

Aldeyra Therapeutics, Inc.  
Form POS AM  
May 14, 2015  
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As filed with the Securities and Exchange Commission on May 14, 2015

Registration No. 333-203077

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

**Post-Effective**  
**Amendment No. 1**  
**to**  
**FORM S-1**  
**REGISTRATION STATEMENT**  
***UNDER***  
***THE SECURITIES ACT OF 1933***

**ALDEYRA THERAPEUTICS, INC.**

**(Exact name of registrant as specified in its charter)**

<b>Delaware</b> (State or other jurisdiction of incorporation or organization)	<b>2834</b> (Primary Standard Industrial Classification Code Number) <b>131 Hartwell Avenue, Suite 320</b>	<b>20-1968197</b> (I.R.S. Employer Identification Number)
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**Lexington, MA 02421**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Todd C. Brady, M.D., Ph.D.**

**President and Chief Executive Officer**

**Aldeyra Therapeutics, Inc.**

**131 Hartwell Avenue, Suite 320**

**Lexington, MA 02421**

**(781) 761-4904**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

*Copies to:*

**Jay K. Hachigian**

**Keith J. Scherer**

**Gunderson Dettmer Stough Villeneuve**

**Franklin & Hachigian, LLP**

**One Marina Park Drive, Suite 900**

**Boston, MA 02210**

**(617) 648-9100**

**Approximate date of commencement of proposed sale to public:** As soon as practicable after this Registration Statement is declared effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

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 definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act.

Large accelerated filer

Accelerated filer

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

Smaller reporting company

**The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.**

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**EXPLANATORY NOTE**

On March 27, 2015, Aldeyra Therapeutics, Inc. ( Aldeyra , the Company , we ) filed a registration statement with the Securities and Exchange Commission, or the SEC, on Form S-1 (File no. 333-203077). The registration statement was declared effective by the SEC on April 7, 2015 to initially register for resale by the selling stockholders identified in the prospectus of up to 1,113,080 shares of our common stock that we sold to the selling stockholders and 1,113,080 shares of common stock that are issuable upon the exercise of outstanding warrants to purchase our common stock issued to the selling stockholders in connection with a private placement completed on January 14, 2015.

This Post-Effective Amendment No. 1 to Form S-1 is being filed to (i) incorporate by reference the Aldeyra s Quarterly Report on Form 10-Q for the quarter ended March 31, 2015 and (ii) update certain other information in the prospectus.

No additional securities are being registered under this Post-Effective Amendment. All applicable filing fees were paid at the time of the original filing of the Registration Statement on March 27, 2015.

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**The information in this prospectus is not complete and may be changed. The selling stockholders named in this prospectus may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and the selling stockholders named in this prospectus are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.**

**SUBJECT TO COMPLETION, DATED MAY 14, 2015**

**PROSPECTUS**

**Aldeyra Therapeutics, Inc.**

**2,226,160 Shares of Common Stock**

This prospectus relates to the resale by the selling stockholders identified in this prospectus of up to 1,113,080 shares of our common stock that we sold to the selling stockholders and 1,113,080 shares of common stock that are issuable upon the exercise of outstanding warrants to purchase our common stock issued to the selling stockholders in connection with a private placement completed on January 14, 2015. We will not receive any proceeds from the sale of these shares by the selling stockholders.

We are not selling any shares of common stock and will not receive any proceeds from the sale of the shares under this prospectus. Upon the exercise of the warrants for 1,113,080 shares of our common stock by payment of cash, however, we will receive the exercise price of the warrants, which is \$9.50 per share.

We have agreed to bear all of the expenses incurred in connection with the registration of these shares. The selling stockholders will pay or assume brokerage commissions and similar charges, if any, incurred for the sale of shares of our common stock.

The selling stockholders identified in this prospectus, or their pledgees, donees, transferees or other successors-in-interest, may offer the shares from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. For additional information on the methods of sale that may be used by the selling stockholders, see the section entitled *Plan of Distribution* on page 30. For a list of the selling stockholders, see the section entitled *Selling Stockholders* on page 28.

We may amend or supplement this prospectus from time to time by filing amendments or supplements as required. You should read the entire prospectus and any amendments or supplements carefully before you make your investment decision.

Our common stock is traded on The NASDAQ Capital Market under the symbol *ALDX*. On May 11, 2015, the closing sale price of our common stock on The NASDAQ Capital Market was \$7.50 per share. You are urged to obtain current market quotations for the common stock.

**Investing in our common stock involves risks. See Risk Factors beginning on page 5.**

We are an emerging growth company under applicable Securities and Exchange Commission rules and are eligible for reduced public company disclosure requirements.

