject to claims alleging that the manufacture, use or sale of Hydros-TA or any future product candidates nor that any activities conducted by us, infringes existing or future third-party patents, or that such claims, if any, will not be successful. We cannot guarantee that we have identified each and every patent and pending application in the United States and abroad owned by others that is relevant or necessary to the commercialization of Hydros-TA. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of Hydros-TA or future product candidates or by the operation of our business. We may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of Hydros-TA or future product candidates. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect.

In addition, coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that Hydros-TA or future product candidates either do not infringe the patent claims of the relevant patent or that the patent claims are invalid and/ or unenforceable, and we may not be able to do this. Proving that a patent is invalid or unenforceable is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Also in proceedings before the courts in Europe, the burden of proving invalidity of the patent usually rests on the party alleging invalidity. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

We may be subject to third-party patent infringement claims in the future against us or a collaboration partner that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing a third-party's patents. We may be required to indemnify our collaboration partners against such claims. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If a patent infringement suit were brought against us or our collaboration partners, we or they could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. As a result of patent infringement claims, or in order to avoid potential claims, we or our collaboration partners may choose to seek, or be required to seek, a license from the third-party and would most likely be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we or our collaboration partners were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or forced to redesign it, or to cease some aspect of our business operations if, as a result of actual or threatened patent infringement claims, we or our collaboration partners are unable to enter into licenses on acceptable terms. Even if we are successful in defending against such claims, such litigation can be expensive and time consuming to litigate and would divert management's attention from our core business. Any of these events could harm our business significantly.

If our intellectual property related to Hydros-TA is not adequate or if we are not able to protect our trade secrets or our confidential information, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to Hydros-TA, our drug discovery and development platform and our development programs. Any disclosure to or misappropriation by third parties of our confidential or proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or license may fail to result in issued patents in the United States or in foreign countries. Even if patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. For example, U.S. patents can be challenged by any person before the new USPTO Patent Trial and Appeals Board at any time before one year after that person is served an infringement complaint based on the patents. Patents granted by the European Patent Office may be similarly opposed by any person within nine months from the publication of the grant. Similar proceedings are available in other jurisdictions, and in the United States, Europe and other jurisdictions third parties can raise questions of validity with a patent office even before a patent has granted. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. For example, a third-party may develop a competitive product that provides therapeutic benefits similar to Hydros-TA but has a sufficiently different composition to fall outside the scope of our patent protection. If the breadth or strength of protection provided by the patents and patent applications we hold or pursue with respect to Hydros-TA is successfully challenged, then our market for Hydros-TA could be negatively affected, and we may face unexpected competition that could have a material adverse impact on our business. Further, if we encounter delays in our clinical trials, the period of time during which we could market Hydros-TA under patent protection would be reduced.

Even where laws provide protection, costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and the outcome of such litigation would be uncertain. If we or a collaboration partner were to initiate legal proceedings against a third-party to enforce a patent covering Hydros-TA, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability against our intellectual property related to Hydros-TA, we would lose at least part, and perhaps all, of the patent protection on Hydros-TA. Such a loss of patent protection would have a material adverse impact on our business. Moreover, our competitors could counterclaim that we infringe their intellectual property, and some of our competitors have substantially greater intellectual property portfolios than we do.

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

We also rely on trade secret protection and confidentiality agreements to protect proprietary know-how that may not be patentable, processes for which patents may be difficult to obtain and/or enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology, to assign their inventions to us, and endeavor to execute confidentiality agreements with all such parties, we cannot be certain that we have executed such agreements with all parties who may have helped to develop our intellectual property or who had access to our proprietary information, nor can we be certain that our agreements will not be breached by such consultants, advisors or third parties, or by our former employees. The breach of such agreements by individuals or entities who are actively involved in the discovery and design of our potential drug candidates, could require us to pursue legal action to protect our trade secrets and confidential information, which would be expensive, and the outcome of which would be unpredictable. If we are not successful in prohibiting the continued breach of such agreements, our business could be negatively impacted. We cannot guarantee that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

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

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. A third-party defendant may also request post grant review or *inter partes* review by the U.S. PTO of any patent we assert. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

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

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

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with in the future will usually expect to be granted rights to publish data arising out of such collaboration, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration, in addition to the opportunity to remove confidential or trade secret information from any such publication. In the future we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation, including the Leahy-Smith America Invents Act signed into law on September 16, 2011. That Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and new venues and opportunities for competitors to challenge patent portfolios. Because of that Act, the U.S. patent system is now a "first to file" system, which may make it more difficult to obtain patent protection for inventions and increase the uncertainties and costs surrounding the prosecution of our or a collaboration partners' patent applications and the enforcement or defense of our or a collaboration partners' issued patents, all of which could materially adversely affect our business, results of operations and financial condition.

The United States Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

The USPTO and various foreign patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions to maintain patent applications and issued patents. Noncompliance with these requirements can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

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

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain and enforce adequate intellectual property protection for our technology.

We may be subject to claims that we or our employees have misappropriated the intellectual property, including know-how or trade secrets, of a third-party, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, consultants and contractors were previously employed at or engaged by other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, consultants and contractors, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees, consultants and contractors do not use the intellectual property and other proprietary information or know-how or trade secrets of others in their work for us, and do not perform work for us that is in conflict with their obligations to another employer or any other entity, we may be subject to claims that we or these employees, consultants and contractors have used or disclosed such intellectual property, including know-how, trade secrets or other proprietary information. In addition, an employee, advisor or consultant who performs work for us may have obligations to a third-party that are in conflict with their obligations to us, and as a result such third-party may claim an ownership interest in the intellectual property arising out of work performed for us. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, or access to consultants and contractors. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

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

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

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the U.S. PTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The U.S. PTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Risks Related to Ownership of our Common Stock

Our stock price is volatile and our stockholders may not be able to resell shares of our common stock at or above the price they paid.

The trading price of our common stock is highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include those discussed in this "Risk Factors" section of this Annual Report on Form 10-K and others such as:

- announcement of a strategic transaction, including the acquisition of our company or its assets;
- our decision to initiate a clinical trial or not to initiate a clinical trial;
- announcements of significant changes in our business or operations, including the decision not to pursue drug development programs;
- additions or departures of key personnel;
- adverse results or delays in clinical trials;
- changes in reimbursement or third-party coverage of treatments for pain associated with OA, or changes to treatment recommendations or guidelines applicable to the treatment of OA or pain from OA;
- announcements relating to collaboration partnerships or other strategic transactions undertaken by us;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to Hydros-TA;
- any adverse changes to our relationship with any manufacturers or suppliers;
- the success of our testing and clinical trials;
- the success of our efforts to acquire or license or discover additional product candidates;
- any intellectual property infringement actions in which we may become involved;
- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our operating results;
- FDA or other U.S. regulatory actions affecting us or our industry or other healthcare reform measures in the United States;
- changes in financial estimates or recommendations by securities analysts;
- trading volume of our common stock;
- sales of our common stock by us, our executive officers and directors or our stockholders in the future;
- general economic and market conditions and overall fluctuations in the United States equity markets; and
- the loss of any of our key scientific or management personnel.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business, which could seriously harm our financial position. Any adverse determination in litigation could also subject us to significant liabilities.

An active, liquid and orderly market for our common stock may not develop or be sustained.

We completed our IPO in April 2015. Prior to that, there had been no public market for shares of our common stock. Following our IPO, the trading volume of our common stock on The NASDAQ Global Market has been limited, and an active public market for our shares may not develop or, if it develops, be sustained. We cannot predict the extent in which investor interest in our company will lead to the development of, or sustain an active trading market on The NASDAQ Global Market or otherwise or how liquid that market might become. The lack of an active market may impair our stockholders' to sell their shares at the time they wish to sell them or at a price that they consider reasonable. An inactive market may also impair our ability to raise capital by selling shares.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If few securities or industry analysts commence coverage of us, the trading price for our stock would be negatively impacted. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

We incur significant costs as a result of operating as a public company, and our management devotes substantial time to compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes-Oxley Act of 2002, which could result in sanctions or other penalties that would harm our business.

We incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and regulations regarding corporate governance practices. The listing requirements of The NASDAQ Global Market require that we satisfy certain corporate governance requirements relating to director independence, distributing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel will need to devote a substantial amount of time to ensure that we comply with all of these requirements, and we will likely need to hire additional accounting and financial staff with appropriate public company reporting experience and technical accounting knowledge. Moreover, the reporting requirements, rules and regulations increase our legal and financial compliance costs and make some activities more time consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms.

We are subject to Section 404 of The Sarbanes-Oxley Act of 2002, or Section 404, and the related rules of the SEC which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Beginning with the second annual report that we will be required to file with the SEC, Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting. However, for so long as we remain an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404.

To date, we have never conducted a review of our internal control for the purpose of providing the reports required by these rules. During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal control over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we are required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The NASDAQ Global Market or other adverse consequences that would materially harm our business.

If we fail to maintain proper internal controls, our ability to produce accurate financial statements or comply with applicable regulations could be impaired.

Pursuant to Section 404 of the Sarbanes-Oxley Act, our management is required annually to deliver a report that assesses the effectiveness of our internal control over financial reporting and, subject to exemptions allowed as an "emerging growth company," our independent registered public accounting firm is required annually to deliver an attestation report on the effectiveness of our internal control over financial reporting. If we are unable to maintain effective internal control over financial reporting or if our independent registered public accounting firm is unwilling or unable to provide us with an attestation report on the effectiveness of internal control over financial reporting for future periods as required by Section 404 of the Sarbanes-Oxley Act, we may not be able to produce accurate financial statements, and investors may therefore lose confidence in our operating results, our stock price could decline and we may be subject to litigation or regulatory enforcement actions.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could significantly reduce the value of our shares to a potential acquirer or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the required approval of at least 66 2/3% of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of at least 66 2/3% of the shares entitled to vote at an election of directors to adopt, amend or repeal certain provisions of our bylaws and our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by or at the direction of our board of directors pursuant to a resolution adopted by a majority of the total number of directors that our board of directors would have if there were no vacancies, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

In addition, these provisions would apply even if we were to receive an offer that some stockholders may consider beneficial.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- We will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.
- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- We will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.
- The rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.
- We may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

Our ability to use our net operating losses to offset future taxable income, if any, may be subject to certain limitations.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" (generally defined as a greater than 50-percentage-point cumulative change (by value) in the equity ownership of certain stockholders over a rolling three-year period) is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, to offset future taxable income. We experienced an ownership change in December 2005 that limited our use of approximately $0.3 million of the NOLs available to us for federal income tax purposes as of December 31, 2015. If we undergo additional ownership changes (some of which changes may be outside our control), our ability to utilize our NOLs could be further limited by Section 382 of the Code. Our NOLs may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs. Furthermore, our ability to utilize our NOLs is conditioned upon our attaining profitability and generating U.S. federal taxable income. We have incurred net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; thus, we do not know whether or when we will generate the U.S. federal taxable income necessary to utilize our NOLs. See the risk factors described above under "—Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements."

We do not currently intend to pay dividends on our common stock, and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock.

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Therefore, our stockholders are not likely to receive any dividends on their common stock for the foreseeable future. In addition, pursuant to our loan and security agreement with SVB, we are prohibited from paying cash dividends without the prior consent of SVB. Since we do not intend to pay dividends, our stockholders' ability to receive a return on their investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

Our employment agreements with our executive officers and certain other employees may require us to pay severance benefits to any of those persons who are terminated under specified circumstances, including in connection with a change of control of us, which could harm our financial condition or results.

Our executive officers and certain other employees are parties to employment agreements that contain change of control and severance provisions providing for severance and other benefits and acceleration of vesting of stock options in the event of a termination of employment under specified circumstances. The payment of these severance benefits could harm our financial condition and results. In addition, these potential severance payments may discourage or prevent third parties from seeking a business combination with us.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our headquarters is currently located in Palo Alto, California, and consists of approximately 16,065 square feet of space, consisting of 10,155 square feet used primarily for our corporate offices and laboratory operations and 5,910 square feet that we subleased to another company. The current term of our lease expires in May 2016, and is cancellable upon 30 days written notice to the landlord.

On July 13, 2015, we entered into a lease for an 18,704 square foot facility located in Newark, California, with office, R&D and laboratory space. The lease has an initial term of approximately six and a half years commences when the landlord delivers us possession of the facility. The monthly rental rate begins at $2.65 per square foot in the first year of the lease, escalating each year by 3.0%. The annual rent obligation is expected to be approximately $595,000 for the first year of the lease. We are responsible for certain other costs, such as insurance, taxes, utilities, maintenance and repairs, a property management fee, and reimbursement of certain expenses related to maintenance of common areas. We delivered a security deposit of approximately $149,000 in connection with the execution of the lease. In March 2016, we determined that we would not occupy the Newark facility and are attempting to sublease the facility. As a result, we may record an impairment relating to assets consisting primarily of leasehold improvements for the facility of approximately $1.2 million. Until such time as we are able to enter into a sublease acceptable to the landlord or otherwise negotiate a termination of the lease, we are still required to make our monthly rent payments.

Item 3. Legal Proceedings.

We are not party to any material legal proceeding. We have been informed that certain law firms are investigating possible violations of federal securities laws by certain Company officers and directors. However, to date, we have not been served with a complaint regarding these matters.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Price Range of Common Stock

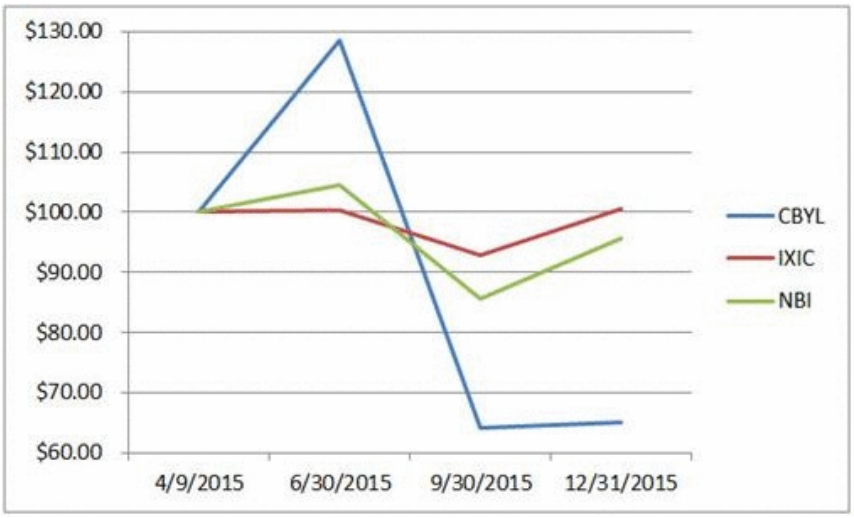
Our common stock commenced trading on The NASDAQ Global Select Market under the symbol "CBYL" on April 9, 2015. Prior to that date, there was no public trading market for our common stock. The following table sets forth, for the periods indicated, the high and low reported sales prices of our common stock as reported on The NASDAQ Global Select Market:

	2015	
	High	Low
Second Quarter (from April 9, 2015)	$ 9.04	$ 5.04
Third Quarter	7.85	3.57
Fourth Quarter	4.71	2.82

As of March 15, 2016, there were 29 holders of record of our common stock. The last reported sale price of the common stock on March 15, 2016 was $0.71 per share.

Stock Price Performance Graph

The following stock performance graph compares our total stock return with the total return for (i) the NASDAQ Composite Index and the (ii) the NASDAQ Biotechnology Index for the period from April 9, 2015 (the date our common stock commenced trading on The NASDAQ Global Market) through December 31, 2015. The figures represented below assume an investment of $100 in our common stock at the closing price of $5.56 on April 9, 2015 and in the NASDAQ Composite Index and the NASDAQ Biotechnology Index on April 9, 2015 and the reinvestment of dividends into shares of common stock. The comparisons in the table are required by the Securities and Exchange Commission, or SEC, and are not intended to forecast or be indicative of possible future performance of our common stock. This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act of 1933, as amended, or the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.



Dividend Policy

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. In addition, pursuant to our loan and security agreement with Silicon Valley Bank, we are prohibited from paying cash dividends without the prior consent of Silicon Valley Bank. Any future determination related to dividend policy will be made at the discretion of our board of directors.

Use of Proceeds from Registered Securities

On April 8, 2015, our registration statement on Form S-1 (File No. 333-201278) relating to our initial public offering ("IPO") of its common stock was declared effective by the SEC. The IPO closed on April 14, 2015 at which time we sold 14,950,000 shares of common stock, which included 1,950,000 shares of common stock purchased by the underwriters upon the full exercise of their option to purchase additional shares of common stock. We received cash proceeds of approximately $66.3 million from the IPO, net of underwriting discounts and commissions and offering costs. There has been no material change in the planned use of proceeds from our IPO as described in the registration statement on Form S-1 (File No. 333-201278). We invested the proceeds from the IPO in money market funds.