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

**The date of this prospectus is \_\_\_\_\_, 2015.**

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We are responsible for the information contained in this prospectus. We have not authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. If anyone provides you with different or inconsistent information, you should not rely on it. The selling stockholders are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front of this prospectus.

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**SUMMARY**

*This summary highlights information contained or incorporated by reference elsewhere in this prospectus. You should read the following summary together with the more detailed information appearing or incorporated by reference in this prospectus, including our consolidated financial statements and related notes, and in Risk Factors beginning on page 5, before deciding whether to purchase shares of our common stock. Unless the context otherwise requires, we use the terms Aldeyra, the company, we, us and our in this prospectus to refer to Aldeyra Therapeutics, Inc.*

**Company Overview**

Aldeyra was formed as a Delaware corporation in 2004, and from inception until December 20, 2012, we operated as Neuron Systems, Inc. and from December 2012 until March 2014 we operated as Aldexa Therapeutics, Inc. Since our incorporation, we have devoted substantially all of our resources to the preclinical and clinical development of our product candidates. Our ability to generate revenues largely depends upon our ability, alone or with others, to complete the development of our product candidates to obtain the regulatory approvals for and to manufacture, market and sell our product candidates. The results of our operations will vary significantly from year-to-year and quarter-to-quarter and depend on a number of factors, including risks related to our business and industry, risks relating to intellectual property and other legal matters, risks related to our common stock, and other risks that are detailed in the section of this prospectus entitled Risk Factors.

We are a biotechnology company focused primarily on the development of new products for immune-mediated, inflammatory, orphan and other diseases that are thought to be caused in part by naturally occurring toxic chemical compounds known as free aldehydes. We have developed a series of product candidates that are designed specifically to trap and allow for the degradation of free aldehydes. In 2015, we began clinical testing of our most advanced product candidate, NS2, in diseases with significant unmet medical need where we believe aldehyde trapping may improve symptoms and slow or prevent disease progression. Since the diseases we plan to study are rare, we intend to request orphan drug designation from the United States Food and Drug Administration (FDA).

In March of 2015, we initiated a clinical trial of NS2 applied topically to skin for the treatment of the dermatologic symptoms of a disease called Sjögren-Larsson Syndrome (SLS), a rare condition that we believe afflicts approximately 1,000 patients in the United States. The disease is caused by mutations in an enzyme, fatty aldehyde dehydrogenase, that metabolizes free fatty (generally 16-18 carbon) aldehydes, resulting in high levels of toxic aldehydes that are the suspected cause of severe skin disease, delay in mental development, spasticity, and, in some patients, retinal dysfunction. In preclinical studies, NS2 traps fatty aldehydes in cells lacking the enzyme that is mutated in SLS. We are not aware of any therapy for SLS that has been approved by the FDA.

Preclinical testing with NS2 suggests that aldehyde trapping has the potential to improve symptoms related to and slow or prevent the progression of a variety of other diseases by reducing inflammation, promoting healing, diminishing the potential for scarring, and protecting a key lipid (fat) that is involved in preventing water loss from tissue.

We believe that inflammatory diseases of the eye may also be mediated in part by free aldehyde toxicity. We have developed an eye drop formulation of NS2 that has completed Phase I clinical testing for safety and tolerability in healthy volunteers. In March of 2015, we initiated a Phase II clinical trial of the NS2 eye drop formulation in a serious and, we believe, poorly treated ocular disease called noninfectious anterior uveitis. In noninfectious anterior uveitis, aldehydes may mediate, at least in part, inflammation, pain, fibrotic changes, and lipid destruction leading to dryness and surface irritation. Patients with noninfectious anterior uveitis generally experience severe pain, sensitivity to light,

and vision loss. We believe that novel medications are needed to improve symptoms and deter disease progression, especially in order to reduce dependence on topical corticosteroids, which can lead to cataracts (ocular lens opacities resulting in vision impairment) and glaucoma (increased intraocular pressure that can, in some cases, lead to blindness).

We intend to initiate other clinical trials with NS2 in SLS and ocular inflammation, as well as in other diseases thought to be mediated in part by free aldehydes, and we may initiate development of injectable formulations of NS2 for diseases for which we believe systemic aldehyde trapping may provide therapeutic benefit. Specifically, we plan to finance additional trials of topically applied NS2 in SLS and uveitis or other forms of ocular inflammation; the formulation of NS2 for subcutaneous and intravenous administration; the completion of Phase I safety and tolerability testing of injectable formulations of NS2 in preparation for potential Phase II clinical trials for systemic treatment of SLS, autoimmune diseases that lead to severe inflammatory crises, and another genetic disease (succinic semi-aldehyde dehydrogenase deficiency) where an aldehyde dehydrogenase is dysfunctional and high aldehyde levels are thought to mediate neurological disease; the synthesis and formulation of novel aldehyde traps other than NS2; and the expansion our clinical development and regulatory infrastructure.