Recent Sale of Unregistered Securities

There were not any sales of unregistered securities by us for the period covered by this Annual Report on Form 10-K that have not been otherwise reported on a Quarterly Report on Form 10-Q or Current Report on Form 8-K.

Issuer Purchases of Equity Securities

None.

Item 6. Selected Financial Data.

The data set forth below is not necessarily indicative of the results of future operations and should be read in conjunction with the financial statements and the notes included elsewhere in this annual report on Form 10-K and also with "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the related notes included in this Annual Report on Form 10-K.

	Year Ended December 31,			
	2015	2014	2013	2012
	(In thousands, except share and per share amounts)			
Statement of Operations Data:				
License revenue	$ 29	$ 29	$ 415	$ 1,538
Operating expenses:				
Research and development	16,199	8,294	4,229	1,959
General and administrative	4,866	3,412	1,402	1,412
Total operating expenses	21,065	11,706	5,631	3,371
Loss from operations	(21,036)	(11,677)	(5,216)	(1,833)
Other income (expense), net				
Interest income	5	2	2	1
Interest expense	(1,188)	(1,082)	(405)	(256)
Net loss on extinguishment of convertible promissory notes	(3,177)	—	—	—
Other income (expense), net	550	(602)	(59)	35
Total other income (expense)	(3,810)	(1,682)	(462)	(220)
Net loss	$ (24,846)	$ (13,359)	$ (5,678)	$ (2,053)
Deemed dividend	—	—	—	$ (111)
Net loss attributable to common shareholders	$ (24,846)	$ (13,359)	$ (5,678)	$ (2,164)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.30)	$ (21.81)	$ (13.42)	$ (5.14)
Weighted average common shares outstanding, basic and diluted	19,082,604	612,525	423,059	421,152

	December 31,			
	2015	2014	2013	2012
Balance Sheet Data:				
Cash and cash equivalents	$ 53,723	$ 3,897	$ 9,781	$ 8,242
Working capital	50,674	(2,506)	5,960	5,257
Total assets	56,791	6,644	10,105	8,529
Loans payable	4,609	4,435	3,063	2,685
Convertible promissory notes	—	2,131	—	—
Derivative liability	—	1,495	—	—
Preferred stock warrant liability	—	463	184	79
Convertible preferred stock	—	39,556	39,556	33,546
Accumulated deficit	(72,621)	(47,775)	(34,416)	(28,738)
Total stockholders' equity (deficit)	49,310	(44,181)	(33,708)	(28,285)

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with the section of this report entitled "Selected Financial Data" and our financial statements and related notes included elsewhere in this report. This discussion and other parts of this report contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section of this report entitled "Risk Factors."

Overview

We are a clinical-stage specialty pharmaceutical company focused on the development and commercialization of novel and proprietary combination therapies that address significant unmet medical needs. Our initial focus is on the development of Hydros-TA, our proprietary, potentially best-in-class intra-articular ("IA"), injectable product candidate to treat pain associated with osteoarthritis ("OA"), of the knee. Hydros-TA is a combination IA product designed to provide both rapid and sustained pain relief. We believe the low dose steroid component of Hydros-TA will provide rapid pain relief as well as sustained pain relief up to six months, from our proprietary hyaluronic acid component. In February 2016, we announced the topline results of our COR1.1 Phase 3 trial of Hydros-TA for the treatment of pain associated with OA of the knee.

In March 2016, we engaged a financial and strategic advisor, Wedbush PacGrow, to advise us on strategic alternatives. Wedbush PacGrow will provide a range of advisory services aimed to enhance shareholder value. The alternatives to be considered will include the potential for an acquisition, merger, strategic partnership or other strategic transactions. We expect to devote substantial time and resources to exploring strategic alternatives, however, there can be no assurance that such activities will result in any agreements or transactions that will enhance shareholder value. Further, any strategic transaction that is completed ultimately may not deliver the anticipated benefits or enhance shareholder value.

Since our inception, we have devoted substantially all our efforts and financial resources to identifying and developing product candidates utilizing our proprietary hyaluronic acid technology and to the clinical development of Hydros-TA. We have not generated any revenue from product sales and, as a result, we have incurred significant losses. Through December 31, 2015, we have funded substantially all of our operations through our initial public offering and prior to that, the sale and issuance of our convertible preferred stock and convertible promissory notes and through various credit facilities.

In November 2012, we entered into a technology license agreement with Shanghai Jingfeng Pharmaceutical Co., Ltd. ("Jingfeng"), pursuant to which we granted to Jingfeng an exclusive license to develop, manufacture and commercialize Hydros-TA in China, Taiwan, Hong Kong and Macau. In consideration for the exclusive license, we received a non-refundable up-front payment of $2.0 million ($1.7 million net of Chinese withholding tax). Additionally, we are eligible to receive future regulatory milestone payments of up to $1.5 million, which are considered non-substantive milestones for accounting purposes, and commercialization royalty payments of up to approximately $5.0 million (each excluding Chinese withholding tax). Other than our arrangement with Jingfeng, we own global development and commercialization rights to Hydros-TA.

We do not have manufacturing facilities and all of our manufacturing activities are contracted out to third parties. Additionally, we currently utilize third-party clinical research organizations ("CROs"), to carry out our clinical trials and we do not yet have a sales organization. We expect to significantly increase our investment in costs relating to our clinical and commercial manufacturing process and inventory of Hydros-TA as we progress through our Phase 3 clinical trials and prepare for a possible commercial launch of Hydros-TA.

We have never been profitable and, as of December 31, 2015, we had an accumulated deficit of $72.6 million. We incurred net losses of approximately $24.8 million, $13.4 million and $5.7 million in the years ended December 31, 2015, 2014, and 2013, respectively. We expect to continue to incur net operating losses as we advance Hydros-TA through clinical development, seek regulatory approval and prepare for and, if approved, proceed to commercialization.

Initial Public Offering

On April 8, 2015, our registration statement on Form S-1 (File No. 333-201278) relating to the IPO of our common stock was declared effective by the SEC. The IPO closed on April 14, 2015 at which time we sold 14,950,000 shares of our common stock, which included 1,950,000 shares of common stock purchased by the underwriters upon the full exercise of their option to purchase additional shares of common stock. We received cash proceeds of approximately $66.3 million from the IPO, net of underwriting discounts and commissions and offering costs incurred by us.

Financial Overview

Revenue

We do not have any products approved for sale, and we have not generated any revenue from product sales since our inception and do not expect to generate any revenue from the sale of products in the near future. We may generate revenue from product sales, license fees, milestone payments and royalties from the sale of products developed using our intellectual property in the future. Our ability to generate revenue and become profitable depends on our ability to successfully commercialize Hydros-TA and any other product candidates that we may advance. If we fail to complete the development of, or obtain regulatory approval for, Hydros-TA or any future product candidates we may advance, our ability to generate future revenue and our results of operations and financial position will be adversely affected.

Our revenue to date has been generated from license revenue pursuant to our agreement with Jingfeng. Revenue under our license arrangement is recognized based on the performance requirements of the contract. Determinations of whether persuasive evidence of an arrangement exists and whether delivery has occurred or services have been rendered are based on management's judgments regarding the fixed nature of the fees charged for deliverables and the collectability of those fees. Should changes in conditions cause management to determine that these criteria are not met for any new or modified transactions, revenue that we are able to recognize could be adversely affected. We have identified all of the deliverables at the inception of the Jingfeng agreement, including an exclusive royalty bearing license to certain of our patents relating to Hydros-TA, know-how and reasonable professional services, clinical or nonclinical data and information, collectively referred to as services, to be provided by us to assist Jingfeng in manufacturing, developing and commercializing the licensed product over the performance period, which is currently estimated to be January 2019. We have determined that the Jingfeng license and the services thereunder, represent two separate units of accounting, as the license has standalone value apart from the services because the development, manufacturing and commercialization rights conveyed would allow Jingfeng to perform all efforts necessary to bring the product to commercialization and begin selling the product upon regulatory approval. Non-substantive regulatory milestone and commercialization royalty payments are recognized in proportion to the two units of accounting identified at the inception of the agreement. Each portion will be recognized in accordance with the underlying unit of accounting.

We determined the best estimate of selling price, or BESP for the license unit of accounting using a discounted cash flow analysis. This measurement is based on the value indicated by current estimates of future payments to be received under the agreement and reflects management determined estimates and assumptions. These estimates and assumptions include but are not limited to estimated sales prices, estimated market opportunity, expected market share, the likelihood that clinical trials will be successful, the likelihood that regulatory approval will be received, the likelihood that the products will be commercialized, the determination of the markets served and the discount rate. We reduced the future payment to be received by the estimated amount of the professional services costs plus an estimated margin, which was based on industry benchmarking of similar companies. These estimates and assumptions formed the basis of an expected net future cash flow that was discounted based on an estimated weighted average cost of capital. The BESP for the services unit of accounting was determined using a similar methodology. This measurement is based on the estimated cost of the professional services plus an estimated margin based on industry benchmarking of similar companies.

The considerations of the Jingfeng agreement have been allocated to the units of accounting based on the relative selling price method. Of the $1.7 million up-front payment received (net of Chinese withholding tax), $1.5 million was allocated to the license and $0.1 million to the services. We recognized license revenue upon execution of the agreement as the associated unit of accounting had been delivered pursuant to the terms of the agreement. The $0.1 million allocated to services will be recognized as revenue on a straight-line basis over the estimated performance period through January 2019.

In November 2013, we received a $0.4 million regulatory milestone payment (net of Chinese withholding tax), and all but $35,000 was allocated to the license. We recognized license revenue upon execution of the agreement as the associated unit of accounting had been delivered pursuant to the terms of the agreement. The $35,000 allocated to services will be recognized as revenue on a straight-line basis over the estimated performance period through January 2019.

We expect that any revenue we generate will fluctuate from year to year as a result of the timing and amount of milestone payments from our license agreement with Jingfeng and any future collaboration partner.

Operating Expenses

Most of our operating expenses to date have been related to the research and development activities of Hydros-TA.

Research and Development Expenses. Since our inception, we have focused our resources on our research and development activities, including nonclinical and pre-clinical studies, clinical trials and chemistry manufacturing and controls. Our development expenses consist primarily of:

- expenses incurred under agreements with consultants, CROs and investigative sites that conduct our pre-clinical studies and clinical trials;
- costs of acquiring, developing and manufacturing clinical trial materials;
- personnel costs, including salaries, benefits, stock-based compensation and travel expenses for employees engaged in scientific research and development functions;
- costs related to compliance with regulatory requirements; and
- allocated expenses for rent and maintenance of facilities, insurance and other general overhead.

Research and development costs are expensed as incurred. Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as subject enrollment, clinical site activations or information provided to us by our third-party vendors.

We do not currently utilize a formal time allocation system to capture expenses on a project-by-project basis, as the majority of our past and planned expenses have been and will be in support of Hydros-TA. We would expect our research and development expenses to increase for the foreseeable future if we initiate further clinical trials.

The following table summarizes our research and development expenses by functional area:

	Year Ended December 31,		
	2015	2014	2013
	(in thousands)		
Clinical development	$ 4,728	$ 2,804	$ 893
Regulatory	1,501	392	213
Preclinical R&D	1,734	1,108	614
Personnel related	2,939	2,345	1,185
Manufacturing	5,297	1,645	1,324
Total research and development expenses	$ 16,199	$ 8,294	$ 4,229

It is difficult to determine with any certainty the duration and completion costs of our current or future clinical trials of Hydros-TA and any future product candidates we may advance, or if, when or to what extent we will generate revenue from the commercialization and sale of Hydros-TA or future product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including the uncertainties of future clinical trials and pre-clinical studies, uncertainties in clinical trial enrollment rate and significant and changing government regulation. In addition, the probability of success for each product candidate will depend on numerous factors, including competition, manufacturing capability and commercial viability.

General and administrative expenses. General and administrative expenses consist of personnel costs, travel expenses and other expenses for outside professional services, including legal, human resources, audit and accounting services. Personnel costs consist of salaries, bonus, benefits and stock-based compensation. We also incur additional expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission ("SEC"), NASDAQ listing standards, additional insurance expenses, investor relations activities and other administration and professional services. General and administrative expenses are expensed as incurred. We would expect that our general and administrative expenses would increase in the future if we continue the development of Hydros-TA and build our corporate infrastructure to support the continued development.

Loss on Extinguishment of Convertible Promissory Notes

Loss on extinguishment of convertible promissory notes was $3.2 million for the year ended December 31, 2015. We incurred a loss as a result of the conversion of the convertible promissory notes into common shares in connection with the IPO. There was no loss on extinguishment of convertible promissory notes for the years ended December 31, 2014 and 2013.

Other Income (Expense), Net

Interest income. Interest income consists of interest earned on our cash and cash equivalents balances. The primary objective of our investment policy is capital preservation.

Interest expense. Interest expense consists of interest expense on amounts outstanding under our debt facility with Silicon Valley Bank ("SVB"), and convertible promissory notes that were issued, as well as non-cash interest expense related to the amortization of loan discounts and final loan interest payments. We expect to incur future interest expense related to the borrowing from SVB until the earlier of maturity or our payoff of the full loan amount. See "— Liquidity and Capital Resources" for a more detailed description of our credit facility.

Other income (expense), net. Other income (expense), net primarily consists of changes in the estimated fair value of the convertible preferred stock warrants and the derivative liability.

Income Taxes

Our effective tax rate is 0% for income tax for the years ended December 31, 2015, 2014 and 2013, respectively. Based on the weight of available evidence, including cumulative losses since inception and expected future losses, the Company has determined that it is more likely than not that the deferred tax asset amount will not be realized, and therefore a valuation allowance has been provided on net deferred tax assets.

We file tax returns for U.S. Federal and State of California. We are not currently subject to any income tax examinations. Since the Company's inception, the Company has incurred losses from operations, which generally allows all tax years to remain open.

We recognizes the financial statement effects of a tax position when it becomes more likely than not, based upon the technical merits, that the position will be sustained upon examination. We do not expect any material changes in the next 12 months in unrecognized tax benefits.

We recognize interest and/or penalties related to uncertain tax positions. To the extent accrued interest and penalties do not ultimately become payable, amounts accrued will be reduced and reflected in the period that such determination is made. Any interest and penalties are recognized as a component of other expense and interest expense, respectively, as necessary. We currently have no interest and penalties related to uncertain tax positions.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of our financial statements and the reported revenue and expenses during the reported periods. We evaluate these estimates and judgments, including those described below, on an ongoing basis. We base our estimates on historical experience, known trends and events, contractual milestones and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Revenue Recognition

We recognize revenue related to our license arrangement in accordance with the provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605-25, *Revenue Recognition — Multiple-Element Arrangements*, or ASC Topic 605-25 which provides guidance on how deliverables in an arrangement should be separated and how the arrangement consideration should be allocated to the separate units of accounting:

- requiring an entity to determine the selling price of a separate deliverable using a hierarchy of (i) vendor-specific objective evidence, or VSOE, (ii) third-party evidence, or TPE, or (iii) BESP; and
- requiring the allocation of the arrangement consideration, at the inception of the arrangement, to the separate units of accounting based on relative fair value.

We evaluate all deliverables within an arrangement to determine whether or not they provide value on a stand-alone basis. Based on this evaluation, the deliverables are separated into units of accounting. The arrangement consideration that is fixed or determinable at the inception of the arrangement is allocated to the separate units of accounting based on their relative selling prices. We may exercise significant judgment in determining whether a deliverable is a separate unit of accounting, as well as in estimating the selling prices of such unit of accounting.

To determine the selling price of a separate deliverable, we use the hierarchy as prescribed in ASC Topic 605-25 based on VSOE, TPE or BESP. VSOE is based on the price charged when the element is sold separately and is the price actually charged for that deliverable. TPE is determined based on third-party evidence for a similar deliverable when sold separately and BESP is the price at which we would transact a sale if the elements of collaboration and license arrangements were sold on a stand-alone basis. We may not be able to establish VSOE or TPE for the deliverables within collaboration and license arrangements as we do not have a history of entering into such arrangements or selling the individual deliverables within such arrangements separately. In addition, there may be significant differentiation in these arrangements, which indicates that comparable third-party pricing may not be available. We may determine that the selling price for the deliverables within collaboration and license arrangements should be determined using BESP. The process for determining BESP involves significant judgment on our part and includes consideration of multiple factors such as estimated direct expenses and other costs and available data.

For each unit of accounting identified within an arrangement, we determine the period over which the performance obligation occurs. We allocate the arrangement consideration to the separate units of accounting based on the relative selling prices. Revenue is recognized immediately if the performance obligation has been met. We recognize the revenue that is deferred using the straight-line method over the expected delivery period of the unit of accounting.

Research and Development Costs

As part of the process of preparing our financial statements, we are required to estimate our accrued and prepaid research and development expenses. We review new and open contracts and communicate with applicable internal and vendor personnel to identify services that have been performed on our behalf and estimate the level of service performed and the associated costs incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost for accrued expenses. In addition, we review and expense contractual liability for which the costs are not recoverable in the event of cancellation. The majority of our service providers invoice us monthly in arrears for services performed; however, some require advanced payments. For any services that require such advanced payments, we perform a review with applicable internal and vendor personnel to estimate the level of services that have been performed and the associated costs that have been incurred at each reporting period.