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**Risks Related to Our Business**

An investment in our common stock involves a high degree of risk. Our business is subject to numerous risks and uncertainties, including those highlighted in the section titled "Risk Factors". These risks represent challenges to the successful implementation of our strategy and to the growth and future profitability of our business. Some of these risks include the following:

We have incurred significant operating losses since our inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability.

Our business is dependent in large part on the success of a single product candidate, NS2. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, NS2.

Because we have limited experience developing clinical-stage compounds, there is a limited amount of information about us upon which you can evaluate our product candidates and business prospects.

If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully develop and commercialize NS2 and our other product candidates.

The results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials, including NS2, may not have favorable results in later clinical trials, if any, or receive regulatory approval.

Because NS2 and our other product candidates are, to our knowledge, new chemical entities, it is difficult to predict the time and cost of development and our ability to successfully complete clinical development of these product candidates and obtain the necessary regulatory approvals for commercialization.

Aldehyde trapping is an unproven approach, the safety and efficacy of which has not been demonstrated in humans.

NS2 and our other product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays, or prevent the receipt of the required approvals to commercialize our product candidates.

Any termination or suspension of, or delays in the commencement or completion of, our planned clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Any product candidate we or any of our future development partners advance into clinical trials may cause unacceptable adverse events or have other properties that may delay or prevent its regulatory approval or commercialization or limit its commercial potential.

If our competitors develop treatments for the target indications of our product candidates that are approved more quickly than ours, marketed more successfully or demonstrated to be safer or more effective than our product candidates, our commercial opportunity will be reduced or eliminated.

We are currently highly dependent on the services of our three senior employees and certain key consultants.

Even if we receive regulatory approval for NS2 or any other product candidate, we still may not be able to successfully commercialize it and the revenue that we generate from its sales, if any, could be limited.

For further discussion of these and other risks you should consider before making an investment in our common stock, see the section titled "Risk Factors" beginning on page 5 of this prospectus.

### **Recent Developments**

On May 13, 2015, we issued and sold a total of 2,700,000 shares of our common stock at a public offering price of \$7.50 per share in an underwritten offering. Net proceeds from the offering was approximately \$18.8 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

### **Our Corporate Information**

Our principal executive offices are located at 131 Hartwell Avenue, Suite 320, Lexington, Massachusetts 02421, and our telephone number is (781) 761-4904. On March 17, 2014, we changed our name from Aldexa Therapeutics, Inc. to Aldeyra Therapeutics, Inc. Our website address is [www.aldeyra.com](http://www.aldeyra.com). Our website and the information contained in, or accessible through, our website will not be deemed to be incorporated by reference into this prospectus and does not constitute part of this prospectus. You should not rely on any such information in making your decision whether to purchase our common stock.

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### **Implications of Being an Emerging Growth Company**

As a company with less than \$1.0 billion in gross revenue during our last fiscal year, we qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of specified reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

being permitted to present only two years of audited financial statements and only two years of related Management's Discussion and Analysis of Financial Condition and Results of Operations in this prospectus;

exemption from complying with the auditor attestation requirements under Section 404 of the Sarbanes-Oxley Act, regarding the effectiveness of our internal controls over financial reporting;

reduced disclosure obligations regarding the company's executive compensation arrangements in our periodic reports, proxy statements and registration statements;

exemptions from the requirements of holding a non-binding advisory vote on executive compensation; and

stockholder approval of any golden parachute arrangements not previously approved.

We may take advantage of these provisions until December 31, 2019, or until such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than \$1.0 billion in annual gross revenue, the date at which we become a large accelerated filer, or issue more than \$1.0 billion of non-convertible debt over a three-year period. We may choose to take advantage of some but not all of these reduced burdens.

We have elected to take advantage of certain of the reduced disclosure obligations and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our stockholders may be different than you might receive from other public reporting companies in which you hold equity interests.