We base our accrued expenses related to clinical trials on estimates of patient enrollment and related expenses at clinical investigator sites, as well as estimates for services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage clinical trials on our behalf. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we modify our estimates of accrued expenses accordingly on a prospective basis.

If we do not identify costs that we have begun to incur, or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. To date, we have not adjusted our estimates at any particular balance sheet date in any material amount.

Stock-Based Compensation

We maintain performance incentive plans under which incentive stock options and non-qualified stock options may be granted to employees and non- employees. We account for stock-based compensation arrangements with employees in accordance with ASC 718, *Compensation—Stock Compensation*.

ASC 718 requires the recognition of compensation expense, using a fair value-based method, for costs related to all share-based payments including stock options. In determining the fair value of the stock-based awards, we use the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected term. The expected term represents the period that our stock-based awards are expected to be outstanding. We used the average of the expected term as disclosed for comparable publicly traded biopharmaceutical companies as we do not have sufficient experience to estimate the expected term based on historical exercises. The expected term of stock options granted to non-employees is equal to the contractual term of the option award.

Expected volatility. Prior to our initial public offering in April 2015, we were privately held and thus have limited trading history for our common stock. Accordingly expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. When selecting comparable publicly traded biopharmaceutical companies on which we have based our expected stock price volatility, we selected companies with comparable characteristics, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Risk-free interest rate. The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected dividend. We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

For all periods prior to our initial public offering, the fair values of the shares of common stock underlying our share-based awards were estimated on each grant date by our board of directors. In order to determine the fair value of our common stock underlying option grants, our board of directors considered, among other things, contemporaneous valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Given the absence of a public trading market for our common stock, our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including our stage of development, progress of our research and development efforts, the rights, preferences and privileges of our preferred stock relative to those of our common stock, equity market conditions affecting comparable public companies and the lack of marketability of our common stock.

For valuations after the completion of our initial public offering, our board of directors determined the fair value of each share of underlying common stock based on the closing price of our common stock as reported on The NASDAQ Global Market as reported on the date of grant.

Estimated Fair Value of Convertible Preferred Stock Warrants

Freestanding warrants for shares that are contingently redeemable are classified as a liability on the balance sheet at their estimated fair value. At the end of each reporting period, the change in estimated fair value during the period is recorded in other income (expense), net in the statement of operations and comprehensive loss. We estimated the fair values of these warrants using the market approach based on the proximity of the valuation date to the closing of an additional Series B financing in December 2012. For each period subsequent to December 2012, we estimated the fair value of the warrant liability by applying a probability of two exit scenarios, going public or remaining private. In all instances, we utilized an OPM to allocate the value of the company to the warrants. Immediately prior to the closing of our initial public offering in April 2015, all convertible preferred stock warrants were converted in to warrants exercisable for common stock.

Results of Operations

Comparison of the Years Ended December 31, 2015 and 2014

License revenue

	Year Ended December 31,		
	2015	2014	Dollar Change
	(in thousands)		
License revenue	$ 29	$ 29	$ —

Revenues from the deferred upfront payments related to our license agreement for the years ended December 31, 2015 and 2014 were $29,000, and $29,000, respectively.

Research and development expenses

	Year Ended December 31,		
	2015	2014	Dollar Change
	(in thousands)		
Research and development	$ 16,199	$ 8,294	$ 7,905

Research and development expenses were $16.2 million, and $8.3 million for the years ended December 31, 2015, and 2014, respectively. The increase in research and development expenses year over year of $7.9 million, or 95%, was primarily due to the following:

- an increase in clinical development expenses of $1.9 million related to our ongoing Phase 3 clinical trial, COR1.1;
- an increase in regulatory expenses of $1.1 million primarily related to the increased use of outside service providers driven by an increase in IND enabling activities; and
- an increase in manufacturing related expenses of $3.7 million, primarily related to an increased use of contract manufacturers preparing for the production of Hydros-TA for our COR1.2 clinical trial.

General and administrative expenses

	Year Ended December 31,		
	2015	2014	Dollar Change
	(in thousands)		
General and administrative	$ 4,866	$ 3,412	$ 1,454

General and administrative expenses were $4.9 million and $3.4 million for the years ended December 31, 2015 and 2014, respectively. The increase in general and administrative expenses year over year of $1.5 million, or 43%, was primarily due to increased expenditures on insurance and outside services associated with being a public company, as well as payroll and related expenses.

Interest income (expense), net

	Year Ended December 31,		
	2015	2014	Dollar Change
	(in thousands)		
Interest income	$ 5	$ 2	$ 3
Interest expense	(1,188)	(1,082)	(106)
Interest income (expense), net	$ (1,183)	$ (1,080)	$ (103)

Interest expense is attributable to our debt facility with SVB and non-cash amortization of debt discounts and final interest payments. Interest income (expense), net was $1.2 million and $1.1 million for the years ended December 31, 2015 and 2014, respectively. The increase in interest expense of $0.1 million was primarily due to amortization of debt discounts.

Other income (expense), net

	Year Ended December 31,		
	2015	2014	Dollar Change
	(in thousands)		
Other income (expense), net	$ 550	$ (602)	$ 1,152

Other income (expense), net was $0.5 million and $(0.6) million for the years ended December 31, 2015 and 2014, respectively. The $0.6 million expense for the year ended December 31, 2014 was primarily related to an increase in the fair value of the derivative liability. The $0.5 million income for the year ended December 31, 2015 was primarily due to a decrease in the fair value of the derivative liability.

Comparison of the Years Ended December 31, 2014 and 2013

License revenue

	Year Ended December 31,		
	2014	2013	Dollar Change
	(in thousands)		
License revenue	$ 29	$ 415	$ (386)

Revenues for the years ended December 31, 2014 and 2013 were $29,000 and $0.4 million, respectively. We received the $0.4 million from Jingfeng in November 2013 upon the successful production by Jingfeng of the first batch of Hydros-TA, and the $29,000 is related to the amortization of deferred revenue associated with the Jingfeng agreement.

Research and development expenses

	Year Ended December 31,		
	2014	2013	Dollar Change
	(in thousands)		
Research and development	$ 8,294	$ 4,229	$ 4,065

Research and development expenses were $8.3 million and $4.2 million for the years ended December 31, 2014 and 2013, respectively. The increase in research and development expenses period over period of $4.1 million, or 98%, was primarily due to the following:

- an increase in clinical development expenses of $1.9 million as we began enrolling patients in our first Phase 3 clinical trial, COR1.1, beginning in January 2014;
- an increase in pre-clinical research and development expenses of $0.5 million primarily related to the increased use of CROs and other outside services driven by an increase in IND enabling activities;
- an increase in personnel related expenses of $1.2 million as we began to build out our in-house regulatory and clinical development team; and
- an increase in manufacturing related expenses of $0.3 million, primarily related to an increased use of contract manufacturers in preparation for the production of Hydros-TA as we began to produce materials for our COR1.2 clinical trial.

General and administrative expenses

	Year Ended December 31,		
	2014	2013	Dollar Change
	(in thousands)		
General and administrative	$ 3,412	$ 1,402	$ 2,010

General and administrative expenses were $3.4 million and $1.4 million for the years ended December 31, 2014 and 2013, respectively. The increase in general and administrative expenses period over period of $2.0 million, or 143%, was primarily due to an increase of $0.3 million in salary and related costs due to an increase in bonus accrual as compared to the prior period, an increase of $0.2 million based on an increased use of outside consulting services and an increase of $1.3 million in professional fees.

Interest income (expense), net

	Year Ended December 31,		
	2014	2013	Dollar Change
	(in thousands)		
Interest income	$ 2	$ 2	$ —
Interest expense	(1,082)	(405)	(677)
Interest income (expense), net	$ (1,080)	$ (403)	$ (677)

Interest expense is attributable to our debt facility with SVB and non-cash amortization of debt discounts and final interest payments. Interest income (expense), net was a net expense of $1.1 million and $0.4 million for the years ended December 31, 2014 and 2013, respectively. The increase in interest expense of $0.7 million was primarily due to expense of the unamortized portion of the final interest payment related to the loan and security agreement with SVB.

Other income (expense), net

	Year Ended December 31,		
	2014	2013	Dollar Change
	(in thousands)		
Other income (expense), net	$ (602)	$ (59)	$ (543)

Other income (expense), net was a net expense of $0.6 million and $59,000 for the years ended December 31, 2014 and 2013, respectively. The increase in expense of $0.5 million was based primarily on an increase in the fair value of the warrant liability of $0.3 million and our increase in the fair value of the derivative liability of $0.4 million.

Liquidity and Capital Resources

To date, we have not generated any revenue from product sales and have incurred losses since our inception in 2004. As of December 31, 2015, we had an accumulated deficit of $72.6 million. We anticipate that we will continue to incur losses for the foreseeable future. If we decide to continue to develop Hydros-TA or another product candidate, we will need additional capital to fund our operations, which we may seek to obtain through one or more equity offerings, debt financings, government or other third-party funding and licensing or collaboration arrangements.

Since our inception and prior to our initial public offering, we funded our operations principally through the receipt of funds from private placements of our equity, the issuance of convertible promissory notes and borrowings under our loan and security agreement with SVB. As of December 31, 2015, we had cash and cash equivalents of $53.7 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to capital preservation.

Indebtedness

In October 2011, we entered into a loan and security agreement with SVB that provided for us to borrow $3.0 million. In September 2014, we entered into a fourth amendment to the loan and security agreement to provide for a new loan of $4.5 million and repayment in full of amounts owing under the prior loans, with net proceeds to us of $0.5 million. We also issued a warrant to purchase 18,709 shares of Series B convertible preferred stock. The interest rate is 3.95% per annum and the loan is repayable in thirty-six equal monthly installments, following a nine month interest-only period. The amendment provided for an extension of the interest-only period by an additional nine months, to April 1, 2016, which became effective upon the completion of our IPO.

The loan and security agreement is collateralized by our personal property but excludes our intellectual property. The agreement also contains customary representations and warranties, covenants, closing and advancing conditions, events of defaults and termination provisions. The negative covenants preclude, among other things, disposing of certain assets, engaging in any merger or acquisition, incurring additional indebtedness, encumbering any collateral or making prohibited investments, in each case, without the prior consent of SVB.

The loan and security agreement provides that an event of default will occur if, among other events, we default in the payment of any amount payable under the agreement when due. As of December 31, 2015, we were in compliance with all the covenants in the loan and security agreement.

On September 29, 2014 and February 19, 2015, we entered into convertible note purchase agreements and issued convertible promissory notes (collectively, the "Notes") in an aggregate principal amount of $5.0 million and $4.0 million, respectively, to several related parties that own more than 10% of our capital stock. The Notes automatically converted into 2,287,120 shares of our common stock immediately prior to the closing of our IPO.

The convertible preferred stock warrants converted in to warrants exercisable for common stock at the completion of our IPO. During June 2015, SVB exercised its common stock warrants and received 56,545 shares of common stock in a cashless exercise.

The following table summarizes our cash flows for the periods indicated (in thousands):

	Year Ended December 31,		
	2015	2014	2013
	($ in thousands)		
Cash used in operating activities	$ (20,863)	$ (11,253)	$ (4,858)
Cash used in investing activities	(1,374)	(159)	(18)
Cash provided by financing activities	72,063	5,528	6,415
Net increase/(decrease) in cash and cash equivalents	49,826	(5,884)	1,539

Operating Activities.

Operating activities used $20.8 million of cash in the year ended December 31, 2015. The cash flow used in operating activities resulted primarily from our net loss of $24.8 million for the year, offset by net non-cash charges of $4.6 million and net cash used by changes in our operating assets and liabilities of $0.6 million. Our non-cash charges consisted primarily of $3.2 million related to the loss on conversion of convertible promissory notes, $0.5 million related to a decrease in the fair value of the preferred stock warrant liability and derivative liability, $0.8 million related to stock-based compensation expense, and $0.8 million related to the amortization of the convertible promissory notes discount. Net cash used by changes in our operating assets and liabilities consisted primarily of a $0.4 million increase in our accounts payable, offset by a $0.3 million decrease in accruals and a decrease in prepaid expenses and other assets of $0.6 million.

Operating activities used $11.3 million of cash in 2014. The cash flow used in operating activities resulted primarily from our net loss of $13.4 million for the period, offset by net non-cash charges of $1.5 million and net cash provided by changes in our operating assets and liabilities of $0.6 million. Our non-cash charges consisted primarily of $0.6 million related to an increase in the fair value of the preferred stock warrant liability and derivative liability, $0.4 million related to stock-based compensation expense and $0.4 million related to the amortization of our convertible debt discount. Net cash provided by changes in our operating assets and liabilities consisted primarily of a $0.5 million increase in our accounts payable and a $0.8 million increase in accruals, offset by a decrease in prepaid expenses of $0.6 million and a decrease in other assets of $0.1 million.

Operating activities used $4.9 million of cash in 2013. The cash flow used in operating activities resulted primarily from our net loss of $5.7 million for the year, offset by net non-cash charges of $0.4 million and net cash provided by changes in our operating assets and liabilities of $0.5 million. Our non-cash charges consisted primarily of $63,000 related to the change in fair value of preferred stock warrant liability, $0.2 million related to stock-based compensation expense and $32,000 related to non-cash interest expense. Net cash provided by changes in our operating assets and liabilities consisted primarily of a $0.3 million increase in our accounts payable and $0.2 million increase in accruals.

Investing activities.

Net cash used in investing activities was $1.4 million, $0.2 million and $18,000 in the years ended December 31, 2015, 2014 and 2013, respectively. Net cash used in investing activities consisted primarily of cash paid to purchase property and equipment, with a deposit for leasehold improvements of $0.7 million in the year ended December 31, 2015.

Financing activities.

Net cash provided by financing activities was $72.1 million, $5.5 million and $6.4 million in the years ended December 31, 2015, 2014 and 2013, respectively. Net cash provided by financing activities in the year ended December 31, 2015 consisted of the receipt of net proceeds of $67.9 million from our initial public offering, after underwriting discounts and commissions and IPO expenses paid by the Company, $4.0 million from the issuance of the Notes and $0.2 million from the issuance of common stock related to option exercises. Net cash provided by financing activities in the year ended December 31, 2014 consisted of the receipt of $5.0 million from the issuance of convertible promissory notes, the receipt of net proceeds of $2.2 million from loans payable and $0.2 million from the issuance of common stock related to option exercise, partially offset by the repayment of $0.7 million in existing borrowings and $1.2 million in deferred costs associated with our IPO. Net cash provided by financing activities in the year ended December 31, 2013 primarily consisted of $6.0 million received from the sale of Series B preferred stock, net of issuance costs, net proceeds of $0.5 million from a $3.0 million loan payable and $2.5 million loan payoff, which was offset by $0.2 million related to repayment of a loan.

Future Funding Requirements

To date, we have not generated any revenue from product sales, and we do not know when, or if, we will generate any revenue from product sales. We do not expect to generate any revenue from product sales unless and until we obtain regulatory approval of and commercialize Hydros-TA or any future product candidates that we may advance. If we decide to continue to develop Hydros-TA or another product candidate, we expect our expenses to increase in connection with any development activities that we decide to pursue and that we will need substantial additional funding in connection with any continuing operations. We also incur additional costs associated with operating as a public company. However, in March 2016, we engaged a financial and strategic advisor, Wedbush PacGrow, to advise us on strategic alternatives. Wedbush PacGrow will provide a range of advisory services aimed to enhance shareholder value. The alternatives to be considered will include the potential for an acquisition, merger, strategic partnership or other strategic transactions.

Based upon our current operating plan, we believe that based on our existing cash and cash equivalents, we will be able to fund our operating expenses and capital requirements for at least the next 12 months. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development and commercialization of our product candidates.

Our future capital requirements will depend on many factors, including:

- our ability to identify and consummate a strategic transaction for the company;
- the timing and nature of any strategic transactions that we undertake, including, but not limited to potential joint developments or partnerships;
- whether, as a result of our strategic and financial review with Wedbush PacGrow, we enter into a partnership or business combination;
- the time and cost necessary to obtain regulatory approvals for Hydros-TA and the costs of post-marketing studies that could be required by regulatory authorities;
- our ability to successfully commercialize Hydros-TA;
- our ability to establish and maintain collaboration partnerships, in-license/out-license or other similar arrangements and the financial terms of such agreements;
- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of Hydros-TA or any other future product candidates; and
- the cost incurred in responding to disruptive actions by activist stockholders.