We have irrevocably elected not to avail ourselves of the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the JOBS Act and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

### **Private Placement of Common Stock and Warrants**

On January 14, 2015, we completed a private placement of 1,113,080 shares of common stock, \$0.001 par value per share, and warrants to purchase 1,113,080 shares of our common stock at an exercise price per share of \$9.50, with a term of three years from the date of issuance resulting in gross proceeds of approximately \$7.8 million and net proceeds of approximately \$7.1 million. We are using the proceeds from the private placement for working capital and

general corporate purposes. As part of this private placement, we entered into a registration rights agreement with the purchasers pursuant to which we agreed to file a registration statement to register for resale the shares of common stock sold in the private placement, including the shares underlying the warrants sold in the private placement, within 75 days following the closing of the private placement. We are required to use our commercially reasonable best efforts to cause the registration statement to be declared effective under the Securities Act of 1933, as amended, as soon as practicable, but in no event later than 120 days after the closing date (or 150 days in the event of a full review of the shelf registration statement by the Securities and Exchange Commission). We agreed to keep the registration statement effective until all registrable securities may be sold pursuant to Rule 144 under the Securities Act of 1933, without the need for current public information or other restriction. The issuance of the shares of common stock and the warrants in connection with the private placement was exempt from registration under the Securities Act of 1933, as amended, pursuant to the exemption for transactions by an issuer not involving a public offering under Section 4(a)(2) of the Securities Act of 1933, as amended, and Regulation D promulgated thereunder.

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**THE OFFERING**

Common stock offered by the selling stockholders	2,226,160 shares, including 1,113,080 shares of our common stock issuable upon exercise of warrants at an exercise price of \$9.50 per share
Common stock outstanding	6,890,021 shares
Use of proceeds	We will not receive any proceeds from the sale of shares in this offering.
Risk Factors	You should read the Risk Factors section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.

NASDAQ Capital Market symbol ALDX

The number of shares of our common stock outstanding is based on 6,890,021 shares of our common stock outstanding as of March 31, 2015, including the 1,113,080 shares of our common stock issued to the selling stockholders in January 2015 in a private placement and excludes the following:

874,032 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2015, at a weighted average exercise price of approximately \$3.10 per share;

583,427 shares of common stock reserved for future grants under our 2014 Equity Incentive Plan as of March 31, 2015 (subject to automatic annual adjustment in accordance with the terms of the plan);

1,384,608 shares of our common stock issuable upon exercise of warrants at a weighted average exercise price of approximately \$9.52 per share; and

2,700,000 shares of our common stock sold pursuant to our registration statement on Form S-1 (File no. 333-203536) on May 13, 2015 and an additional 405,000 shares of our common stock which may be purchased by the underwriters to cover over-allotments under such registration statement.

Unless otherwise indicated, all information in this prospectus assumes no exercise of the outstanding options or warrants described above.

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**RISK FACTORS**

*Investing in our common stock involves a high degree of risk. You should consider carefully the risks and uncertainties described below, together with all of the other information contained or incorporated by reference in this prospectus, including our consolidated financial statements and related notes, before deciding whether to purchase shares of our common stock. If any of the following risks actually occurs, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that event, the price of our common stock could decline and you could lose part or all of your investment.*

**Risks Related to our Business**

***We have incurred significant operating losses since inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability.***

We have incurred significant operating losses since we were founded in 2004 and expect to incur significant losses for the next several years as we continue our clinical trial and development programs for NS2 and our other product candidates. Net loss attributable to common stockholders for the three months ended March 31, 2015 and 2014 was approximately \$2.1 million and \$13,237, respectively. As of March 31, 2015, we had total stockholders' equity of \$13.8 million. Losses have resulted principally from costs incurred in our clinical trials, research and development programs and from our general and administrative expenses. In the future, we intend to continue to conduct research and development, clinical testing, regulatory compliance activities and, if NS2 or any of our other product candidates is approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in our incurring further significant losses for the next several years.

We currently generate no revenue from sales, and we may never be able to commercialize NS2 or our other product candidates. We do not currently have the required approvals to market any of our product candidates and we may never receive them. We may not be profitable even if we or any of our future development partners succeed in commercializing any of our product candidates. Because of the numerous risks and uncertainties associated with developing and commercializing our product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

***Our business is dependent in large part on the success of a single product candidate, NS2. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, NS2.***

Our product candidates are in the early stage of development and will require additional preclinical studies, substantial clinical development and testing, and regulatory approval prior to commercialization. We have not yet completed development of any product. We have only one product candidate that has been the focus of significant development: NS2, a novel small molecule chemical entity that is believed to trap and allow for the degradation of free aldehydes, toxic chemical species suspected to cause and exacerbate numerous diseases in humans and animals. We are largely dependent on successful continued development and ultimate regulatory approval of this product candidate for our future business success. We have invested, and will continue to invest, a significant portion of our time and financial resources in the development of NS2. We will need to raise sufficient funds for, and successfully enroll and complete, our current and planned clinical trials of NS2. The future regulatory and commercial success of this product candidate is subject to a number of risks, including the following:

we may not have sufficient financial and other resources to complete the necessary clinical trials for NS2;

we may not be able to timely finalize the design or formulation of any product candidate or demonstrate that a formulation of our product candidate will be stable for commercially reasonable time periods;

we may not be able to provide evidence of safety and efficacy for NS2;

the results of later phases of our clinical trials may not confirm the results of our Phase I trial of NS2 as an eye drop in healthy volunteers, particularly because the safety of NS2 has not been confirmed in a diseased population nor has NS2 been tested in humans in any other dosage form other than an eye drop;

there may be variability in patients, adjustments to clinical trial procedures and inclusion of additional clinical trial sites;

the results of our clinical trials may not meet the level of statistical or clinical significance for marketing approval required by the FDA, or comparable foreign regulatory bodies;

patients in our clinical trials may suffer other adverse effects or die for reasons that may or may not be related to NS2;

if approved for certain diseases, NS2 will compete with well-established products already approved for marketing by the FDA, including corticosteroids and other agents that have demonstrated varying levels of efficacy in some of the diseases for which we may attempt to develop NS2; and

we may not be able to obtain, maintain or enforce our patents and other intellectual property rights. Of the large number of drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a New Drug Application (NDA) to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market NS2, any such approval may be subject to limitations on the indicated uses for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we cannot assure you that NS2 will be successfully developed or commercialized. If we or any of our future development partners are unable to develop, or obtain regulatory approval for or, if approved, successfully commercialize, NS2, we may not be able to generate sufficient revenue to continue our business.

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*Because we have limited experience developing clinical-stage compounds, there is a limited amount of information about us upon which you can evaluate our product candidates and business prospects.*

We commenced our first clinical trial in 2010, and we have limited experience developing clinical-stage compounds upon which you can evaluate our business and prospects. In addition, as an early-stage clinical development company, we have limited experience in conducting clinical trials, and we have never conducted clinical trials of a size required for regulatory approvals. Further, we have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan we will need to successfully:

execute our product candidate development activities, including successfully completing our product design and formulation and our clinical trial programs;

obtain required regulatory approvals for our product candidates;

manage our spending as costs and expenses increase due to the performance and completion of clinical trials, attempting to obtain regulatory approvals, manufacturing and commercialization;

secure substantial additional funding;

develop and maintain successful strategic relationships;

build and maintain a strong intellectual property portfolio;

build and maintain appropriate clinical, sales, distribution, and marketing capabilities on our own or through third parties; and

gain broad market acceptance for our product candidates.

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

***The scientific rationale for our Sjögren-Larsson Syndrome clinical program does not necessarily predict the clinical success of NS2.***

Sjögren-Larsson Syndrome (SLS) is a rare disease afflicting an estimated 1 in 250,000 people worldwide, equivalent to approximately 1,000 patients in the United States and a larger number in Europe. SLS is caused by genetic mutations in an enzyme, Fatty Aldehyde Dehydrogenase (FALDH) that converts long-chain aldehydes into fatty acids. In addition to manifesting what is believed to be severe aldehyde toxicity, SLS patients also have elevated levels of fatty alcohols and may manifest diminished levels of fatty acids.

The dermal pathology of SLS is thought to be due to aldehyde-mediated damage of lipids (fats) that contribute to the formation of the dermal moisture barrier. As a result, SLS patients are thought to lose water from skin, leading to compensatory mechanisms that include proliferation of the superficial layers of skin that may be only partially effective in preventing water loss. Increased levels of skin proliferation in SLS patients lead to ichthyosis, a severe skin disorder characterized by plaques and scales, thickening, dryness, redness, inflammation and pruritus (itching).

NS2 traps aldehydes and has been shown to prevent fatty aldehyde-mediated modification of lipids in vitro, in human skin cells and in cells that have been genetically modified to lack FALDH. Thus, NS2 may be partially or wholly effective in preventing and treating ichthyosis or other dermal symptoms, signs, or pathologies in SLS. However, the proposed mechanism of action of NS2 in SLS has not been demonstrated in humans. Further, our assumptions about the pathogenesis of skin disease in SLS patients may not be accurate. For instance, SLS skin disease may be caused by elevated fatty alcohol levels or decreased fatty acid levels, neither of which NS2 is predicted to affect directly. In addition, the presumed mechanisms of aldehyde-mediated inflammation are distinct from the presumed aldehyde-mediated pathology in SLS, and the outcome of clinical trials of NS2 in SLS is unlikely to predict the outcome of clinical trials with NS2 in inflammatory diseases.