Until such time, if ever, as we can generate substantial revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, government or other third-party funding and licensing or collaboration arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through government or other third-party funding, marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2015:

	Payments Due By Period				
	Total	Less Than 1 Year	1 – 3 Years	3 – 5 Years	More Than 5 Years
	(in thousands)				
Long-term debt (including interest)(1)	$ 5,778	$ 1,775	$ 4,003	$ —	$ —
Operating lease obligations(2)	4,274	618	1,240	1,316	1,100
Total(3)	$ 10,052	$ 2,393	$ 5,243	$ 1,316	$ 1,100

(1) Represents the contractually required principal and interest payments on our credit facility in accordance with the required payment schedule. Amounts associated with future interest payments to be made were calculated based on a stated loan rate of 3.95% plus a final interest payment of $0.5 million.

(2) Represents the contractually required payments under our operating lease obligations in existence as of December 31, 2015 in accordance with the required payment schedule. No assumptions were made with respect to renewing the lease terms at the expiration date of their initial terms.

(3) This table does not include a liability for unrecognized tax benefits related to various federal and state income tax matters of $0.7 million at December 31, 2015. The timing of the settlement of these amounts was not reasonably estimable at December 31, 2015. We do not expect payment of amounts related to the unrecognized tax benefits within the next twelve months.

The tables above reflect only payment obligations that are fixed or determinable. We enter into contracts in the normal course of business with CROs for clinical trials and clinical supply manufacturing and with vendors for pre-clinical research studies, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore we believe that our non-cancellable obligations under these agreements are not material.

JOBS Act Accounting Election

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards update ("ASU") 2014-09, "*Revenue from Contracts with Customers*," requiring an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. The updated standard will replace most existing revenue recognition guidance in U.S. GAAP when it becomes effective and permits the use of either the retrospective or cumulative effect transition method. In July 2015, the FASB voted to defer the effective date for annual reporting periods beginning after December 15, 2017 (including interim reporting periods within those periods) and permitted early adoption of the standard, but not before the original effective date of December 15, 2016. We expect to adopt the updated standard in the first quarter of fiscal 2018. We have not yet selected a transition method, and we are currently evaluating the effect that the updated standard will have on our financial statements and related disclosures.

In August 2014, the FASB issued ASU NO. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, or ASU 2014-15. ASU 2014-15 requires management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date the financial statements are issued and provides guidance on determining when and how to disclose going concern uncertainties in the financial statements. Certain disclosures will be required if conditions give rise to substantial doubt about an entity's ability to continue as a going concern. ASU 2014-15 applies to all entities and is effective for annual and interim reporting periods ending after December 15, 2016, with early adoption permitted. We do not expect that the adoption of this guidance will have a material effect on our financial statements.

In April 2015, the FASB issued ASU No. 2015-03, *Simplifying the Presentation of Debt Issuance Costs*. ASU 2015-03 requires that debt issuance costs be presented in the balance sheet as a direct deduction from the carrying amount of the related debt liability, similar to debt discounts. The standard will be effective for financial statements issued for annual periods beginning after December 15, 2015, and interim periods within those annual periods. We are currently evaluating the effect that the standard will have on our financial statements.

In November 2015, the FASB issued ASU No. 2015-17 (Topic 740), *Balance Sheet Classification of Deferred Taxes*. ASU 2015-17 requires deferred tax liabilities and assets to be classified as noncurrent in the balance sheet. The standard will be effective for financial statements issued for annual periods beginning after December 15, 2016, and interim periods within those annual periods. Early adoption is permitted for financial statements that have not been previously issued. The ASU may be applied either prospectively to all deferred tax liabilities and assets or retrospectively to all periods presented. We adopted this ASU on a prospective basis in the fourth quarter of fiscal 2015. The adoption did not have a material effect on our financial statements.

In February 2016, the FASB issued new lease accounting guidance in Accounting Standards Update No. 2016-02, Leases (Topic 842). Under the new guidance, lessees will be required to recognize for all leases (with the exception of short-term leases) at the commencement date: (1) a lease liability, which is a lessee's obligation to make lease payments arising from a lease, measured on a discounted basis; and (2) a right-of-use asset, which is an asset that represents the lessee's right to use, or control the use of, a specified asset for the lease term. Lessor accounting, however, remains largely unchanged. In addition, the new lease guidance simplified the accounting for sale and leaseback transactions primarily because lessees must recognize lease assets and lease liabilities. Lessees will no longer be provided with a source of off-balance sheet financing. The new lease guidance is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. Early application is permitted, however, we do not intend to early adopt. We also believe that adoption of this new guidance will not have a material impact on our financial statements.

Off-Balance Sheet Arrangements

Since our inception, we have not engaged in any off-balance sheet arrangements, as defined in the rules and regulations of the SEC. Refer to Note 5, "Commitments and Contingencies" regarding our indemnification arrangements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10.0% change in interest rates would not have a material effect on the fair market value of our portfolio. Accordingly, we would not expect our operating results or cash flows to be affected to any significant degree by a sudden change in market interest rates on our investment portfolio.

We do not believe that our cash and cash equivalents have significant risk of default or illiquidity. While we believe our cash and cash equivalents and certificates of deposit do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash and cash equivalents at a financial institution that are in excess of federally insured limits.

Item 8. Financial Statements and Supplementary Data.

CARBYLAN, INC.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Carbylan Therapeutics, Inc:

In our opinion, the accompanying balance sheets and the related statements of operations and comprehensive loss, of convertible preferred stock and stockholders' equity (deficit) and of cash flows present fairly, in all material respects, the financial position of Carbylan Therapeutics, Inc. at December 31, 2015 and 2014 , and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2015 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

San Jose, California

March 30, 2016

Carbylan Therapeutics, Inc.
Balance Sheets
(in thousands, except share and per share amounts)

	December 31, 2015	December 31, 2014
Assets		
Current assets:		
Cash and cash equivalents	$ 53,723	$ 3,897
Prepaid expenses and other current assets	1,222	690
Total current assets	54,945	4,587
Property and equipment, net	805	180
Restricted cash	50	50
Deferred public offering costs	—	1,648
Other assets	991	179
Total assets	**$ 56,791**	**$ 6,644**
Liabilities, Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 1,460	$ 1,024
Accrued expenses	1,327	1,605
Loans payable	1,455	4,435
Deferred licensing revenue	29	29
Total current liabilities	4,271	7,093
Loans payable, net of current portion	3,154	—
Convertible promissory notes	—	2,131
Derivative liability	—	1,495
Preferred stock warrant liability	—	463
Deferred licensing revenue, net of current portion	56	85
Deferred rent, net of current portion	—	2
Total liabilities	7,481	11,269
Commitments and contingencies (Note 5)		
Convertible preferred stock, $0.001 par value; no shares authorized as of December 31, 2015 and 34,371,305 shares authorized as of December 31, 2014; no shares issued and outstanding as of December 31, 2015 and 8,268,531 shares issued and outstanding as of December 31, 2014	—	39,556
Stockholders' equity (deficit)		
Preferred stock, $0.001 par value; 5,000,000 shares authorized as of December 31, 2015 and none authorized as of December 31, 2014: no shares issued and outstanding as of December 31, 2015 and December 31, 2014	—	—
Common stock, $0.001 par value; 100,000,000 shares authorized as of December 31, 2015 and 45,000,000 shares authorized as of December 31, 2014; 26,322,494 shares issued and outstanding as of December 31, 2015 and 691,312 shares issued and outstanding as of December 31, 2014	27	1
Additional paid-in capital	121,904	3,593
Accumulated deficit	(72,621)	(47,775)
Total stockholders' equity (deficit)	49,310	(44,181)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	**$ 56,791**	**$ 6,644**

The accompanying notes are an integral part of these financial statements.

Carbylan Therapeutics, Inc.
Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Year Ended December 31,		
	2015	**2014**	**2013**
License Revenue	$ 29	$ 29	$ 415
Operating Expenses:			
Research and development	16,199	8,294	4,229
General and administrative	4,866	3,412	1,402
Total operating expenses	21,065	11,706	5,631
Loss from Operations	(21,036)	(11,677)	(5,216)
Other Income (expense):			
Interest income	5	2	2
Interest expense	(1,188)	(1,082)	(405)
Loss on extinguishment of convertible promissory notes	(3,177)	—	—
Other income (expense), net	550	(602)	(59)
Total other income (expense)	(3,810)	(1,682)	(462)
Net Loss and Comprehensive Loss	$ (24,846)	$ (13,359)	$ (5,678)
Net loss per share to common stockholders, basic and diluted	$ (1.30)	$ (21.81)	$ (13.42)
Weighted average common shares outstanding, basic and diluted	19,082,604	612,525	423,059

The accompanying notes are an integral part of these financial statements.

Carbylan Therapeutics, Inc.
Statements of Changes in Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share and per share amounts)

	Series A and B Convertible Preferred Stock		Common Stock		Additional Paid-in-Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Balance at December 31, 2012	7,016,037	$ 33,546	421,152	$ —	$ 453	$ (28,738)	$ (28,285)
Exercise of stock options	—	—	21,254	—	17	—	17
Issuance of Series B Preferred Stock at $4.8104, net of issuance costs of $14	1,252,494	6,010	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	238	—	238
Net loss	—	—	—	—	—	(5,678)	(5,678)
Balance at December 31, 2013	8,268,531	39,556	442,406	—	708	(34,416)	(33,708)
Exercise of stock options	—	—	248,906	1	228	—	229
Stock-based compensation expense	—	—	—	—	381	—	381
Beneficial conversion feature of convertible promissory notes	—	—	—	—	2,276	—	2,276
Net loss	—	—	—	—	—	(13,359)	(13,359)
Balance at December 31, 2014	8,268,531	39,556	691,312	1	3,593	(47,775)	(44,181)
Exercise of stock options	—	—	78,986	1	154	—	155
Stock-based compensation expense	—	—	—	—	785	—	785
Issuance of common stock upon initial public offering, net of underwriting discounts, commissions and offering costs	—	—	14,950,000	15	66,247	—	66,262
Conversion of convertible preferred stock to common stock	(8,268,531)	(39,556)	8,268,531	8	39,548	—	39,556
Conversion of convertible promissory notes to common stock	—	—	2,287,120	2	11,230	—	11,232
Conversion of preferred stock warrants to common stock warrants	—	—	—	—	347	—	347
Cashless exercise of common stock warrants	—	—	56,545	—	—	—	0
Net loss	—	—	—	—	—	(24,846)	(24,846)
Balance at December 31, 2015	—	$ —	26,332,494	$ 27	$ 121,904	$ (72,621)	$ 49,310

The accompanying notes are an integral part of these financial statements.

Carbylan Therapeutics, Inc.
Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2015	**2014**	**2013**
Cash Flows from Operating Activities			
Net loss	$ (24,846)	$ (13,359)	$ (5,678)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	133	54	27
Stock based compensation	785	381	238
Change in fair value of preferred stock warrant liability and derivative liability	(520)	605	63
Non-cash interest expense	229	64	32
Amortization of loan and convertible promissory notes discount	780	384	—
Loss on extinguishment of convertible promissory notes	3,177	—	—
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(532)	(561)	(46)
Other assets	(97)	(109)	—
Accounts payable	355	487	315
Accrued expenses	(298)	830	185
Deferred licensing revenue	(29)	(29)	6
Net cash used in operating activities	(20,863)	(11,253)	(4,858)
Cash Flows from Investing Activities			
Purchase of property and equipment	(659)	(159)	(18)
Deposit for leasehold improvements	(715)	—	—
Net cash used in investing activities	(1,374)	(159)	(18)
Cash Flows from Financing Activities			
Proceeds from issuance of common stock upon exercise of options, net	155	229	17
Proceeds from issuance of common stock, net	67,908	(1,201)	—
Proceeds from issuance of convertible preferred stock, net	—	—	6,010
Proceeds from loans payable	—	2,208	546
Repayment of loans payable	—	(708)	(158)
Proceeds from convertible promissory notes	4,000	5,000	—
Net cash provided by financing activities	72,063	5,528	6,415
Net increase/(decrease) in cash and cash equivalents	49,826	(5,884)	1,539
Cash and cash equivalents at beginning of year	3,897	9,781	8,242
Cash and cash equivalents at end of year	$ 53,723	$ 3,897	$ 9,781
Supplemental Cash Flow Information			
Cash paid for interest	$ 180	$ 626	$ 367
Supplemental Disclosures of Non-cash Financing Activities			
Issuance of preferred stock warrants	$ —	$ 103	$ 42
Conversion of preferred stock warrants to common stock warrants	$ 347	$ —	$ —
Conversion of preferred stock to common stock	$ 39,556	$ —	$ —
Increase of accrual for deferred public offering costs	$	$ 447	$ —
Increase of derivative related to convertible promissory notes	$ 1,196	$ 1,067	$ —
Increase of beneficial conversion feature for convertible promissory notes	$ 519	$ 2,275	$ —
Property and equipment additions in accounts payable and accrued expenses	$ 99	$ —	$ —

The accompanying notes are an integral part of these financial statements.

Note 1. Formation and Business of the Company

Carbylan Therapeutics, Inc. (the "Company") is a clinical-stage specialty pharmaceutical company focused on the development and commercialization of novel and proprietary combination therapies that address significant unmet medical needs. The Company's initial focus is on the development of Hydros-TA, its proprietary, potentially best-in-class intra-articular injectable product candidate to treat pain associated with osteoarthritis of the knee. The Company was incorporated in the state of Delaware on March 26, 2004 as Sentrx Surgical, Inc. The name of the Company was changed to Carbylan Biosurgery, Inc. on December 14, 2005. The name of the Company was changed to Carbylan Therapeutics, Inc. on March 7, 2014.

Since commencing operations in 2004, the Company has devoted substantially all of its efforts to identifying and developing product candidates for therapeutic markets, recruiting personnel and raising capital. The Company has devoted predominantly all of its resources to the preclinical and clinical development of, and manufacturing capabilities for, Hydros-TA. The Company has never been profitable and has not yet commenced commercial operations.

At December 31, 2015, the Company had an accumulated deficit of approximately $72.6 million. The Company expects to incur increased research and development expenses during the current Phase 3 trial of Hydros-TA. Management's plans with respect to these matters include utilizing a substantial portion of the Company's capital resources and efforts in completing the development and obtaining regulatory approval for Hydros-TA and expanding the Company's organization.

In March 2015, the Company's board of directors and stockholders approved a 4-for-1 reverse stock split of the Company's common and preferred stock. The Company filed an amendment to its certificate of incorporation effecting the reverse stock split on March 13, 2015. All share and per share amounts contained in these financial statements and notes thereto, have been adjusted retroactively to reflect the reverse stock split.

On April 8, 2015, the Company's registration statement on Form S-1 (File No. 333-201278) relating to the IPO of its common stock was declared effective by the SEC. The IPO closed on April 14, 2015 at which time the Company sold 14,950,000 shares of common stock, which included 1,950,000 shares of common stock purchased by the underwriters upon the full exercise of their option to purchase additional shares of common stock. The Company received cash proceeds of approximately $66.3 million from the IPO, net of underwriting discounts and commissions and offering costs paid by the Company.

Prior to the closing of the IPO, all outstanding shares of convertible preferred stock converted into 8,268,531 shares of common stock with the related carrying value of $39.6 million reclassified to common stock and additional paid-in capital. In addition, all convertible preferred stock warrants were converted into warrants exercisable for common stock and the convertible promissory notes were converted in to 2,287,120 shares of common stock.

On April 14, 2015, the Company filed its Amended and Restated Certificate of Incorporation, authorizing 105,000,000 shares of capital stock, including 100,000,000 shares of authorized common stock and 5,000,000 shares of authorized undesignated preferred stock. Both the common stock and preferred stock have a par value of $0.001 per share. There are no shares of preferred stock outstanding at December 31, 2015.

Note 2. Summary of Significant Accounting Policies and Basis of Presentation

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP").

Use of Estimates

The preparation of the Company's financial statements in accordance with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting periods. On an ongoing basis, the Company evaluates its estimates, including those related to common stock, stock-based compensation expense, warrant liabilities, accruals, derivative liability, deferred tax valuation allowance and revenue recognition. Management bases its estimates on historical experience or on various other assumptions, including information received from its service providers, which it believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Risks and Uncertainties

The product candidates developed by the Company require approvals from the U.S. Food and Drug Administration ("FDA") or foreign regulatory agencies prior to commercial sales. There can be no assurance that the Company's current and future product candidates will receive the necessary approvals. If the Company is denied approval or approval is delayed, it may have a material adverse impact on the Company's business and its financial statements.

The Company is subject to risks common to companies in the pharmaceutical industry with no commercial operating history, including, but not limited to, dependency on the clinical and commercial success of its product candidates, ability to obtain regulatory approval of its product candidates, the need for substantial additional financing to achieve its goals, uncertainty of broad adoption of its approved products, if any, by physicians and consumers, significant competition and untested manufacturing capabilities.

The Company expects to incur substantial operating losses for the next several years and will need to obtain additional financing in order to launch and commercialize any products or product candidates for which it receives regulatory approval. There can be no assurance that such financing will be available or will be at terms acceptable by the Company.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash and cash equivalents. The Company invests its excess cash in money market accounts. The Company's cash and cash equivalents are held by a single financial institution and all cash is held in the United States. Such deposits may, at times, exceed federally insured limits. The Company has not recognized any losses during the periods presented and management does not believe that the Company is exposed to significant credit risk from its cash and cash equivalents.

Segment Reporting

The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions. The Company is a specialty pharmaceutical company focused on the development and commercialization of novel and proprietary combination therapies that address significant unmet medical needs. No product revenue has been generated since inception, and all assets are held in North America.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with an original maturity date of 90 days or less on the date of purchase to be cash equivalents. The Company invests its cash in bank deposits and money market funds.

Restricted Cash

The Company is required to guarantee the credit limit on its corporate credit card with a certificate of deposit of $50,000. The balance is included as restricted cash on the accompanying financial statements.

Beneficial Conversion Feature

From time to time, the Company may issue convertible promissory notes that have conversion prices that create an embedded beneficial conversion feature on the issuance date. A beneficial conversion feature exists on the date a convertible promissory note is issued when the fair value of the underlying common stock to which the note is convertible into is in excess of the remaining unallocated proceeds of the note after first considering the allocation of a portion of the note proceeds to the fair value of any attached equity instruments, if any related equity instruments were granted with the debt. The intrinsic value of the beneficial conversion feature is recorded as a debt discount with a corresponding amount to additional paid-in capital. The debt discount is amortized to interest expense over the term of the note using the effective interest method.

Embedded Derivatives Related to Convertible Promissory Notes

Embedded derivatives that are required to be bifurcated from the underlying debt instrument (i.e. host) are accounted for and valued as a separate financial instrument. The Company evaluated the terms and features of the convertible promissory notes issued in September 2014 and February 2015 and identified embedded derivatives requiring bifurcation and accounting at fair value because the economic and contractual characteristics of the embedded derivatives met the criteria for bifurcation and separate accounting due to the conversion features (see Note 8 for a description of the conversion features).

Fair Value of Financial Instruments

Fair value accounting is applied for all financial assets and liabilities, and non-financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually).

Property and Equipment, Net

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, which are as follows:

Computer equipment	3 years
Lab equipment	3 years
Furniture and fixtures	5 years
Machinery and equipment	3 years
Manufacturing equipment	7 years

Leasehold improvements are amortized over the lesser of their useful lives or the term of the lease. Upon sale or retirement of the assets, the cost and related accumulated depreciation are removed from the balance sheet and the resulting gain or loss is recognized in the accompanying statement of operations and comprehensive loss in other income (expense), net. Maintenance and repairs are charged to operations as incurred.

Pre-clinical and Clinical Trial Accruals

The Company's clinical trial accruals are based on estimates of patient enrollment and related costs at clinical investigator sites as well as estimates for the services received and efforts expended pursuant to contracts with clinical research organizations that conduct and manage preclinical and clinical trials on the Company's behalf. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, the Company modifies the estimates of accrued expenses accordingly. To date, there have been no material differences from its estimates to the amount actually incurred.

Preferred Stock Warrant Liability

The Company accounts for its warrants as either equity or liabilities based upon the characteristics and provisions of each instrument. Warrants classified as derivative liabilities are recorded on the Company's accompanying balance sheets at their fair value on the date of issuance and are revalued at each subsequent balance sheet date, with fair value changes recognized as increases or reductions to other income (expense), net in the statements of operations and comprehensive loss.

License Revenue

Revenue under the Company's license arrangement is recognized based on the performance requirements of the contract. Determinations of whether persuasive evidence of an arrangement exists and whether delivery has occurred or services have been rendered are based on management's judgments regarding the fixed nature of the fees charged for deliverables and the collectability of those fees. Should changes in conditions cause management to determine that these criteria are not met for any new or modified transactions, revenue recognized could be adversely affected.

The Company recognizes revenue related to its license arrangement in accordance with the provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605-25, *Revenue Recognition — Multiple-Element Arrangements* ("ASC Topic 605-25,") which provides guidance on how deliverables in an arrangement should be separated and how the arrangement consideration should be allocated to the separate units of accounting:

- requiring an entity to determine the selling price of a separate deliverable using a hierarchy of (i) vendor-specific objective evidence ("VSOE,"), (ii) third-party evidence ("TPE,") or (iii) best estimate of selling price ("BESP"); and
- requiring the allocation of the arrangement consideration, at the inception of the arrangement, to the separate units of accounting based on relative fair value.

The Company evaluates all deliverables within an arrangement to determine whether or not they provide value on a stand-alone basis. Based on this evaluation, the deliverables are separated into units of accounting. The arrangement consideration that is fixed or determinable at the inception of the arrangement is allocated to the separate units of accounting based on their relative selling prices. The Company may exercise significant judgment in determining whether a deliverable is a separate unit of accounting, as well as in estimating the selling prices of such unit of accounting.

To determine the selling price of a separate deliverable, the Company uses the hierarchy as prescribed in ASC Topic 605-25 based on VSOE, TPE or BESP. VSOE is based on the price charged when the element is sold separately and is the price actually charged for that deliverable. TPE is determined based on third-party evidence for a similar deliverable when sold separately and BESP is the price at which the Company would transact a sale if the elements of collaboration and license arrangements were sold on a stand-alone basis. The Company may not be able to establish VSOE or TPE for the deliverables within collaboration and license arrangements, as the Company does not have a history of entering into such arrangements or selling the individual deliverables within such arrangements separately. In addition, there may be significant differentiation in these arrangements, which indicates that comparable third-party pricing may not be available. The Company may determine that the selling price for the deliverables within collaboration and license arrangements should be determined using BESP. The process for determining BESP involves significant judgment on the Company's part and includes consideration of multiple factors such as estimated direct expenses and other costs, and available data.

For each unit of accounting identified within an arrangement, the Company determines the period over which the performance obligation occurs. The Company allocates the arrangement consideration to the separate units of accounting based on the relative selling prices. Revenue is recognized immediately if the performance obligation has been met. The Company recognizes the revenue that is deferred using the straight-line method over the expected delivery period of the unit of accounting. Non-substantive regulatory milestone and commercialization royalty payments are recognized in proportion to the two units of accounting identified at the inception of the agreement. Each portion will be recognized in accordance with the underlying unit of accounting. The Company accounts for revenue net of applicable foreign taxes.

Research and Development Expenditures

Costs incurred to further the Company's research and development include salaries and related employee benefits, stock-based compensation expense, costs associated with clinical studies, nonclinical research and development activities, regulatory activities, research-related overhead expenses and fees paid to external service providers and contract research and manufacturing organizations that conduct certain research and development activities on behalf of the Company.

Stock-Based Compensation

The Company maintains performance incentive plans under which incentive stock options and non-qualified stock options may be granted to employees and non-employees. The Company accounts for stock-based compensation arrangements with employees in accordance with ASC 718, *Compensation — Stock Compensation.* ASC 718 requires the recognition of compensation expense, using a fair value-based method, for costs related to all share-based payments including stock options.

The Company's determination of the fair value of stock options on the date of grant utilizes the Black-Scholes option-pricing model, and is impacted by its common stock price as well as changes in assumptions regarding a number of subjective variables. These variables include, but are not limited to, expected term that options will remain outstanding, expected common stock price volatility over the term of the option awards, risk-free interest rates and expected dividends.

The fair value is recognized over the period during which an optionee is required to provide services in exchange for the option award, known as the requisite service period (usually the vesting period), on a straight-line basis. Stock-based compensation expense recognized at fair value includes the impact of estimated forfeitures. The Company estimates future forfeitures at the date of grant and revises the estimates, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Income Taxes

The Company accounts for income taxes under the asset and liability method. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amounts expected to be realized.

The Company accounts for uncertain tax positions in accordance with ASC 740-10, *Accounting for Uncertainty in Income Taxes.* The Company assesses all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon ultimate settlement. As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and the Company will determine whether (i) the factors underlying the sustainability assertion have changed and (ii) the amount of the recognized tax benefit is still appropriate. The recognition and measurement of tax benefits requires significant judgment. Judgments concerning the recognition and measurement of a tax benefit might change as new information becomes available.

It is the Company's policy to include penalties and interest expense related to income taxes as a component of other expense and interest expense as necessary. There was no interest or penalties accrued at December 31, 2015, 2014 and 2013.

Net Loss per Share Attributable to Common Stockholders

The Company calculates its basic and diluted net income (loss) per share attributable to common stockholders in conformity with the two-class method required for companies with participating securities, which are securities other than common stock that are entitled to receive dividends. The Company's convertible preferred stockholders are entitled to participate in dividends and earnings of the Company when dividends are paid on common stock. Under the two-class method, the Company determines whether it has net income attributable to common stockholders, which includes the results of operations, capital contributions and deemed dividends less current period convertible preferred stock non-cumulative dividends. If it is determined that the Company does have net income attributable to common stockholders during a period, the related undistributed earnings are then allocated between common stock and the convertible preferred stock based on the weighted average number of shares outstanding during the period to determine the numerator for the basic net income per share attributable to common stockholders. In computing diluted net income attributable to common stockholders, undistributed earnings are re- allocated to reflect the potential impact of dilutive securities to determine the numerator for the diluted net income per share attributable to common stockholders.

The Company's basic net income (loss) per share attributable to common stockholders is calculated by dividing the net income (loss) by the weighted average number of shares of common stock outstanding for the period. The diluted net income (loss) per share attributable to common stockholders is computed by giving effect to all potential dilutive common stock equivalents outstanding for the period. For purposes of this calculation, options to purchase common stock and common stock warrants are considered common stock equivalents. For periods in which the Company has reported net losses, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders for the years ended December 31, 2015, 2014 and 2013.

Reverse Stock Split

In March 2015, the Company's board of directors and stockholders approved a 4-for-1 reverse stock split of the Company's common and preferred stock. The Company filed an amendment to its certificate of incorporation effecting the reverse stock split on March 13, 2015. All share and per share amounts for all periods presented in these financial statements and notes thereto, have been adjusted retroactively to reflect the reverse stock split.

Recent Accounting Pronouncement

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards update ("ASU") 2014-09, *"Revenue from Contracts with Customers*," requiring an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. The updated standard will replace most existing revenue recognition guidance in U.S. GAAP when it becomes effective and permits the use of either the retrospective or cumulative effect transition method. In July 2015, the FASB voted to defer the effective date for annual reporting periods beginning after December 15, 2017 (including interim reporting periods within those periods) and permitted early adoption of the standard, but not before the original effective date of December 15, 2016. The Company expects to adopt the updated standard in the first quarter of fiscal 2018. The Company has not yet selected a transition method and is currently evaluating the effect that the updated standard will have on the financial statements and related disclosures.

In August 2014, the FASB issued ASU NO. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, or ASU 2014-15. ASU 2014-15 requires management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date the financial statements are issued and provides guidance on determining when and how to disclose going concern uncertainties in the financial statements. Certain disclosures will be required if conditions give rise to substantial doubt about an entity's ability to continue as a going concern. ASU 2014-15 applies to all entities and is effective for annual and interim reporting periods ending after December 15, 2016, with early adoption permitted. The Company does not expect that the adoption of this guidance will have a material effect on its financial statements.

In April 2015, the FASB issued ASU No. 2015-03, *Simplifying the Presentation of Debt Issuance Costs*. ASU 2015-03 requires that debt issuance costs be presented in the balance sheet as a direct deduction from the carrying amount of the related debt liability, similar to debt discounts. The standard will be effective for financial statements issued for annual periods beginning after December 15, 2015, and interim periods within those annual periods. Early adoption is permitted for financial statements that have not been previously issued. The Company is evaluating the effect that the standard will have on our financial statements.

In November 2015, the FASB issued ASU No. 2015-17 (Topic 740), *Balance Sheet Classification of Deferred Taxes*. ASU 2015-17 requires deferred tax liabilities and assets to be classified as noncurrent in the balance sheet. The standard will be effective for financial statements issued for annual periods beginning after December 15, 2016, and interim periods within those annual periods. Early adoption is permitted for financial statements that have not been previously issued. The ASU may be applied either prospectively to all deferred tax liabilities and assets or retrospectively to all periods presented. The Company adopted this ASU on a prospective basis in the fourth quarter of fiscal 2015. The adoption did not have a material effect on the Company's financial statements.

In February 2016, the FASB issued new lease accounting guidance in Accounting Standards Update No. 2016-02, Leases (Topic 842). Under the new guidance, lessees will be required to recognize for all leases (with the exception of short-term leases) at the commencement date: (1) a lease liability, which is a lessee's obligation to make lease payments arising from a lease, measured on a discounted basis; and (2) a right-of-use asset, which is an asset that represents the lessee's right to use, or control the use of, a specified asset for the lease term. Lessor accounting, however, remains largely unchanged. In addition, the new lease guidance simplified the accounting for sale and leaseback transactions primarily because lessees must recognize lease assets and lease liabilities. Lessees will no longer be provided with a source of off-balance sheet financing. The new lease guidance is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. Early application is permitted, however, the Company does not intend to early adopt. The Company also believes that adoption of this new guidance will not have a material impact on the Company's financial statements.

Note 3. Fair Value Measurements

The Company follows ASC 820-10, Fair Value Measurements and Disclosures, which among other things, defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or nonrecurring basis. Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, a three-tier fair value hierarchy has been established, which prioritizes the inputs used in measuring fair value as follows:

Level 1	Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.
Level 2	Inputs (other than quoted prices included in Level 1) are either directly or indirectly observable for the asset or liability through correlation with market data at the measurement date and for the duration of the instrument's anticipated life.
Level 3	Inputs reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

The Company's investments in money market funds are measured at fair value on a recurring basis. The fair value of the money market fund investments is classified as Level 1.

The fair value of the certificates of deposit is classified as Level 2 due to the nature of a contractual restriction with a financial institution that requires the certificate of deposit to remain in place as collateral, and therefore the ability to liquidate the investment is limited.

As of December 31, 2015, based on borrowing rates that are available to the Company for loans of similar terms and consideration of the Company's credit risk, the carrying value of the loan payable approximates the fair value using Level 2 inputs.

There were no transfers between Level 1 and Level 2 during the periods presented.

In certain cases where there is limited activity or less transparency around inputs to valuation, securities are classified as Level 3. On a recurring basis, the Company estimates the fair value of the warrant liability. The Company used the Black-Scholes option-pricing method to calculate the fair value of the warrant liability. Generally, increases or decreases in the fair value of the underlying convertible preferred stock would result in a similar impact in the fair value measurement of the warrant liability.

The fair value of the derivative of the September 2014 and February 2015 convertible promissory notes (see Note 8) was recorded as a derivative liability instrument that is measured at fair value at each reporting period. In connection with the IPO, the convertible promissory notes were converted in to shares of common stock, and therefore there is no derivative liability at December 31, 2015. At December 31, 2014, the Company remeasured the fair value of the derivative for the September 2014 convertible promissory notes by estimating the fair value of the convertible promissory notes with and without the conversion derivative. To calculate the fair value of the convertible promissory notes without the conversion derivative, the Company estimated the present value of the expected cash payments at an assumed discount rate. To calculate the fair value of the convertible promissory notes with the conversion feature, the Company calculated the present value of the convertible promissory notes upon conversion at an initial public offering, and the present value of the convertible promissory notes at an equity financing. The Company applied a probability of occurrence to all of the conversion scenarios and estimated a weighted value of the notes with the conversion feature. The difference between the fair value of the convertible promissory notes with and without the conversion features is the fair value of the derivative.

The following table presents the Company's fair value hierarchy for assets and liabilities measured at fair value on a recurring basis:

	Fair Value Measurements as of December 31, 2015 (in thousands)			
	Quoted Price in Active Markets for Identical Assets Level 1	Significant other Observable Inputs Level 2	Significant Unobservable Inputs Level 3	Total
Assets				
Money market funds(1)	$ 53,625	$ —	$ —	$ 53,625
Certificate of deposit	—	50	—	50
	$ 53,625	$ 50	$ —	$ 53,675

	Fair Value Measurements as of December 31, 2014 (in thousands)			
	Quoted Price in Active Markets for Identical Assets Level 1	Significant other Observable Inputs Level 2	Significant Unobservable Inputs Level 3	Total
Assets				
Money market funds(1)	$ 3,825	$ —	$ —	$ 3,825
Certificate of deposit	—	50	—	50
	$ 3,825	$ 50	$ —	$ 3,875
Liabilities				
Derivative liability	$ —	$ —	$ 1,495	$ 1,495
Preferred stock warrant liability	—	—	463	463
	$ —	$ —	$ 1,958	$ 1,958

(1) Included in cash and cash equivalents in the Company's balance sheet.

The change in the fair value of the preferred stock warrant liability is summarized below:

Fair value as of December 31, 2013	$ 184
Fair value of new warrant issued	103
Change in fair value recorded in other income (expense), net	176
Fair value as of December 31, 2014	$ 463
Change in fair value recorded in other income (expense), net	(116)
Conversion to common stock warrants at IPO date	(347)
Fair value as of December 31, 2015	$ —

The following is a summary of the activity of the derivative liability:

Fair value as of December 31, 2013	$ —
Embedded derivative liability upon issuance of convertible promissory notes	1,067
Change in fair value recorded in other income (expense), net	428
Fair value as of December 31, 2014	$ 1,495
Embedded derivative liability upon issuance of convertible promissory notes	1,196
Change in fair value recorded in other income (expense), net	(404)
Conversion of convertible promissory notes	(2,287)
Fair value as of December 31, 2015	$ —

The fair value of the derivative liability was determined using the following assumptions (see Note 8):

	At Issuance	At December 31, 2014	At December 31, 2015
Discount Rate	8.25%	8.25%	—
Embedded derivative liability upon issuance of convertible promissory notes	0.05%	0.05%	—
Change in fair value recorded in other income (expense), net	0.15%	0.12%	—

Note 4. Balance Sheet Components

Property and Equipment, Net

The following table represents the components of property and equipment (in thousands):

	December 31, 2015	December 31, 2014
Computer equipment	$ 30	$ 30
Lab equipment	697	543
Furniture and fixtures	21	21
Machinery and equipment	262	26
Leasehold improvements	55	55
Construction in progress	368	—
	1,433	675
Less: Accumulated depreciation and amortization	(628)	(495)
Total property and equipment, net	$ 805	$ 180

Depreciation expense for the years ended December 31, 2015, 2014 and 2013, was $133,000, $54,000 and $27,000, respectively.

Accrued Liabilities

(in thousands)

	December 31, 2015	December 31, 2014
Accrued payroll and related expenses	$ 727	$ 723
Accrued legal expenses	77	159
Accrued research and clinical trial expenses	338	380
Accrued professional services	185	343
	$ 1,327	$ 1,605

Note 5. Commitments and Contingencies

Operating Lease

The Company leases facilities in Palo Alto, California under a noncancelable operating lease which expires May 2016. The terms of the lease agreement required the Company to provide a security deposit of $69,000. The security deposit is included in other assets on the accompanying balance sheets. The Company had a sub-lease agreement with a tenant for approximately thirty-seven percent of the square footage of the corporate headquarters. Under this agreement, the Company received $16,000 per month as rental income which is accounted for as a reduction of rent expense. The sub-lease agreement expired February 29, 2016.

Gross rent expense for the years ended December 31, 2015, 2014 and 2013 was $431,000, $429,000 and $413,000 , respectively. The rental expense is reduced by the sublease rental income amounts of $195,000, $190,000 and $186,000, respectively, for the same periods.

On July 13, 2015, the Company entered into a lease for an approximately 18,700 square foot facility located in Newark, California (the "Newark Lease"), with office, R&D and laboratory space. Under the Newark Lease, the landlord provided an allowance of $599,000 to fund certain improvements to the facility. In March 2016, the Company determined not occupy to the Newark facility and is attempting to sublease the facility. (See Note 18.)

The Newark Lease has an initial term of approximately six and a half years, with a monthly rental rate starting at $2.65 per square foot in the first year of the lease, escalating each year by 3.0%. The annual rent obligation is expected to be approximately $599,000 for the first year of the lease. The Company is also responsible for certain other costs, including insurance, taxes, utilities, maintenance and repairs, a property management fee, and reimbursement of certain expenses related to maintenance of common areas. The Company delivered a security deposit of approximately $149,000 in connection with the execution of the Newark lease, which is recorded in other assets on the balance sheets.

The aggregate future minimum lease payments under the current and future operating lease are as follows:

Years ending December 31,	(in thousands)
2016	$ 618
2017	611
2018	629
2019	648
2020	668
Remaining years	1,100
Total minimum lease payments	$ 4,274

Indemnification

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for general indemnification. The Company's exposure under these agreements is unknown because it involves future claims that may be made against the Company but have not yet been made. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. However, the Company may record charges in the future as a result of these indemnification obligations No amounts associated with such indemnifications have been recorded to date.

Contingencies

From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of business activities. The Company accrues a liability for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. There have been no contingent liabilities requiring accrual or disclosure at December 31, 2015.

Note 6. License Agreement with Shanghai Jingfeng Pharmaceutical Co. Ltd.

In November 2012, the Company entered into a technology license agreement (the "Agreement") with Shanghai Jingfeng Pharmaceutical Co. Ltd. ("Jingfeng"), pursuant to which the Company granted to Jingfeng the exclusive right and license under certain patents to develop, manufacture and commercialize Hydros-TA for human and veterinary uses in China, Taiwan, Hong Kong and Macau. In these countries, Jingfeng is responsible for the manufacture and supply of Hydros-TA, the management and funding of all development activities, regulatory submissions and regulatory approvals for Hydros-TA and the commercialization of Hydros-TA. The Company has also agreed to provide know-how and reasonable professional and technical support services to Jingfeng until Jingfeng performs all efforts necessary to bring the product to commercialization and begins selling the product upon regulatory approval in the aforementioned territory. The Agreement provides for an up-front license payment of $2,000,000 ($1,674,000 net of Chinese withholding taxes), regulatory milestone payments of up to $2,000,000 (excluding Chinese withholding taxes) and future commercial milestone payments of up to approximately $5,000,000 (excluding Chinese withholding taxes) at current exchange rates based on Jingfeng achieving certain gross sales thresholds.

The Company has identified the following non-contingent performance deliverables at the inception of the Agreement: (i) an exclusive royalty bearing license to certain of the Company's patents relating to Hydros-TA (the "License"), which was transferred immediately upon signing of the Agreement, and (ii) know-how, reasonable professional and technical support services to be provided by the Company to assist Jingfeng in manufacturing, developing and/or commercializing the licensed product (the "Services") throughout the period of the Agreement. The Company has determined that the License represents a separate unit of accounting as the License has standalone value apart from the Services because the development, manufacturing and commercialization rights conveyed would allow Jingfeng to perform all efforts necessary to use the Company's technologies to bring the product to commercialization and begin selling the product upon regulatory approval. Jingfeng can sublicense its rights to the License; and the Services provided by the Company could be performed by a third-party. Therefore, the License and Services represent separate units of accounting.

The Company has determined the BESP for the License unit of accounting using a discounted cash flow analysis. This measurement is based on the value indicated by current estimates of future payments to be received under the agreement and reflects management determined estimates and assumptions. These estimates and assumptions include but are not limited to estimated sales prices, estimated market opportunity, expected market share, the likelihood that clinical trials will be successful, the likelihood that regulatory approval will be received, the likelihood that the products will become commercialized, the determination of the markets served and the discount rate. The Company reduced the future payment to be received by the estimated amount of the professional service costs plus an estimated margin, which was based on industry benchmarking of similar companies. These estimates and assumptions formed the basis of an expected net future cash flow that was discounted based on an estimated weighted average cost of capital. The Company has also determined the BESP for the Services unit of accounting based on the estimated cost of the professional services plus an estimated margin which was based on industry benchmarking of similar companies. These estimates and assumptions formed the basis of an expected net future cash flow that was discounted based on an estimated weighted average cost of capital.

The considerations of the Agreement have been allocated to the units of accounting based on the relative selling price method. Of the $1,674,000 upfront payment received, $1,534,000 was allocated to the License and $140,000 to the Services. The Company has recognized license revenue upon execution of the Agreement as the license has been delivered pursuant to the terms of the Agreement. The $140,000 allocated to Services will be recognized as revenue on a straight-line over the estimated performance period through January 2019. The way in which the Company will provide professional services does not give rise to a more precise pattern of recognition and the Company therefore will recognize revenue on a straight-line basis over the performance period.

Of the $421,000 regulatory milestone payment received in November 2013 upon the successful production by Jingfeng of the first batch of Hydros-TA, $385,000 was allocated to the License and $35,000 was allocated to the Services. The Company has recognized license revenue upon execution of the Agreement as the associated unit of accounting had been delivered pursuant to the terms of the Agreement. The $35,000 allocated to Services will be recognized as revenue on a straight-line basis over the performance period which is currently estimated to be January 2019.

Total revenue recognized with respect to the Agreement consisted of the following (in thousands):

	Year Ended December 31,		
	2015	2014	2013
License and Services revenue	$ 29	$ 29	$ 415

The Company has determined that the regulatory milestones and commercialization royalty are contingent revenue that will be allocated to the two units of accounting (License and Services) described above, rather than recognized immediately upon satisfaction of the milestone, as they do not meet the definition of a milestone as described in the applicable accounting literature. Certain regulatory milestones do not require performance by the Company to be achieved. The payments the Company would receive for the remaining regulatory milestones are not commensurate with the performance by the Company to achieve such milestones.

Note 7. Loan and Security Agreement

In October 2011, the Company entered into a loan and security agreement (the "Loan and Security Agreement") with a financial institution. In September 2014, the Loan and Security Agreement was amended to provide for a new loan of $4,500,000 and repayment of the outstanding principal of the loan amounts previously disbursed in February 2013 and January 2014, with the remaining proceeds of approximately $0.5 million provided to the Company. The interest rate is 3.95% per annum and the loan is repayable in thirty-six equal monthly installments, following an eighteen-month interest only period. The final balloon interest payment is approximately $0.5 million and is accreted over the life of the loan. As a result of the Company's IPO, the interest only period has been extended to April 1, 2016. The amendment was accounted for as a modification of loans payable, and the unamortized debt discount as of the date of the modification will be amortized over the new loan period, using the effective interest rate method.

The Loan and Security Agreement contains customary representations and warranties, covenants, closing and advancing conditions, events of defaults and termination provisions. The Loan and Security Agreement provides that an event of default will occur if (1) the financial institution determines that it is the clear intention of the Company's investors to not continue to fund the Company in the amounts and timeframe necessary to enable the Company to satisfy the Company's financial obligations, (2) there is a material impairment in the financial institution's security interest in the personal property that is the collateral, (3) the Company defaults in the payment of any amount payable under the agreement when due or (4) the Company breaches any negative covenant or certain affirmative covenants in the agreement (subject to a grace period in certain cases). The repayment of the loan is accelerated following the occurrence of an event of default or otherwise, which would require the Company to immediately pay an amount equal to: (i) all outstanding principal plus accrued but unpaid interest, (ii) the final payment, plus (iii) all other sums, that shall have become due and payable but have not been paid, including interest at the default rate with respect to any past due amounts. As of December 31, 2015, the Company was in compliance with all the covenants in the Loan and Security Agreement.

Aggregated annual payments due under the Loan and Security Agreement are as follows:

As of December 31, 2015 (in thousands)		
2016	$	1,775
2017		2,095
2018		1,391
Total payments		5,261
Less: Interest		(761)
Present value of loans payable		4,500
Less: Debt discount		(83)
Add: Final balloon payment		517
Less: Unamortized portion of final balloon payment		(325)
Loans payable		4,609
Less: Current portion		(1,455)
Loans payable, net of current portion	$	3,154

Note 8. Convertible Promissory Notes

On September 29, 2014 and February 19, 2015, the Company entered into convertible note purchase agreements and issued convertible promissory notes (the "Notes") in an aggregate principal amount of $5.0 million and $4.0 million, respectively, to several related parties that own more than 10% of the Company's capital stock. All principal and accrued interest on the Notes was converted to the Company's common stock upon the completion of the Company's initial public offering in April 2015. Upon conversion, 2,287,120 shares of common stock were issued.

The Notes provided that upon completion of an initial public offering, the Notes would automatically convert into a number of shares of the Company's common stock equal to the quotient obtained by dividing the entire principal amount and accrued interest on the Notes by 80% of the initial public offering price per share of the Company's common stock. The Notes bore interest at a rate of 5% per annum, compounded annually.

Due to the automatic conversion features contained in the Notes, the actual number of shares of common stock or preferred stock that would be required if a conversion of the Notes was made through the issuance of the Company's common or preferred stock could not be predicted prior to the conversion taking place. In addition, the conversion that would occur upon a change in control of the Company met the definition of a put option and was not closely related to the debt. As a result, the automatic conversion features and put option, exclusive of the Series B conversion feature, required derivative accounting treatment and were bifurcated from the Notes and marked to market each reporting period through the statement of operations and comprehensive loss. The fair value of the automatic conversion features and put option of the Notes, exclusive of the Series B conversion feature, were recorded as a derivative liability instrument and measured at fair value at each reporting period.

As of December 31, 2014, the Company estimated the fair value of the derivative by estimating the fair value of the Notes with and without the conversion derivative. To calculate the fair value of the Notes without the conversion derivative, the Company estimated the present value of the expected cash payments at an assumed discount rate of 8.25%. To calculate the fair value of the Notes with the conversion feature, the Company calculated the present value of the Notes upon conversion at an initial public offering, and the present value of the Notes at an equity financing. The risk-free rate for the assumed discount period is estimated at 0.05% and 0.15% in the respective conversion scenarios. The risk-free rate for the assumed discount period is estimated at 0.05% and 0.12% in the respective conversion scenarios at the valuation date of December 31, 2014. The Company applied a probability of occurrence to all of the conversion scenarios associated with the derivative and estimated a weighted value of the Notes with the conversion feature. The difference between the fair value of the Notes with and without the conversion features is the derivative. The fair value of the derivative was $1,495,000 as of December 31, 2014.

Upon issuance of the February 2015 Notes, the Company calculated the derivative liability using the same methodology and assumptions as those used as of December 31, 2014 because there were not significant changes in the Company or in the operations of the Company that had occurred in that intervening time period. The additional derivative liability recorded upon issuance of the February 2015 Notes was $1,196,000.

At April 8, 2015, the Company remeasured the fair value of the derivative liability for the Notes using a methodology similar to the methodology used at December 31, 2014, with a minimal discount period. The fair value of the derivative was $2,287,000.

The Company determined that the Notes contain a beneficial conversion feature related to the conversion feature of the Notes into Series B convertible preferred stock. The beneficial conversion feature results from the difference between the fair value of the Company's common stock at the date of issuance and the Series B Preferred Stock Conversion price of $4.8104 at the date of issuance. The beneficial conversion feature amounted to $2,275,000 for the September 2014 Notes and $158,000 for the February 2015 Notes as of the date of issuance of the respective Notes, and was recorded as a debt discount that would be amortized through the maturity date of the Notes.

At April 8, 2015, the beneficial conversion feature amounted to $202,000 for the September 2014 Notes and $158,000 for the February 2015 Notes. The fair value of the shares issued upon conversion of the convertible promissory notes was first allocated to the beneficial conversion feature of $360,000.

At April 8, 2015, the loss on extinguishment of the convertible promissory notes was calculated as follows:

Fair value of common stock issued upon conversion of convertible promissory notes and accrued interest	$	11,435
Less:		
Fair value of beneficial conversion feature on conversion date		(360)
Net book value of convertible promissory notes		(5,611)
Fair Value of derivative liability at conversion date		(2,287)
Loss on extinguishment of convertible promissory notes	$	3,177

Note 9. Convertible Preferred Stock

The Company has no outstanding convertible preferred stock as of December 31, 2015.

Convertible preferred stock as of December 31, 2014 consisted of the following (in thousands, except share data):

Series	Shares Authorized	Shares Outstanding	Liquidation Amount	Proceeds Net of Issuance Costs
A	6,574,364	1,611,089	$ 7,750	$ 7,595
B	27,796,941	6,657,442	32,025	31,961
	34,371,305	8,268,531	$ 39,775	$ 39,556

The rights, privileges and preferences of convertible preferred stock are as follows:

Dividends

The holders of the Series A and Series B convertible preferred stock were entitled to receive noncumulative annual dividends at the rate of 8% of the original issuance price, or approximately $0.38 per share, respectively, when, as and if declared by the Board of Directors. Dividends on preferred stock shall be payable in preference to and prior to payment of dividends on common stock. In the event that dividends are paid on common stock, an additional dividend shall be paid on preferred stock in an amount equal per share (on an as-if-converted basis) to the amount paid for each share of common stock. No dividends were declared from inception to December 31, 2014.

Liquidation Rights

In the event of any liquidation, dissolution or winding up of the Company, the holders of the Company's convertible preferred stock shall be entitled to receive, prior to any distribution of the Company's assets to the holders of common stock, an amount equal to $4.8104 per share for each outstanding share of Series A and Series B convertible preferred stock, plus any declared but unpaid dividends. If the Company's assets shall be insufficient to provide for such preferential distributions, the preferred stockholders shall be entitled to pro rata distributions. The remaining assets of the Company shall be distributed among the preferred stockholders and the common stockholders pro rata on an as-if-converted basis until the holders of Series A and Series B preferred stock have received an aggregate of $14.43 per share, respectively. Thereafter, if assets remain in the Company, the common stockholders shall receive all of the Company's remaining assets on a pro rata basis. A sale of all or substantially all of the assets of the Company, merger or consolidation, which result in the Company's stockholders immediately prior to such transaction not holding at least 50% of the voting power of the surviving, continuing or purchasing entity shall be deemed a liquidation of the Company.

Due to the liquidation rights in a deemed liquidation, the Company's convertible preferred stock was classified outside of permanent equity (deficit) as mezzanine.

Modification of Series B Convertible Preferred Stock

In December 2012, the Company approved the adjustment of the Series B convertible preferred stock liquidation preference from $5.52 per share to $4.8104 per share. In order to preserve the aggregate liquidation preference of the Series B convertible preferred stockholders at that time, the Company issued 534,467 shares of Series B convertible preferred stock to such holders. As part of this analysis, the Company assessed the economic characteristics and risks of its convertible preferred stock, including conversion, liquidation and redemption features, as well as dividend and voting rights. Based on the Company's determination that each series of its convertible preferred stock is an "equity host," the Company determined that the features of the convertible preferred stock are most closely associated with an equity host and, although the convertible preferred stock includes conversion features, such conversion features do not require bifurcation as a derivative liability. The Company also determined that the conversion option with a contingent reduction in the conversion price, upon occurrence of certain dilutive events, is a potential contingent beneficial conversion feature. In accordance with certain antidilution provisions contained in the Series B convertible preferred stock agreements, issuances of Series B convertible preferred stock in 2012 resulted in an antidilution adjustment of the conversion prices for the Series B convertible preferred stock during the year ended December 31, 2012. As a result, the Company performed a calculation to determine if a beneficial conversion feature was triggered for the Series B convertible preferred stock at each issuance of Series B in 2012. The fair value of common stock, as determined by management and the Board of Directors, on the corresponding issuance dates of Series B convertible preferred stock in each instance was below the adjusted accounting conversion prices. Therefore, no beneficial conversion feature was identified. The Company will continue to evaluate if a beneficial conversion feature needs to be recorded upon each subsequent adjustment of the conversion price based upon the difference between the adjusted conversion price and the fair market value of common stock at the original issuance date. This change is treated as a modification of the Series B preferences and results in a deemed dividend of Series B convertible preferred stock of $111,000. This amount is recorded as a reduction of additional paid-in-capital and an increase in the Series B convertible preferred stock in the accompanying financial statements.

Conversion Rights

The Company's preferred stock was convertible, at the option of the holder, into common stock on a one-for-one basis with the conversion ratio subject to adjustment in the event of certain dilutive stock issuances or other future events. Conversion was automatic upon the closing of a firm commitment underwritten public offering in which the aggregate gross proceeds equals or exceeds $30,000,000, or the date specified by written agreement of the holders of at least two-thirds of the preferred stock then issued and outstanding on an as-if-converted basis.

Voting Rights

The holder of each share of the Company's convertible preferred stock had the right to one vote for each share of common stock into which such convertible preferred stock could be converted. The holders of Series A convertible preferred stock and series B convertible preferred stock, voting as separate classes, were entitled to elect two members each of the Board of Directors, and the holders of common stock, voting as a separate class, were entitled to elect one member of the Board of Directors. The holders of common stock and preferred stock, voting together as a single class on an as-if-converted basis, were entitled to elect all remaining members of the Board of Directors.

Prior to the closing of the IPO, all outstanding shares of convertible preferred stock converted into 8,268,531 shares of common stock with the related carrying value of $39.6 million reclassified to common stock and additional paid-in capital. In addition, all convertible preferred stock warrants were converted into warrants exercisable for common stock and the convertible promissory notes were converted in to 2,287,120 shares of common stock.

Note 10. Convertible Preferred Stock Warrants

The Company issued warrants to purchase shares of the Company's convertible preferred stock at various times in connection with loans payable. Immediately prior to the closing of the IPO, all convertible preferred stock warrants were converted in to warrants exercisable for common stock. The convertible preferred stock warrants outstanding as of December 31, 2014 were as follows (in thousands, except share and per share amounts):

	Number of Shares Underlying Warrants	Exercise Price per Share	Fair Value, as of December 31, 2014
Series A preferred stock	20,788	$ 4.8104	$ 46
Series B preferred stock	103,941	$ 4.8104	$ 417
	124,729		$ 463

The fair value of the convertible preferred stock warrant liability was remeasured as of each period end. As of December 31, 2014, the Company remeasured the fair value using a Black-Scholes option-pricing method with the following assumptions: a weighted average remaining life of 6.7 years, an expected volatility of 58.9%, a weighted average risk-free interest rate of 1.80% and no expected dividend. As of April 14, 2015, the Company remeasured the fair of the convertible preferred stock warrant liability using a Black-Scholes option-pricing method with the following assumptions: the Company's IPO price of $5.00 per share, a weighted average remaining life of 6.4 years, an expected volatility of 58.3%, a weighted average risk-free interest rate of 1.51% and no expected dividend. The Company evaluated the down-round protection provisions of the warrant agreements by using a Monte Carlo simulation model and determined that the impact of such provisions was immaterial to the fair value of the warrants at the reporting dates. The assumptions are further described as follows:

Expected Time to liquidity event — The Company estimated the time to liquidity event based on management's analysis of the business, market conditions and clinical development.

Expected Volatility — The Company estimates the expected volatility based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected time to liquidity event. When selecting the publicly traded biopharmaceutical companies, the Company selected companies with comparable characteristics to it, including enterprise value and risk profiles, and with historical share price information sufficient to meet the time to liquidity event. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Risk-Free Interest Rate — The risk-free interest rate is based on U.S. Treasury zero-coupon issues with remaining terms similar to the expected time to the liquidity event.

Expected Dividend Rate — The Company has never paid any dividends and does not plan to pay dividends in the foreseeable future, and, therefore, used an expected dividend rate of zero in the valuation model.

On April 8, 2015, the convertible preferred stock warrants automatically converted to common stock warrants. The convertible preferred stock warrant liability was reclassified to additional paid-in capital. During June 2015, the holder of the common stock warrants exercised those warrants for 56,545 shares of common stock in a cashless exercise.

Note 11. Common Stock

As of December 31, 2015 the Company's Amended and Restated Certificate of Incorporation, as amended, has authorized 100,000,000 shares of common stock at $0.001 par value.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the board of directors, if any, subject to the preferential dividend rights of the holders of the Series A and B convertible preferred stock. As of December 31, 2015, no dividends have been declared.

Note 12. 401(k) Plan

The Company sponsors a 401(k) Plan that stipulates that eligible employees can elect to contribute to the 401(k) Plan, subject to certain limitations, on a pretax basis. Pursuant to the 401(k) Plan, the Company does not match any employee contributions.

Note 13. Stock Option Plan

2004 Stock Option Plan

In 2004, the Board of Directors approved the 2004 Stock Option Plan (the 2004 Plan), which provides for the granting of incentive and non-statutory stock options to employees, directors, and consultants at the discretion of management and the Board of Directors. In December 2005, the Board of Directors authorized the number of shares available for grant under the Plan to be 239,825. In February 2006, the Board of Directors authorized an additional 62,500 shares available for grant under the Plan. In June 2007, the Board of Directors authorized an additional 20,000 shares available for grant under the Plan. In November 2007, the Board of Directors authorized an additional 625,000 shares available for grant under the Plan. In December 2012, the Board of Directors authorized an additional 564,290 shares available for grant under the Plan. In June 2013, the Board of Directors authorized an additional 173,218 shares available for grant under the Plan.

Incentive stock options are granted with exercise prices not less than the estimated fair value of common stock, and non-statutory stock options may be granted with an exercise price of not less than 100% of the estimated fair value of the common stock on the date of grant. Options granted under the Plan expire no later than 10 years from the date of grant. Incentive stock options granted under the Plan vest over periods determined by the Board of Directors, generally over four years. Non-statutory stock options vest based on the terms of the individual agreement, generally from nine months to four years.

Performance Grants

In 2013, the Company granted options to purchase 1,038,473 shares of common stock, and options to purchase 207,362 of those shares contained a performance based vesting condition. Standard monthly vesting commenced for options to purchase 103,681 of those shares upon the successful recruitment of a specific number of patient subjects in the Company's COR1.1 clinical study. The grant date fair value of the performance options was $120,000. The performance based vesting condition commenced on September 30, 2014. Expense of $26,000 and $3,000 was recognized for the years ended December 31, 2015 and 2014, respectively, and the performance options will continue to vest over the remaining vesting period. The remaining options to purchase 103,681 shares vest over a 48 month period.

2014 Stock Incentive Plan

In April 2014, the Company terminated the 2004 Plan and the board of directors approved the 2014 Stock Option Plan (the 2014 Plan), authorizing 250,000 shares for issuance under the 2014 Plan. Shares underlying any outstanding stock awards or stock option grants previously awarded remain subject to the terms of the 2004 Plan. Any shares available for grant or any shares canceled or forfeited prior to vesting or exercise subsequent to the termination of the 2004 Plan became available for use under the 2014 Plan. Upon the effectiveness of the 2014 Plan, the Company ceased granting any equity awards under the 2004 Plan.

2015 Equity Plan

In January and February 2015, the board of directors and stockholders, respectively, approved the 2015 Equity Plan (the "2015 Equity Plan"). All future awards will be granted under the 2015 Plan. In connection with the IPO, the Company terminated the 2014 Plan. Shares underlying any outstanding stock option grants previously awarded under the 2014 Plan remain subject to the terms of such plan. Any shares available for grant or any shares canceled or forfeited prior to vesting or exercise subsequent to the termination of the 2014 Plan became available for use under the 2015 Plan.

As of December 31, 2015, options for 661,306 shares have been issued under the 2015 Equity Plan. The maximum number of shares of the Company's common stock that may be delivered in satisfaction of awards under the 2015 Equity Plan is 1,532,534 shares, inclusive of 750,000 shares authorized upon creation of the 2015 Plan. The number of shares available for issuance under the Company's 2015 Equity Plan will be increased on the first day of each fiscal year beginning in 2016, by an amount equal to the lessor of (1) 1,200,000 shares of stock and (2) four percent (4%) of the outstanding shares of stock on the last day of the immediately preceding year.

The following table summarizes the activity under the Company's Plans (in thousands, except share and per share amounts):

		Options Issued and Outsanding			
	Shares Available for Grant	Number of Shares	Weighted Average Exercise Price	Remaining Contractual Life (in Years)	Aggregate Intrinsic Value
Balance at December 31, 2013	83,557	1,650,122	$ 0.77	6.91	
Increase in shares reserved for issuance	250,000	—			
Options granted	(428,072)	428,072	$ 7.24		
Options exercised	—	(248,909)	$ 0.92		
Options cancelled	500,412	(500,412)	$ 1.52		
Balance at December 31, 2014	405,897	1,328,873	$ 2.54	7.99	$ 7,521
Increase in shares reserved for issuance	750,000	—			
Options granted	(661,306)	661,306	$ 6.71		
Options exercised	—	(78,983)	$ 1.96		
Options cancelled	183,691	(183,691)	$ 6.98		
Balance at December 31, 2015	678,282	1,727,505	$ 3.69	7.75	$ 2,624
Vested at December 31, 2015		794,044	$ 2.01	6.39	$ 1,842
Vested and expected to vest at December 31, 2015		1,653,998	$ 3.60	7.68	$ 2,587

The following table summarizes information concerning outstanding and exercisable options under the Plan as of December 31, 2015:

	Options Outstanding and Exercisable at December 31, 2015		Options Vested and Exercisable at December 31, 2015	
Exercise Price	Number Outstanding	Weighted Average Remaining Contractual Life (in Years)	Number Outstanding	Weighted Average Remaining Contractual Life (in Years)
$0.56	687,001	7.24	431,485	7.16
$0.80–$1.12	114,396	2.65	114,396	2.65
$1.20	89,000	2.38	89,000	2.38
$4.01	50,415	9.84	—	—
$6.91	547,776	9.59	74,154	9.59
$7.00	120,925	8.84	54,477	8.84
$7.45	30,625	9.31	1,389	9.31
$8.20	87,367	8.98	29,143	8.98
	1,727,505	7.74	794,044	6.39

The intrinsic value of options exercised was $368,000, $1,015,000 and $35,000 for the years ended December 31, 2015, 2014 and 2013. The intrinsic value was calculated as the difference between the exercise price of the options and the estimated fair value of the Company's common stock at those reporting dates.

The total estimated grant date fair value of options vested during the years ended December 31, 2015, 2014 and 2013 was $694,000, $343,000 and $103,000, respectively.

In July and October 2015, the board of directors approved non-qualified stock option grants of 165,903 and 50,000 shares, respectively, of the Company's common stock for employees as inducement grants in connection with the commencement of employment. The grants were issued outside of the 2015 Equity Plan. Stockholder approval was not required for these grants in reliance upon the employment inducement award exemption provided by NASDAQ Rule 5635(c)(4).

Stock-Based Compensation

Total stock-based compensation expense related to options and awards granted was allocated as follows (in thousands):

	Year Ended December 31,		
	2015	2014	2013
Research and Development	$ 235	$ 171	$ 45
General and administrative	550	210	193
Total	$ 785	$ 381	$ 238

At December 31, 2015, there was $2,900,000 of unrecognized stock-based compensation expense, net of estimated forfeitures, related to unvested share options with a weighted-average remaining recognition period of 3.10 years. The non-employee stock-based compensation expense was not material for all periods presented.

In determining the fair value of the stock-based awards, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

For all periods prior to the initial public offering, the fair values of the shares of common stock underlying the share-based awards were estimated on each grant date by the board of directors. In order to determine the fair value of the common stock underlying option grants, the board of directors considered, among other things, contemporaneous valuations of the common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Given the absence of a public trading market for the common stock, the board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of the common stock, including the stage of development, progress of the research and development efforts, the rights, preferences and privileges of the preferred stock relative to those of the common stock, equity market conditions affecting comparable public companies and the lack of marketability of the common stock.

For valuations after the completion of the initial public offering on April 14, 2015, the board of directors determined the fair value of each share of underlying common stock based on the closing price of the common stock as reported on The NASDAQ Global Market as reported on the date of grant.

Expected Term — The Company's expected term represents the period that the Company's stock-based awards are expected to be outstanding. The Company used the average of the expected term as disclosed for comparable publicly traded biopharmaceutical companies since the Company does not have sufficient experience to estimate the expected term based on historical exercises. The expected term of stock options granted to non-employees is equal to the contractual term of the option award.

Expected Volatility — The Company has been trading for less than one year and therefore does not have trading history equal to the expected term for its common stock. The expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. When selecting comparable publicly traded biopharmaceutical companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

Risk-Free Interest Rate — The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend — The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

The fair value of stock option awards to employees was estimated at the date of grant using a Black-Scholes option-pricing model with the following weighted-average assumptions:

	Year Ended December 31,		
	2015	2014	2013
Expected term (in years)	5.57	5.39	5.39
Expected volatility	62.9% to 66.6%	56%	80.7%
Risk-free interest rate	1.43 to 1.67%	1.70 to 1.82%	0.87 to 1.47%
Dividend yield	0%	0%	0%

The weighted-average, estimated grant-date fair value of employee stock options granted during the years ended December 31, 2015, 2014 and 2013 was $3.39, $5.10 and $0.29 per share, respectively

Note 14. Related Party Transactions

In November 2012, the Company entered into a technology license agreement with Shanghai Jingfeng Pharmaceutical Co., Ltd. pursuant to which the Company granted to Jingfeng an exclusive license to develop, manufacture and commercialize Hydros-TA in China, Taiwan, Hong Kong and Macau. Vivo Ventures, which is an investor in the Company with board representation, is also an investor in Jingfeng with board representation.

In June 2013, the Company issued 1,252,494 shares of Series B convertible preferred stock for net cash proceeds of $6.0 million. As part of this offering, 1,247,297 shares were sold to entities owning more than 10% of the Company's outstanding capital stock as of December 2013.

In September 2014 and February 2015, the Company issued the Notes to several related parties that own more than 10% of the Company's capital stock (see Note 8). Upon completion of the IPO, those Notes were converted in to shares of common stock.

Note 15. Income Taxes

Since inception, the Company has generated losses from operations. The Company did not record a benefit from the income taxes for those losses during the years ended December 31, 2015, 2014 and 2013, respectively, due to its uncertainty of realizing a benefit from those losses.

The components of the income tax expense are as follows (in thousands):

	Year Ended		
	2015	2014	2013
Current income tax expense:			
State	$ —	$ —	$ —
Deferred income tax benefit:			
State	—	—	—
Total income tax expense	$ —	$ —	$ —

Income tax expense in 2015, 2014 and 2013 differed from the amount expected by applying the statutory federal tax rate to the loss before taxes as summarized below:

	Year Ended		
	2015	2014	2013
Federal tax benefit at statutory rate	34%	34%	34%
Change in valuation allowance	(41%)	(36%)	(41%)
State income taxes, net of federal benefits	6%	4%	6%
Research and development credits	1%	1%	3%
Non-deductible expenses and other	—	(3%)	(2%)
Total	—	—	—

Significant components of the Company's net deferred tax assets as of December 31, 2015, 2014 and 2013 consist of the following (in thousands):

	Year Ended		
	2015	2014	2013
Deferred tax assets			
Net operating loss carryforwards	$ 26,916	$ 17,439	$ 13,211
Accruals and reserves	325	910	96
Stock based compensation	188	59	80
Research and development credit carryforwards	1,416	1,016	873
Property and equipment	1	3	5
	28,846	19,427	14,265
Less: Valuation allowance	(28,783)	(18,243)	(14,265)
Deferred tax assets, net of valuation allowance	63	1,184	—
Convertible promissory notes discount	0	(1,168)	—
Property and equipment	(63)	(16)	—
Net deferred tax assets (liabilities)	$ 0	$ 0	$ 0

The Company has established a full valuation allowance against its deferred tax assets due to the uncertainty surrounding realization of these assets.

Realization of deferred tax assets is dependent on future earnings, if any, the timing and amount of which are uncertain. Accordingly, the deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $10,540,000, $3,978,000, and $2,345,000 for the years ended December 31, 2015, 2014 and 2013, respectively.

The Company's deferred tax assets do not include the excess tax benefit related to stock-based compensation that are a component of its federal and state net operating loss carryforwards in the amount of $0.9 million as of December 31, 2015. The excess tax benefit reflected in the Company's net operating loss carryforwards will be accounted for as a credit to additional paid-in capital within stockholders' equity, if and when realized. In determining if and when excess tax benefits have been realized, the Company has elected to utilize the with-and-without approach with respect to such excess tax benefits. The Company has also elected to ignore the indirect tax effects of stock-based compensation deductions for financial and accounting reporting purposes, and specifically to recognize the full effect of the research tax credit in income from operations.

At December 31, 2015, the Company had net operating loss ("NOL") carryforwards for federal income tax purposes of approximately $68,494,000 that expire beginning in 2024 if not utilized, and federal research and development tax credit carryforwards of approximately $904,000 that expire beginning in 2026 if not utilized. In addition, the Company had NOL carryforwards for state income tax purposes of approximately $67,995,000 that expire beginning in 2026 if not utilized, and state research and development tax credit carryforwards of approximately $800,000, which do not expire.

Utilization of the NOL and tax credit carryforwards may be subject to substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code and similar state provisions. Such an annual limitation could result in the expiration of the NOL and tax credit carryforwards before their utilization. In general, if the Company experiences a greater than 50 percentage point aggregate change (by value) in the equity ownership of certain stockholders over a rolling three-year period (a Section 382 ownership change), utilization of its pre-change NOL carryforwards are subject to an annual limitation under Section 382 of the Internal Revenue Code (California has similar laws). Such limitations may result in expiration of a portion of the NOL carryforwards before utilization. The Company has determined that an ownership change occurred in December 2005, which resulted in a permanent loss of $287,000 of the federal net operating loss carryforwards. The ability of the Company to use its remaining NOL carryforwards may be further limited if the Company experiences a Section 382 ownership change in connection with this offering or as a result of future changes in its stock ownership.

At December 31, 2015, 2014 and 2013, the Company's reserve for unrecognized tax benefits is approximately $720,000, $521,000 and $454,000, respectively. Due to the full valuation allowance at December 31, 2015, current adjustments to the unrecognized tax benefit will have no impact on the Company's effective income tax rate; any adjustments made after the valuation allowance is released will have an impact on the tax rate. The Company does not anticipate any significant change in its uncertain tax positions within 12 months of this reporting date. The Company includes penalties and interest expense related to income taxes as a component of other expense and interest expense, respectively, as necessary.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	Year Ended		
	2015	2014	2013
Balance at beginning of year	$ 521	$ 454	$ 363
Gross increases related to current year tax positions	201	102	69
Gross increases related to prior year tax positions	—	—	22
Reductions of prior year tax positions for:			
Changes in estimate	(2)	(35)	—
Balance at end of year	$ 720	$ 521	$ 454

The Company files U.S. federal and California state income tax returns with varying statutes of limitations, and currently does not have any tax audits or other proceedings pending. All tax returns will remain open for examination by the federal and state authorities for three and four years from the date of utilization of any net operating loss or credits.

Note 16. Net Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted-average number of common shares outstanding as of January 1, 2014 or the issuance date, if later, less shares subject to repurchase, and excludes any dilutive effects of share-based awards and warrants. Diluted net loss per common share is computed giving effect to all potential dilutive common shares, including common stock issuable upon exercise of stock options, and unvested restricted common stock and stock units. As the Company had net losses for the years ended December 31, 2015, 2014 and 2013, all potential common shares were determined to be anti-dilutive.

The following table sets forth the computation of net loss per common share (in thousands, except per share amounts):

	Year Ended		
	2015	2014	2013
Net loss attributable to common stockholders, basic	$ (24,846)	$ (13,359)	$ (5,678)
Adjustments to net loss for dilutive securities	—	—	—
Net loss attributable to common stockholders, diluted	$ (24,846)	$ (13,359)	$ (5,678)
Net loss per share attributable to common stockholders, Basic and diluted	$ (1.30)	$ (21.81)	$ (13.42)
Weighted-average shares used in computing net loss per share attributable to common stockholders:			
Basic and diluted	19,082,604	612,525	423,059

Potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows:

	Year Ended		
	2015	2014	2013
Stock options	1,727,505	1,328,873	1,650,122
Convertible preferred stock	—	8,268,531	8,268,531
Convertible preferred stock warrants	—	124,729	95,626
Common stock warrant	—	1,203	1,203
Convertible promissory notes	—	1,052,799	—

Note 17. Selected Quarterly Financial Data (Unaudited)

Selected quarterly financial results from operations for the years ended December 31, 2015 and 2014 are as follows (in thousands, except per share amounts):

	2015 Quarter End			
	March 31	June 30	September 30	December 31
License revenue	$ 7	$ 7	$ 7	$ 7
Total operating expenses	4,908	5,674	4,906	5,576
Net loss and comprehensive loss	(5,184)	(9,012)	(4,991)	(5,659)
Net loss per share to common stockholders, basic and diluted	(7.38)	(0.40) [1]	(0.19)	(0.21)

	2014 Quarter End			
	March 31	June 30	September 30	December 31
License revenue	$ 6	$ 5	$ 10	$ 8
Total operating expenses	1,862	2,441	3,578	3,825
Net loss and comprehensive loss	(2,015)	(2,635)	(3,995)	(4,714)
Net loss per share to common stockholders, basic and diluted	(4.39)	(4.26)	(5.89)	(6.82)

(1) Revised from a net loss of $0.37 per share as previously reported

Note 18. Subsequent Events

In March 2016, the Company engaged a financial and strategic advisor, Wedbush PacGrow, to advise the Company on strategic alternatives. Wedbush PacGrow will provide a range of advisory services aimed to enhance shareholder value. The alternatives to be considered will include the potential for an acquisition, merger, strategic partnership or other strategic transactions.

In March 2016, the Company determined that it would not occupy the Newark Lease facility. As a result, the Company may record an impairment relating to assets consisting primarily of leasehold improvements for the Newark Lease of approximately $1.2 million.

In March 2016, the Company received a deficiency letter from the Listing Qualifications Department (the "Staff") of The NASDAQ Stock Market notifying the Company that, for the last 30 consecutive business days, the bid price for the Company's common stock had closed below the minimum $1.00 per share requirement for continued inclusion on The NASDAQ Global Market pursuant to NASDAQ Listing Rule 5450(a)(1) (the "Rule"). In accordance with NASDAQ Listing Rule 5810(c)(3)(A), the Company has been provided an initial period of 180 calendar days, or until September 12, 2016, to regain compliance with the Rule. If, at any time before September 12, 2016, the bid price for the Company's common stock closes at $1.00 or more for a minimum of 10 consecutive business days as required under Listing Rule 5810(c)(3)(A), the Staff will provide written notification to the Company that it complies with the Rule.

If the Company does not regain compliance with the Rule by September 12, 2016, the Company may be eligible for an additional 180 calendar day compliance period. To qualify, the Company will be required to meet the continued listing requirement for market value of publicly held shares and all other initial listing standards, with the exception of the bid price requirement, and will need to provide written notice to the Staff of its intention to cure the deficiency during the second compliance period by effecting a reverse stock split if necessary.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

As required by Rule 13a-15(b) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), our management, under the supervision and with the participation of our principal executive and principal financial officers, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures as of December 31, 2015. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2015, our principal executive and principal financial officers have concluded that, as of December 31, 2015, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of the Company's independent registered public accounting firm due to a transition period established by the rules of the Securities and Exchange Commission for newly public companies.

Changes in Internal Controls over Financial Reporting

There has been no change in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) during the quarter ended December 31, 2015, that has materially affected, or is reasonably likely to materially affect our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information called for by this item will be set forth in our Proxy Statement for the Annual Meeting of Stockholders to be filed with the SEC within 120 days of the fiscal year ended December 31, 2015 (the "Proxy Statement") and is incorporated herein by reference.

We have adopted a code of business conduct and ethics that applies to all of our officers, including those officers responsible for financial reporting, directors and employees. We have posted a copy of our code of business conduct and ethics, and intend to post amendments to this code, or any waivers of its requirements, on our website at www.carbylan.com, as permitted under SEC rules and regulations. The reference to our web address does not constitute incorporation by reference of the information contained on or available through this site.

Item 11. Executive Compensation.

The information called for by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information, if any, required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item will be set forth in our Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this report:

(1) Financial statements

See Index to Financial Statements at Item 8 herein

(2) Financial statement schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto

(3) Exhibits

See the Exhibit Index immediately following the signature page of this Annual Report on Form 10-K.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

Carbylan Therapeutics, Inc.

Date: March 30, 2016

By: /s/ David M. Renzi
David M. Renzi
President, Chief Executive Officer and Director

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints David M. Renzi his or her true and lawful attorney-in-fact and agent, with full power of substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this annual report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

IN WITNESS WHEREOF, each of the undersigned has executed this Power of Attorney as of the date indicated opposite his/her name.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ David M. Renzi **David M. Renzi**	President, Chief Executive Officer and Director (Principal Executive Officer)	March 30, 2016
/s/ John McKune **John McKune**	Principal Financial and Accounting Officer	March 30, 2016
/s/ Steven Basta **Steven Basta**	Director	March 30, 2016
/s/ Albert Cha **Albert Cha, M.D., Ph.D.**	Director	March 30, 2016
/s/ David Clapper **David Clapper**	Director	March 30, 2016
/s/ Keith Katkin **Keith Katkin**	Director	March 30, 2016
/s/ Guy Nohra **Guy Nohra**	Director	March 30, 2016
/s/ David Saul **David Saul**	Director	March 30, 2016
/s/ Edward Unkart **Edward Unkart**	Director	March 30, 2016
/s/ Reza Zadno **Reza Zadno, Ph.D.**	Director	March 30, 2016

Exhibit Index

Exhibit Number	Exhibit Description	Incorporated by Reference Form	Date	Number	Filed Herewith
3.1	Amended and Restated Certificate of Incorporation	8-K	04/16/2015	3.1	
3.2	Amended and Restated Bylaws	8-K	04/16/2015	3.2	
4.1	Reference is made to exhibits 3.1 and 3.2				
4.2	Form of Common Stock Certificate	S-1/A	01/23/2015	4.2	
4.3	Warrant to purchase shares of Series A Preferred Stock issued to Silicon Valley Bank, dated December 13, 2006	S-1	12/29/2014	4.4	
4.4.1	Warrant to purchase shares of Series B Preferred Stock issued to Silicon Valley Bank, dated October 26, 2011	S-1	12/29/2014	4.5.1	
4.4.2	First Amendment to October 26, 2011 Warrant to purchase shares of Series B Preferred Stock issued to Silicon Valley Bank, dated July 27, 2012	S-1	12/29/2014	4.5.2	
4.4.3	Second Amendment to October 26, 2011 Warrant to purchase shares of Series B Preferred Stock issued to Silicon Valley Bank, dated February 12, 2013	S-1	12/29/2014	4.5.3	
4.5	Warrant to purchase shares of Series B Preferred Stock issued to Silicon Valley Bank, dated February 15, 2013	S-1	12/29/2014	4.6	
4.6	Warrant to purchase shares of Series B Preferred Stock issued to Silicon Valley Bank, dated September 25, 2014	S-1	12/29/2014	4.7	
10.1#	Amended and Restated 2004 Stock Option Plan and forms of agreements	S-1	12/29/2014	10.1	
10.2#	2014 Stock Option Plan and forms of agreements	S-1	12/29/2014	10.2	
10.3#	2015 Equity Incentive Plan and forms of agreements	S-1/A	01/23/2015	10.3	
10.4†	Technology License Agreement, dated November 15, 2012, by and between the Registrant and Shanghai Jingfeng Pharmaceutical Co., Ltd	S-1	12/29/2015	10.4	
10.5.1	Loan and Security Agreement, dated October 26, 2011, by and between the Registrant and Silicon Valley Bank	S-1	12/29/2014	10.5.1	
10.5.2	First Amendment to Loan and Security Agreement, dated July 27, 2012, by and between the Registrant and Silicon Valley Bank	S-1	12/29/2014	10.5.2	
10.5.3	Second Amendment to Loan and Security Agreement, dated February 15, 2013, by and between the Registrant and Silicon Valley Bank	S-1	12/29/2014	10.5.3	
10.5.4	Third Amendment to Loan and Security Agreement, dated December 10, 2013, by and between the Registrant and Silicon Valley Bank	S-1	12/29/2014	10.5.4	

Exhibit Number	Exhibit Description	Incorporated by Reference Form	Date	Number	Filed Herewith
10.5.5	Fourth Amendment to Loan and Security Agreement, dated September 25, 2014, by and between the Registrant and Silicon Valley Bank	S-1	12/29/2015	10.5.5	
10.6	Commercial Lease, dated January 26, 2012, by and between the Registrant and the Board of Trustees of the Leland Stanford University	S-1	12/29/2015	10.6	
10.7#	Executive Employment Agreement, dated May 30, 2013, by and between the Registrant and David Renzi	S-1	12/29/2015	10.7	
10.8#	Employment Offer Letter, dated June 26, 2014, by and between the Registrant and T. Michael White.	S-1	12/29/2015	10.8	
10.9#	Amended and Restated Employment Agreement Letter, dated July 21, 2014, by and between the Registrant and David Gravett	S-1	12/29/2015	10.9	
10.10#	Amended and Restated Employment Agreement Letter, dated July 21, 2014, by and between the Registrant and Marcee M. Maroney	S-1	12/29/2015	10.10	
10.11#	Employment Offer Letter, dated April 18, 2014, by and between the Registrant and Hayley Lewis	S-1	10/03/2014	10.12	
10.12	Form of Indemnification Agreement entered into by and between the Registrant and each of its directors and executive officers	S-1	10/03/2014	10.14	
10.13	Convertible Note Purchase Agreements, dated as of September 29, 2014 and February 19, 2015, respectively, by and between the Registrant and the purchasers named therein and forms of Convertible Promissory Note	S-1/A	04/06/2015	10.15	
10.14#	Non-Employee Director Compensation Policy	S-1/A	01/23/2015	10.16	
10.15#	Annual Incentive Plan	S-1/A	04/06/2015	10.17	
10.16	Amended and Restated Registration Rights Agreement, dated December 21, 2012, by and among the Registrant and certain of its stockholders	S-1/A	12/29/2014	4.3	
10.17	Facility Lease, dated as of July 13, 2015, by and between BMR-Pacific Research Center LP and the Registrant	8-K	07/14/2015	10.1	
23.1	Consent of Independent Registered Public Accounting Firm				X
24.1	Power of Attorney (included on signature page to this Annual Report on Form 10-K)				X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				X

Exhibit Number	Exhibit Description	Incorporated by Reference Form	Date	Number	Filed Herewith
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				X
32.1**	Certification of Principal Executive Officer and Principal Accounting Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				X
101.INS	XBRL Instance				X
101.SCH	XBRL Taxonomy Extension Schema				X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase				X
101.LAB	XBRL Taxonomy Extension Label Linkbase				X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase				X

† Confidential treatment has been granted for certain information contained in this exhibit. Such information has been omitted and filed separately with the Securities and Exchange Commission.

# Indicates management contract or compensatory plan.

** The certification attached as Exhibit 32.1 that accompanies this Form 10-K is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Carbylan Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-203721) of Carbylan Therapeutics, Inc. of our report dated March 30, 2016 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
San Jose, California
March 30, 2016

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, David M. Renzi, certify that:

1. I have reviewed this Annual Report on Form 10-K of Carbylan Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 30, 2016

By: /s/ David M. Renzi
David M. Renzi
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, John McKune, certify that:

1. I have reviewed this Annual Report on Form 10-K of Carbylan Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 30, 2016

By: /s/ John McKune
John McKune
Principal Accounting Officer

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Carbylan Therapeutics, Inc. (the "Company") on Form 10-K for the period ending December 31, 2015 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 30, 2016

By: /s/ David M. Renzi
David M. Renzi
President and Chief Executive Officer

Date: March 30, 2016:

By: /s/ John McKune
John McKune
Principal Accounting Officer