***The results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials, including NS2, may not have favorable results in later clinical trials, if any, or receive regulatory approval.***

Drug development has inherent risk. We or any of our future development partners will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates are safe and effective, with a favorable benefit-risk profile, for use in their target indications before we can seek regulatory approvals for their commercial sale. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of development, including after commencement of any of our clinical trials. In addition, success in early clinical trials does not mean that later clinical trials will be successful because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through initial clinical testing. Furthermore, our future trials will need to demonstrate sufficient safety and efficacy for approval by regulatory authorities in larger patient populations. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results. In addition, only a small percentage of drugs under development result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

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***Because NS2 and our other product candidates are, to our knowledge, new chemical entities, it is difficult to predict the time and cost of development and our ability to successfully complete clinical development of these product candidates and obtain the necessary regulatory approvals for commercialization.***

Our product candidates are, to our knowledge, new chemical entities, and unexpected problems related to such new technology may arise that can cause us to delay, suspend or terminate our development efforts. NS2 administered as an eye drop has completed a Phase I clinical trial in healthy volunteers. Prior to our SLS Phase II clinical trial which commenced in March 2015, NS2 had not been administered to humans by any other route. Further, NS2 has not demonstrated efficacy in humans for any disease. Because NS2 is a novel chemical entity with limited use in humans, short and long-term safety, as well as prospects for efficacy, are poorly understood and difficult to predict due to our and regulatory agencies' lack of experience with them. Regulatory approval of new product candidates such as NS2 can be more expensive and take longer than approval for other more well-known or extensively studied pharmaceutical or biopharmaceutical product candidates.

***Aldehyde trapping is an unproven approach, the safety and efficacy of which has not been demonstrated in humans.***

Aldehydes are thought to be mediators of inflammation and other pathology. However, we are aware of only a limited number of attempts to lower aldehyde levels and modulate disease in animals or humans. Thus, there is only moderate justification for the approach of lowering aldehyde levels to treat disease. Despite evidence suggestive of benefit in animal models, clinical trials may indicate that aldehyde trapping has no effect or negative effects in humans on the diseases we intend to test. Animal studies may not predict safety or efficacy in humans.

***Our dermatologic topical formulation of NS2 is unlikely to affect other clinical manifestations of SLS, which may decrease the likelihood of regulatory and commercial acceptance.***

While the primary day-to-day complaint of SLS patients and their caregivers are symptoms associated with severe skin disease, SLS patients also manifest varying degrees of delay in mental development, spasticity, seizures and retinal disease. Due to expected low systemic exposure of NS2 when administered topically to the skin, it is unlikely that NS2 will affect the non-dermatologic conditions of SLS. Lack of effect in neurologic and ocular manifestations of SLS may negatively impact regulatory discussions with the FDA and may also negatively impact reimbursement, pricing and commercial acceptance of NS2 if it is approved.

***The FDA or other regulatory agencies may prohibit us from initiating clinical trials that are necessary for demonstrating drug safety and efficacy in patients.***

NS2 and the activities associated with its development and potential commercialization, including its testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other jurisdictions.

We are not permitted to initiate clinical trials of a new drug under an IND in the United States until the FDA has no objection to the initial IND submission. To date, we have completed one Phase I clinical trial for NS2 administered as an eye drop in healthy volunteers. In 2014, we filed two IND applications to initiate a Phase II clinical trial in SLS and a Phase II trial in noninfectious anterior uveitis. We will have to submit separate INDs for each additional indication that we intend to study, which could mean additional delays in the commencement of each of the related trials and the performance of additional preclinical studies. We have not demonstrated efficacy of NS2 in any patient population.

There is no guarantee that future trials will be allowed by the FDA to proceed or generate successful results, or that regulators will agree with our assessment of the clinical trials for NS2. In addition, we expect to rely on consultants and third party contract research organizations to assist us with regulatory filings and the conduct of our clinical trials. The FDA and other regulators have substantial discretion and may refuse to accept any application or may decide that our current data is insufficient for clinical trial initiation and require additional clinical trials, or preclinical or other studies.

*NS2 and our other product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays, or prevent the receipt of the required approvals to commercialize our product candidates.*

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The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing, and distribution of our product candidates are subject to extensive regulation by the FDA in the United States and by comparable authorities in foreign markets. In the United States, we are not permitted to market our product candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive, often takes many years, and can vary substantially based upon the type, complexity, and novelty of the products involved, as well as the target indications, and patient population. Approval policies or regulations may change and the FDA has substantial discretion in the drug approval process, including the ability to delay, limit, or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed.

The FDA or comparable foreign regulatory authorities can delay, limit, or deny approval of a product candidate for many reasons, including:

such authorities may disagree with the design or implementation of our or any of our future development partners' clinical trials;

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we or any of our future development partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a product candidate is safe and effective for any indication;

such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from the United States;

the results of clinical trials may not demonstrate the safety or efficacy required by such authorities for approval;

we or any of our future development partners may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;

such authorities may disagree with our interpretation of data from preclinical studies or clinical trials;

such authorities may find deficiencies in the manufacturing processes or facilities of third-party manufacturers with which we or any of our future development partners contract for clinical and commercial supplies; or

the approval policies or regulations of such authorities may significantly change in a manner rendering our or any of our future development partners' clinical data insufficient for approval.

With respect to foreign markets, approval procedures vary among countries and, in addition to the aforementioned risks, can involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our future development partners from commercializing our product candidates.

***Any termination or suspension of, or delays in the commencement or completion of, our planned clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.***

Before we can initiate clinical trials in the United States for our product candidates, we must submit the results of preclinical testing to the FDA as part of an IND, along with other information including information about product candidate chemistry, manufacturing, and controls and our proposed clinical trial protocol. We may rely in part on preclinical, clinical, and quality data generated by contract research organization (CROs) and other third parties for obtaining the data for and preparing regulatory submissions for our product candidates. If these third parties do not make timely regulatory submissions for our product candidates, it will delay our clinical development. If those third parties do not make this data available to us, we will likely have to develop all necessary preclinical and clinical data on our own, which will lead to significant delays and increase development costs of the product candidate. In addition, the FDA may require us to conduct additional preclinical testing for any product candidate before it allows us to initiate clinical testing under any IND for future clinical trials, which may lead to additional delays and increase the

costs of our preclinical and clinical development. Delays in the commencement or completion of our planned clinical trials for NS2 or other product candidates could significantly affect our product development costs. We do not know whether future trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

the FDA failing to grant permission to proceed or placing the clinical trial on hold;

subjects failing to enroll or remain in our trial at the rate we expect;

subjects choosing an alternative treatment for the indication for which we are developing NS2 or other product candidates, or participating in competing clinical trials;

lack of adequate funding to continue the clinical trial;

subjects experiencing severe or unexpected drug-related adverse effects;

a facility manufacturing NS2, any of our other product candidates or any of their components being ordered by the FDA or other government or regulatory authorities, to temporarily or permanently shut down due to violations of current Good Manufacturing Practices, or cGMP, or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;

any changes to our manufacturing process that may be necessary or desired;

third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, Good Clinical Practice or regulatory requirements, or other third parties not performing data collection or analysis in a timely or accurate manner;

inspections of clinical trial sites by the FDA or the finding of regulatory violations by the FDA or an institutional review board, or IRB, that require us to undertake corrective action, result in suspension or termination of one or more sites or the imposition of a clinical hold on the entire trial, or that prohibit us from using some or all of the data in support of our marketing applications;

third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; or

one or more IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial.

Product development costs will increase if we have delays in testing or approval of NS2 or if we need to perform more or larger clinical trials than planned. Additionally, changes in regulatory requirements and policies may occur and we may need to amend clinical trial protocols

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to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in completion of or if we, the FDA or other regulatory authorities, the IRB, other reviewing entities, or any of our clinical trial sites suspend or terminate any of our clinical trials, the commercial prospects for a product candidate may be harmed and our ability to generate product revenues will be delayed. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. Further, if one or more clinical trials are delayed, our competitors may be able to bring products to market before we do, and the commercial viability of NS2 or other product candidates could be significantly reduced.

***Any product candidate we or any of our future development partners advance into clinical trials may cause unacceptable adverse events or have other properties that may delay or prevent its regulatory approval or commercialization or limit its commercial potential.***

Unacceptable adverse events caused by any of our product candidates that we advance into clinical trials could cause us or regulatory authorities to interrupt, delay, or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications and markets. This in turn could prevent us from completing development or commercializing the affected product candidate and generating revenue from its sale.

We have not yet completed testing of any of our product candidates in humans for the treatment of the indications for which we intend to seek approval, and we currently do not know the extent of adverse events, if any, that will be observed in patients who receive any of our product candidates. NS2, for example, has been observed to be toxic at high concentrations in *in vitro* human dermal tissue. If any of our product candidates cause unacceptable adverse events in clinical trials, we may not be able to obtain regulatory approval or commercialize such product candidate.

***Final marketing approval for NS2 or our other product candidates by the FDA or other regulatory authorities for commercial use may be delayed, limited, or denied, any of which would adversely affect our ability to generate operating revenues.***

After the completion of our clinical trials and, assuming the results of the trials are successful, the submission of an NDA, we cannot predict whether or when we will obtain regulatory approval to commercialize NS2 or our other product candidates and we cannot, therefore, predict the timing of any future revenue. We cannot commercialize NS2 or our other product candidates until the appropriate regulatory authorities have reviewed and approved the applicable applications. We cannot assure you that the regulatory agencies will complete their review processes in a timely manner or that we will obtain regulatory approval for NS2 or our other product candidates. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. If marketing approval for NS2 or our other product candidates is delayed, limited or denied, our ability to market the product candidate, and our ability to generate product sales, would be adversely affected.

***Even if we obtain marketing approval for NS2 or any other product candidate, it could be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidate, when and if any of them are approved.***

Even if United States regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly and time consuming post-approval studies, post-market surveillance or clinical trials. Following approval, if any, of NS2 or any other product candidates,

such candidate will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, recordkeeping and reporting of safety and other post-market information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements, including those relating to quality control, quality assurance and corresponding maintenance of records and documents. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requesting recall or withdrawal of the product from the market or suspension of manufacturing.

If we or the manufacturing facilities for NS2 or any other product candidate that may receive regulatory approval, if any, fail to comply with applicable regulatory requirements, a regulatory agency may:

issue warning letters or untitled letters;

seek an injunction or impose civil or criminal penalties or monetary fines;

suspend or withdraw regulatory approval;

suspend any ongoing clinical trials;

refuse to approve pending applications or supplements or applications filed by us;

suspend or impose restrictions on operations, including costly new manufacturing requirements; or

seize or detain products, refuse to permit the import or export of product, or request us to initiate a product recall.

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The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue.

The FDA has the authority to require a risk evaluation and mitigation strategy plan as part of a NDA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry.

In addition, if NS2 or any of our other product candidates is approved, our product labeling, advertising and promotion would be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The 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 sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

***Even if we receive regulatory approval for NS2 or any other product candidate, we still may not be able to successfully commercialize it and the revenue that we generate from its sales, if any, could be limited.***

Even if our product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payors, and the medical community. Coverage and reimbursement of our product candidates by third-party payors, including government payors, is also generally necessary for commercial success. The degree of market acceptance of our product candidates will depend on a number of factors, including:

demonstration of clinical efficacy and safety compared to other more-established products;

the limitation of our targeted patient population and other limitations or warnings contained in any FDA-approved labeling;

acceptance of a new formulation by health care providers and their patients;

the prevalence and severity of any adverse effects;

new procedures or methods of treatment that may be more effective in treating or may reduce the incidences of SLS or other conditions for which our products are intended to treat;

pricing and cost-effectiveness;

the effectiveness of our or any future collaborators' sales and marketing strategies;

our ability to obtain and maintain sufficient third-party coverage or reimbursement from government health care programs, including Medicare and Medicaid, private health insurers and other third-party payors;

unfavorable publicity relating to the product candidate; and

the willingness of patients to pay out-of-pocket in the absence of third-party coverage.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors or patients, we may not generate sufficient revenue from that product candidate and may not become or remain profitable. Our efforts to educate the medical community and third-party payors on the benefits of NS2 or any of our other product candidates may require significant resources and may never be successful. In addition, our ability to successfully commercialize our product candidate will depend on our ability to manufacture our products, differentiate our products from competing products and defend the intellectual property of our products.

***Reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our product candidates profitably.***

Market acceptance and sales of our product candidates will depend significantly on the availability of adequate insurance coverage and reimbursement from third-party payors for any of our product candidates and may be affected by existing and future health care reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Reimbursement by a third-party payor may depend upon a number of factors including the third-party payor's determination that use of a product candidate is:

a covered benefit under its health plan;

safe, effective, and medically necessary;

appropriate for the specific patient;

cost-effective; and

neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product candidate from a government or other third-party payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of the applicable



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product candidate to the payor. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Further, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our product candidates. If reimbursement is not available or is available only in limited levels, we may not be able to commercialize certain of our product candidates profitably, or at all, even if approved.

As a result of legislative proposals and the trend toward managed health care in the United States, third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. They may also refuse to provide coverage of approved product candidates for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for their use of newly approved drugs, which in turn will put pressure on the pricing of drugs. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations, and additional legislative proposals as well as country, regional or local healthcare budget limitations.

***If we fail to develop and commercialize other product candidates, we may be unable to grow our business.***

As part of our growth strategy, we plan to evaluate the development and commercialization of other therapies related to immune-mediated, inflammatory, orphan and other diseases. We will evaluate internal opportunities from our compound libraries, and also may choose to in-license or acquire other product candidates as well as commercial products to treat patients suffering from immune-mediated or orphan or other disorders with high unmet medical needs and limited treatment options. These other product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives.