

IDERA PHARMACEUTICALS, INC.

Form 424B5

April 13, 2012

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Filed Pursuant to Rule 424(b)(5)

Registration No. 333-169060

PROSPECTUS SUPPLEMENT

(To Prospectus dated August 26, 2010)

\$10,000,000

Common Stock

We have entered into a sales agreement with Cowen and Company, LLC, or Cowen, relating to shares of our common stock, \$0.001 par value per share, offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$10,000,000.

Our common stock is listed on The NASDAQ Global Market under the symbol IDRA. The last reported sale price of our common stock on April 11, 2012 was \$1.87 per share.

Upon our delivery of a placement notice and subject to the terms and conditions of the sales agreement, Cowen may sell our common stock by methods deemed to be an at the market offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on The NASDAQ Global Market, on any other existing trading market for our common stock or to or through a market maker. In addition, with our prior written approval, Cowen may also sell our common stock by any other method permitted by law, including in privately negotiated transactions. Cowen will act as sales agent using its commercially reasonable efforts consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of The NASDAQ Stock Market, Inc.

We will pay Cowen a commission, or allow a discount, for its services in acting as agent in the sale of common stock equal to 3.0% of the gross sales price per share of all shares sold through it as agent under the sales agreement. As of the date of this prospectus supplement, we have not offered any securities pursuant to General Instruction I.B.6 of Form S-3 during the prior 12 calendar month period that ends on, and includes, the date of this prospectus supplement.

Investing in our securities involves a high degree of risk. See Risk Factors, beginning on page S-5 of this prospectus supplement and page 2 of the accompanying prospectus, as well as the documents incorporated by reference in this prospectus supplement, for a discussion of the factors you should carefully consider before deciding to purchase our securities.

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

Cowen and Company

Prospectus Supplement dated April 12, 2012

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is the prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, provides more general information. Generally, when we refer to this prospectus supplement, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, as well as the additional information described under *Where You Can Find Additional Information* on page S-9 of this prospectus supplement. These documents contain information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document filed after the date of this prospectus supplement and incorporated by reference in this prospectus supplement and the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectuses we may provide to you in connection with this offering. We have not, and Cowen has not, authorized any other person to provide you with any information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement outside the United States. This prospectus supplement does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information about us, this offering and information appearing elsewhere in this prospectus supplement, in the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all the information you should consider before investing in our common stock pursuant to this prospectus supplement and the accompanying prospectus. Before making an investment decision, to fully understand this offering and its consequences to you, you should carefully read this entire prospectus supplement and the accompanying prospectus, including Risk Factors beginning on page S-5 of this prospectus supplement and the financial statements and related notes and the other information that we incorporated by reference herein, including our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q that we file from time to time.

Idera Pharmaceuticals, Inc.

Overview

We are a clinical stage biotechnology company engaged in the discovery and development of novel synthetic DNA- and RNA- based drug candidates. We are developing drug candidates that are designed to modulate immune responses mediated through Toll-like Receptors, or TLRs. We believe that the modulation of immune responses through TLRs provides a rationale for the development of drug candidates to treat a broad range of diseases. We are also evaluating gene silencing oligonucleotides, or GSOs, which inhibit the production of disease-associated proteins by targeting RNA. We believe that our GSO technology provides us with a platform from which drug candidates for diverse disease indications can be developed.

TLRs are specific receptors present in immune system cells. Using a chemistry-based approach, we have created synthetic DNA- and RNA-based compounds that are targeted to TLRs 3, 7, 8, and 9. A TLR agonist is a compound that stimulates an immune response through the targeted TLR. A TLR antagonist is a compound that blocks activation of an immune response through the targeted TLR. Drug candidates are compounds that we are developing and that have not been approved for any commercial use.

We are focusing our internal development efforts on TLR-targeted clinical candidates for autoimmune and inflammatory diseases and cancer, and on the advancement of our GSO technology platform. We are seeking to advance our TLR-targeted programs in infectious diseases, respiratory diseases, hematologic oncology, and the use of TLR3 agonists in vaccine adjuvant applications through collaborative alliances with pharmaceutical companies. We currently are collaborating with Merck Sharp & Dohme Corp. (formerly Merck & Co., Inc.), which is referred to herein as Merck, for the use of agonists of TLRs 7, 8, and 9 as vaccine adjuvants for cancer, infectious diseases, and Alzheimer's disease.

Autoimmune and Inflammatory Disease Program. We are developing IMO-3100, an antagonist of TLR7 and TLR9, for the treatment of psoriasis. We plan to conduct a Phase 2 clinical trial of IMO-3100 in adult patients with moderate to severe plaque psoriasis, randomized into three arms over a four-week treatment period, which we expect to initiate in the second quarter of 2012. In the trial, we plan to evaluate two dose levels of IMO-3100 and a concurrent placebo arm. In addition, we have

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selected IMO-8400, an antagonist of TLRs 7, 8, and 9, for development in the treatment of lupus. We are conducting nonclinical studies of IMO-8400 to support the submission of an Investigational New Drug Application, or IND, for IMO-8400. We expect to submit this IND to the United States Food and Drug Administration, or FDA, in the fourth quarter of 2012. We have evaluated IMO-3100 and IMO-8400 in preclinical models of several autoimmune diseases including psoriasis, lupus, rheumatoid arthritis, and multiple sclerosis. In these models, treatment with IMO-3100 or IMO-8400 was associated with improvement in a number of disease parameters.

Cancer Program. IMO-2055, an agonist of TLR9, is in clinical development for the treatment of cancer. In November 2011, we reacquired rights to IMO-2055 from Merck KGaA, Darmstadt, Germany, our former collaborator. We believe that IMO-2055 can be developed for use as an immune modifier in combination with targeted anticancer agents. Recently, we announced favorable data from a Phase 1b clinical trial of IMO-2055 in combination with erlotinib and bevacizumab in patients with advanced non-small cell lung cancer. We anticipate top-line data from a randomized Phase 2 clinical trial of IMO-2055 in combination with cetuximab in second-line patients with squamous cell carcinoma of the head and neck in the second quarter of 2012. We also expect to have top-line data from a Phase 1b clinical trial of IMO-2055 in combination with cetuximab and chemotherapy in patients with advanced colorectal cancer in the second quarter of 2012.

Gene Silencing Oligonucleotide Technology Platform. Our GSOs are single-stranded RNA or DNA constructs that are complementary to targeted mRNA sequences of therapeutic interest. In preclinical studies, our GSOs have inhibited in vivo gene expression without requiring a delivery enhancement technology.

Additional Programs. In addition to our clinical programs in autoimmune and inflammatory diseases and in cancer, we have identified TLR drug candidates for applications in the treatment of infectious diseases, respiratory diseases and hematological malignancies, and TLR3 agonists for use as vaccine adjuvants. We are seeking to enter into collaborations with pharmaceutical companies to advance these applications.

Corporate Information

Our executive offices are located at 167 Sidney Street, Cambridge, MA 02139, our telephone number is (617) 679-5500 and our Internet address is www.iderapharma.com. The information on our Internet website is not incorporated by reference in this prospectus and should not be considered to be part of this prospectus. Our website address is included in this prospectus as an inactive technical reference only. Unless the context otherwise requires, references in this prospectus to Idera Pharmaceuticals, we, us, and our refer to Idera Pharmaceuticals, Inc.

Idera® and IMO® are our trademarks. All other trademarks and service marks appearing in this registration statement are the property of their respective owners.

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The Offering

| | |
|-----------------------------|--|
| Common stock offered by us | Shares having an aggregate offering price up to \$10,000,000. |
| Manner of offering | At-the-market offering that may be made from time to time through our agent, Cowen and Company, LLC. See Plan of Distribution. |
| Use of proceeds | We plan to use the net proceeds from this offering for working capital and other general corporate purposes. Please see Use of Proceeds on page S-6. |
| Risk factors | See Risk Factors beginning on page S-5 of this prospectus supplement, as well as the other information included in or incorporated by reference in this prospectus supplement and the accompanying prospectus, for a discussion of risks you should carefully consider before investing in our securities. |
| NASDAQ Global Market symbol | IDRA |

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RISK FACTORS

Investing in our securities involves a high degree of risk and uncertainty. In addition to the other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus, you should carefully consider the risks described in the Risk Factors section of our Annual Report on Form 10-K for the year ended December 31, 2011 which is incorporated by reference herein, before making an investment decision with respect to the securities. We expect to update these Risk Factors from time to time in the periodic and current reports that we file with the SEC after the date of this prospectus supplement. These updated Risk Factors will be incorporated by reference in this prospectus supplement and the accompanying prospectus. Please refer to these subsequent reports for additional information relating to the risks associated with investing in our common stock. If any of such risks and uncertainties actually occurs, our business, financial condition, and results of operations could be severely harmed. This could cause the trading price of our common stock to decline, and you could lose all or part of your investment.

The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Related to this Offering

Our management will have broad discretion over the use of the net proceeds from this offering, you may not agree with how we use the proceeds and the proceeds may not be invested successfully.

We have not designated any portion of the net proceeds from this offering to be used for any particular purpose. Accordingly, our management will have broad discretion as to the use of the net proceeds from any offering by us and could use them for purposes other than those contemplated at the time of this offering. Accordingly, you will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the proceeds will be invested in a way that does not yield a favorable, or any, return for our company.

You may experience immediate and substantial dilution in the book value per share of the common stock you purchase.

Because the prices per share at which shares of our common stock are sold in this offering may be substantially higher than the book value per share of our common stock, you may suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. The shares sold in this offering, if any, will be sold from time to time at various prices. After giving effect to the sale of our common stock in the maximum aggregate offering amount of \$10,000,000 at an assumed offering price of \$1.87 per share, the last reported sale price of our common stock on The NASDAQ Global Market on April 11, 2012, and after deducting estimated offering commissions and expenses payable by us, our net tangible book value as of December 31, 2011 would have been \$27,380,000, or \$0.83 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.18 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of \$1.04 per share to new investors who purchase our common stock in the offering. See Dilution for a more detailed discussion of the dilution you may incur in connection with this offering.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the SEC filings that are incorporated by reference into this prospectus supplement and the accompanying prospectus contain or incorporate by reference forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements, other than statements of historical fact, included or incorporated in this prospectus supplement or the accompanying prospectus regarding our strategy, future operations, collaborations, intellectual property, financial position, future revenues, projected costs, prospects, plans, and objectives of management are forward-looking statements. The words believes, anticipates, estimates, plans, expects, intends, may, could, should, potential, likely, projects, continue, will, and would and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we actually will achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. There are a number of important factors that could cause our actual results to differ materially from those indicated or implied by forward-looking statements. These important factors include those set forth above under Risk Factors. These factors and the other cautionary statements made in this prospectus supplement should be read as being applicable to all related forward-looking statements whenever they appear in this prospectus supplement and the accompanying prospectus. We do not assume any obligation to update any forward-looking statements. We disclaim any intention or obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for working capital and other general corporate purposes. These purposes may include the funding of research and product development activities including nonclinical and clinical trials, general and administrative expenses, the acquisition of companies, businesses or assets and capital expenditures.

We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, our management will retain broad discretion over the allocation of net proceeds.

DILUTION

Purchasers of common stock offered by this prospectus supplement and the accompanying prospectus will suffer immediate and substantial dilution in the net tangible book value per share of common stock. Our net tangible book value as of December 31, 2011 was approximately \$17,945,000, or approximately \$0.65 per share of common stock. Net tangible book value per share represents the amount of total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding as of December 31, 2011.

Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers in this offering and the net tangible book value per share of our common

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stock immediately after this offering. After giving effect to the assumed sale of shares of common stock in the aggregate amount of \$10,000,000 at an assumed public offering price of \$1.87 per share, the last reported sale price of our common stock on April 11, 2012, and after deduction of commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2011 would have been approximately \$27,380,000, or \$0.83 per share of common stock. This represents an immediate increase in net tangible book value of \$0.18 per share of common stock to our existing stockholders and an immediate dilution in net tangible book value of \$1.04 per share of common stock to investors participating in this offering. The following table illustrates this per share dilution:

| | |
|---|---------|
| Assumed offering price per share | \$ 1.87 |
| Net tangible book value per share as of December 31, 2011 | \$ 0.65 |
| Increase per share attributable to this offering | \$ 0.18 |
| As adjusted net tangible book value per share as of December 31, 2011, after giving effect to this offering | \$ 0.83 |
| Dilution per share to new investors participating in this offering | \$ 1.04 |

Changes in the assumed public offering price of \$1.87 per share would not affect our as adjusted net tangible book value after this offering because this offering is currently limited to \$10,000,000. However, each \$1.00 increase (decrease) in the assumed public offering price of \$1.87 per share would increase (decrease) our as adjusted per share net tangible book value after this offering by approximately \$0.05 per share, and the dilution per share to new investors by approximately \$0.95 per share, assuming that the aggregate dollar amount of shares offered by us, as set forth above, remains at \$10,000,000 and after deducting the commissions and estimated offering expenses payable by us. We may also increase or decrease the aggregate dollar amount of shares we are offering from the amount set forth above. The information discussed above is illustrative only and will adjust based on the actual public offering price, the actual number of shares that we offer in this offering, and other terms of this offering determined at the time of each offer and sale.

The above table is based on 27,637,007 shares of our common stock outstanding as of December 31, 2011 and excludes, as of December 31, 2011:

1,926 shares of common stock reserved for issuance upon conversion of our series A convertible preferred stock;

5,621,300 shares of common stock reserved for issuance upon conversion of our series D convertible preferred stock;

4,439,052 shares of common stock reserved for issuance upon exercise of outstanding warrants at a weighted average exercise price of \$2.39;

5,943,759 shares of common stock reserved for issuance upon exercise of outstanding stock options at a weighted average exercise price of \$4.96; and

2,194,395 shares of common stock reserved for future issuance under our 2008 Stock Incentive Plan and our 1995 Employee Stock Purchase Plan.

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To the extent that any options or warrants are exercised, new options are issued under our equity incentive plans, additional shares of common stock are sold under our employee stock purchase plan or we otherwise issue additional shares of common stock in the future at prices per share below the price per share for any shares sold in this offering, there will be further dilution to new investors.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Cowen and Company, LLC, or Cowen, under which we may issue and sell from time to time up to \$10,000,000 of our common stock through Cowen as our sales agent. Sales of the common stock, if any, will be made at market prices by any method that is deemed to be an at the market offering as defined in Rule 415 under the Securities Act, including sales made directly on The NASDAQ Global Market and any other trading market for the common stock, and sales to or through a market maker other than on an exchange. In addition, with our prior written approval, Cowen may also sell our common stock by any other method permitted by law, including in privately negotiated transactions.

Cowen will offer the common stock subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and Cowen. We will designate the maximum amount of common stock to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. We or Cowen may suspend the offering of the common stock being made through Cowen under the sales agreement upon proper notice to the other party. We and Cowen each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party's sole discretion at any time.

The aggregate compensation payable to Cowen as sales agent equals 3.0% of the gross proceeds from the sale of shares of our common stock pursuant to the terms of the sales agreement.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

Cowen will provide written confirmation to us following the close of trading on The NASDAQ Global Market as applicable, each day in which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the gross sales price per share, the net proceeds to us and the compensation payable by us to Cowen.

We will report at least quarterly the number of shares of common stock sold through Cowen under the sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the third business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

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In connection with the sales of the common stock on our behalf, Cowen may be deemed to be an underwriter within the meaning of the Securities Act, and the compensation paid to Cowen may be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act. In addition, we have agreed, under certain circumstances, to reimburse a portion of the expenses of Cowen in connection with this offering up to a maximum of \$50,000. As sales agent, Cowen will not engage in any transactions that stabilize our common stock.

We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately \$265,000.

In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker deal may not exceed 8.0% of the aggregate amount of securities offered pursuant to this prospectus supplement.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Cowen and Company, LLC is being represented in connection with this offering by LeClairRyan, A Professional Corporation, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2011, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file annual, quarterly and other reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room.

Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K, including any amendments to those reports, and other information that we file with or furnish to the SEC pursuant to Section 13(a) or 15(d) of the Exchange Act can also be accessed free of charge by linking directly from our website at <http://www.iderapharma.com> under the Investors' SEC Filings caption to the SEC's Edgar Database. These filings will be available as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information contained on our website is not part of this prospectus supplement.

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This prospectus supplement is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus regarding us and the securities, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's internet site.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus supplement. We incorporate by reference the following information or documents that we have filed with the SEC (excluding those portions of any Form 8-K that are not deemed filed pursuant to the General Instructions of Form 8-K):

Our Annual Report on Form 10-K for the year ended December 31, 2011 filed with the SEC on March 14, 2012;

The information specifically incorporated by reference into the Annual Report on Form 10-K for the fiscal year ended December 31, 2010 from our definitive proxy statement for the 2011 Annual Meeting of Stockholders; and

The descriptions of our capital stock contained in (a) our Registration Statement on Form 8-A dated December 4, 2003, as amended on August 17, 2007 and as further amended on December 7, 2007 and (b) Item 5.03 of our Current Report on Form 8-K dated November 10, 2011, including any amendments or reports filed for the purpose of updating such descriptions.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and deemed to be part of this prospectus supplement from the date of the filing of such reports and documents.

Any statement contained in any document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or any additional prospectus supplements modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

We will provide without charge to each person, including any beneficial owner, to whom this prospectus supplement is delivered, upon written or oral request, a copy of any or all documents that are incorporated by reference into this prospectus supplement, but not delivered with the prospectus supplement, other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the documents that this prospectus supplement incorporates. You should direct written requests to: Idera Pharmaceuticals, Inc., 167 Sidney Street, Cambridge, Massachusetts 02139, or you may call us at (617) 679-5500.

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PROSPECTUS

\$75,000,000

IDERA PHARMACEUTICALS, INC.

Common Stock

Warrants

We may from time to time sell common stock and warrants to purchase common stock in one or more offerings for an aggregate initial offering price of \$75,000,000. We refer to the common stock and the warrants to purchase common stock collectively as the securities. This prospectus describes the general terms of these securities and the general manner in which these securities may be offered. We will provide the specific terms of these securities to be offered and sold in supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any applicable prospectus supplement before you invest.

We may offer these securities in amounts, at prices and on terms determined at the time of offering. The securities may be sold directly to you, through agents, or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in the accompanying prospectus supplement.

Our common stock is traded on the Nasdaq Global Market under the symbol IDRA. On August 23, 2010, the closing sale price of our common stock on the Nasdaq Global Market was \$3.37 per share. You are urged to obtain current market quotations for our common stock.

Investing in our securities involves certain risks. See Risk Factors on page 2 of this prospectus, as well as in the documents incorporated by reference in this prospectus, for a discussion of the factors you should carefully consider before deciding to purchase our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

Prospectus dated August 26, 2010.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, which we refer to as the SEC, utilizing a shelf registration process. Under this shelf registration process, we may from time to time sell a combination of the securities described in this prospectus in one or more offerings for an aggregate initial offering price of up to \$75,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with documents incorporated by reference in this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus does not, and together with the accompanying prospectus supplement will not, constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

To the extent there is a conflict between the information contained in this prospectus and the prospectus supplement, you should rely on the information in the prospectus supplement, provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus or any prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement.

Unless the context otherwise requires, references in this prospectus to Idera, we, us, and our refer to Idera Pharmaceuticals, Inc.

ABOUT IDERA PHARMACEUTICALS, INC.

We are engaged in the discovery and development of DNA- and RNA-based drug candidates targeted to Toll-Like Receptors, or TLRs, to treat infectious diseases, autoimmune and inflammatory diseases, cancer, and asthma and allergies, and for use as vaccine adjuvants. Drug candidates are compounds that we are developing and that have not been approved for any commercial use. TLRs are specific receptors present in immune system cells that recognize the DNA or RNA of bacteria or viruses and initiate an immune response. Relying on our expertise in DNA and RNA chemistry, we have designed and created proprietary TLR agonists and antagonists to modulate immune responses. A TLR agonist is a compound that stimulates an immune response through the targeted TLR. A TLR antagonist is a compound that blocks activation of an immune response through the targeted TLR.

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Our business strategy is to advance applications of our TLR-targeted drug candidates in multiple disease areas simultaneously. We are advancing some of these applications through internal programs, and we seek to advance other applications through collaborative alliances with pharmaceutical companies. Collaborators provide the necessary resources and drug development experience to advance our compounds in their programs. Upfront payments and milestone payments received from collaborations help to provide us with the financial resources for our internal research and development programs.

Our executive offices are located at 167 Sidney Street, Cambridge, MA 02139, our telephone number is (617) 679-5500 and our Internet address is www.iderapharma.com. The information on our Internet website is not incorporated by reference in this prospectus and should not be considered to be part of this prospectus. Our website address is included in this prospectus as an inactive technical reference only. Our name and logo and the names of our products are our trademarks or registered trademarks.

RISK FACTORS

An investment in our securities involves significant risks. You should carefully consider the risk factors contained in any prospectus supplement and in our filings with the SEC, as well as all of the information contained in this prospectus, any prospectus supplement and the documents incorporated by reference in this prospectus, before you decide to invest in our securities. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING INFORMATION

This prospectus, any prospectus supplement and the documents we incorporate by reference in this prospectus contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. All statements, other than statements of historical fact, that we include in this prospectus, any prospectus supplement and in the documents we incorporate by reference in this prospectus, may be deemed forward-looking statements for purposes of the Securities Act and the Exchange Act. We use the words anticipate, believe, estimate, expect, intend, may, plan, project, will, w expressions to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we actually will achieve the plans, intentions or expectations disclosed in our forward-looking statements and, accordingly, you should not place undue reliance on our forward-looking statements. There are a number of important factors that could cause actual results or events to differ materially from the forward-looking statements that we make, including the factors included in the documents we incorporate by reference in this prospectus. You should read these factors and the other cautionary statements made in the documents we incorporate by reference as being applicable to all related forward-looking statements wherever they appear in this prospectus, any prospectus supplement and any document incorporated by reference. We caution you that we do not undertake any obligation to update forward-looking statements we make.

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USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include the funding of research and product development activities, the acquisition of companies, businesses or assets, repayment and refinancing of debt (if any is outstanding at such time), working capital and capital expenditures.

We expect to invest the net proceeds in investment-grade, interest-bearing securities until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, our management will retain broad discretion over the allocation of net proceeds.

THE SECURITIES WE MAY OFFER

The descriptions of the securities contained in this prospectus, together with the applicable prospectus supplement, summarize the material terms and provisions of the various types of securities that we may offer. We will describe in the applicable prospectus supplement relating to any securities the particular terms of the securities offered by that prospectus supplement. If we so indicate in the applicable prospectus supplement, the terms of the securities may differ from the terms we have summarized below. We will also include in the prospectus supplement information, where applicable, about material United States federal income tax considerations relating to the securities, and the securities exchange, if any, on which the securities will be listed.

We may sell from time to time, in one or more offerings, one or more of the following securities:

common stock; and

warrants to purchase common stock.

The total initial offering price of all securities that we may sell in these offerings will not exceed \$75,000,000.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

Common Stock

The following description of our common stock is intended as a summary only and is qualified in its entirety by reference to our restated certificate of incorporation, as amended, our amended and restated by-laws, and our stockholder rights plan, as amended, filed as exhibits to this registration statement, and to Delaware corporate law. We refer herein to our restated certificate of incorporation, as amended, as our certificate of incorporation, and we refer to our amended and restated by-laws as our by-laws.

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We are authorized to issue 70,000,000 shares of common stock, \$0.001 par value per share. As of June 30, 2010, 23,498,637 shares of common stock were outstanding.

Voting. For all matters submitted to a vote of stockholders, each holder of common stock is entitled to one vote for each share registered in that stockholder's name on our books. Our common stock does not have cumulative voting rights. As a result, subject to the voting rights, of which there currently are none, of any outstanding preferred stock, persons who hold more than 50% of the outstanding common stock entitled to elect members of our board of directors can elect all of the directors who are up for election in a particular year.

Dividends. If our board of directors declares a dividend, holders of common stock will receive payments from our funds that are legally available to pay dividends. However, this dividend right is subject to any preferential dividend rights that we have granted or may grant to the persons who hold preferred stock.

Liquidation and Dissolution. If we are liquidated or dissolved, the holders of our common stock will be entitled to share ratably in all the assets that remain after we pay our liabilities, including without limitation liabilities under the unit purchase agreement described below, and any amounts we may owe to the persons who hold preferred stock, if any is outstanding.

Other Rights and Restrictions. The outstanding shares of our common stock are validly issued, fully paid and nonassessable. Holders of our common stock do not have preemptive rights, and they have no right to convert their common stock into any other securities. Our common stock is not subject to redemption by us. The rights, preferences and privileges of common stockholders are subject to the rights of the stockholders of any series of preferred stock that are issued and outstanding or that we may issue in the future. Our certificate of incorporation and by-laws do not restrict the ability of a holder of common stock to transfer his or her shares of common stock.

Transfer Agent and Registrar. The transfer agent and registrar for our common stock is BNY Mellon Shareowner Services.

Put Right. Pursuant to the terms of a unit purchase agreement dated as of May 5, 1998, we issued and sold a total of 1,199,684 shares of common stock, which we refer to as the put shares, at a price of \$16.00 per share. Under the terms of the unit purchase agreement, the initial purchasers, which we refer to as the put holders, of the put shares have the right, which we refer to as the put right, to require us to repurchase the put shares. The put right may not be exercised by any put holder unless all of the following occur:

we liquidate, dissolve or wind up our affairs pursuant to applicable bankruptcy law, whether voluntarily or involuntarily,

all of our indebtedness and obligations, including without limitation the indebtedness under our outstanding notes, has been paid in full, and

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all rights of the holders of any series or class of capital stock ranking prior and senior to the common stock with respect to liquidation, including without limitation the series A convertible preferred stock, have been satisfied in full.

We may terminate the put right upon written notice to the put holders if the closing sales price of our common stock exceeds \$32.00 per share for the 20 consecutive trading days prior to the date of notice of termination. Because the put right is not transferable, in the event that a put holder has transferred put shares since May 5, 1998, the put right with respect to those shares has terminated. As a consequence of the put right, in the event we are liquidated, holders of shares of common stock that do not have put rights with respect to such shares may receive smaller distributions per share upon our liquidation than if there were no put rights outstanding.

As of December 31, 2009, we had repurchased or received documentation of the transfer of 399,950 put shares and 99,261 of the put shares continued to be held in the name of put holders. We cannot determine at this time what portion of the put rights of the remaining 700,473 put shares have terminated.

Stockholder Rights Plan

On December 10, 2001, our board of directors adopted a stockholder rights plan. The stockholder rights plan was subsequently amended on August 27, 2003, March 24, 2006 and January 16, 2007. Under the plan, each holder of our common stock at the close of business on January 7, 2002 received a dividend of one preferred stock purchase right, or a right, for each outstanding share of common stock that the stockholder owned. In addition, each share of our common stock issued after January 7, 2002 receives one right. The rights trade automatically with our shares of common stock and become exercisable only under the circumstances described below. The rights will expire on the close of business on December 10, 2011, subject to earlier expiration or termination as described in the rights plan.

The purpose of the rights is to encourage potential acquirors to negotiate with our board of directors before attempting a takeover bid and to provide our board of directors with leverage in negotiating on behalf of our stockholders the terms of any proposed takeover. The rights may have anti-takeover effects. They should not, however, interfere with any merger or other business combination approved by our board of directors.

The following description is a summary of the material terms of our stockholder rights plan. It does not restate all of the terms of the plan. The stockholder rights plan, and not this description, defines the terms and provisions of the plan.

Exercise of Rights. Until a right is exercised, the holder of a right will not have any rights as a stockholder. Currently, the rights are not exercisable. When the rights become exercisable, if ever, holders of the rights will be able to purchase from us a unit equal to 1/1000th of a share of our series C junior participating preferred stock at a purchase price of \$13.00 per unit.

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In general, the rights will become exercisable upon the earlier of:

ten business days following a public announcement that a person or group, other than an exempted person, has acquired beneficial ownership of 15% or more of the outstanding

ten business days after the beginning of a tender offer or exchange offer that would result in a person or group, other than an exempted person, beneficially owning 15% or more of our common stock.

Flip-In Event. If a person or group, other than an exempted person, becomes the beneficial owner of 15% or more of our common stock, then each right, other than those rights held by the person or group that exceeded the 15% threshold, will then entitle its holder to receive, upon exercise, a number of shares of our common stock which is equal to the exercise price of the right divided by one-half of the market price of our common stock on the date of the occurrence of the flip-in event. However, the rights are not exercisable following such an event until such time as the rights are no longer redeemable by us, as described below.

Flip-Over Event. If at any time after a person or group, other than an exempted person, becomes the beneficial owner of 15% or more of our common stock,

we are acquired in a merger or other transaction in which we do not survive or in which our common stock is changed or exchanged; or

50% or more of our assets or earning power is sold or transferred, then each holder of a right, other than the person or group that exceeded the 15% threshold, will be entitled to receive, upon exercise, a number of shares of common stock of the acquiring company in the transaction equal to the exercise price of the right divided by one-half of the market price of the acquiring company's common stock on the date of the occurrence of the flip-over event.

Exchange of Rights. At any time after a flip-in event, our board of directors may exchange the rights, other than those rights held by the person or group that exceeded the 15% threshold, in whole or in part, at an exchange ratio of one share of our common stock or one one-thousandth of a share of our series C junior participating preferred stock for each right.

Redemption of Rights. At any time prior to the tenth business day after the occurrence of a flip-in event, we may redeem the rights in whole, but not in part, at a price of \$0.001 per right.

Certain Effects of Authorized but Unissued Stock

We have shares of common stock and preferred stock available for future issuance without stockholder approval. We may use these additional shares for a variety of corporate purposes, including future public offerings to raise additional capital, facilitating corporate acquisitions or paying a dividend on our capital stock.

The existence of unissued and unreserved shares of common stock and preferred stock may enable our board of directors to issue shares to persons friendly to current management or to issue preferred stock with terms that could render more difficult or discourage a third party's

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attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise, thereby protecting the continuity of our management. In addition, our issuance of preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation.

Delaware Law and Specified Certificate of Incorporation and By-law Provisions

Staggered Board. Our certificate of incorporation and by-laws provide for the division of our board of directors into three classes as nearly equal in size as possible with staggered three-year terms. In addition, our certificate of incorporation and by-laws provide that directors may be removed only for cause by the affirmative vote of the holders of two-thirds of the shares of our capital stock entitled to vote. Under our certificate of incorporation and by-laws, any vacancy on the board of directors, however occurring, including a vacancy resulting from an enlargement of the board, may only be filled by vote of a majority of the directors then in office. The classification of the board of directors and the limitations on the removal of directors and filling of vacancies could have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from acquiring, control of us.

Stockholder Action; Special Meeting of Stockholders. Our certificate of incorporation and by-laws provide that stockholders may take action only at a duly called annual or special meeting of stockholders and may not take action by written consent. Our certificate of incorporation and by-laws further provide that special meetings of our stockholders may be called only by a majority of the board of directors or by our chief executive officer or, if the office of chief executive officer is vacant, our president, and in no event may the stockholders call a special meeting.

Advance Notice Requirements for Stockholder Proposals and Director Nominations. Our by-laws provide that stockholders seeking to bring business before an annual meeting of stockholders, or to nominate candidates for election as directors at an annual meeting of stockholders, must meet specified procedural requirements. The by-laws also include a similar requirement for making nominations for directors. These provisions may preclude stockholders from bringing matters before an annual meeting of stockholders or from making nominations for directors at an annual or special meeting of stockholders.

Supermajority Votes Required. The General Corporation Law of Delaware provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or by-laws, unless a corporation's certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our certificate of incorporation and by-laws require the affirmative vote of the holders of at least 75% of the shares of our capital stock issued and outstanding and entitled to vote to amend or repeal any of the provisions described in the prior three paragraphs.

Limitation of Liability; Indemnification. Our certificate of incorporation contains provisions permitted under the General Corporation Law of Delaware relating to the liability of directors. The provisions eliminate a director's liability for monetary damages for a breach of fiduciary duty, except in circumstances involving wrongful acts, such as the breach of a director's duty of loyalty or acts or omissions that involve intentional misconduct or a knowing

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violation of law. This limitation of liability does not alter the liability of our directors and officers under federal securities laws. Furthermore, our certificate of incorporation contains provisions to indemnify our directors and officers to the fullest extent permitted by the General Corporation Law of Delaware. These provisions do not limit or eliminate our right or the right of any of our stockholders to seek non-monetary relief, such as an injunction or rescission in the event of a breach by a director or an officer of his or her duty of care. We believe that these provisions will assist us in attracting and retaining qualified individuals to serve as directors.

Business Combinations. We are subject to the provisions of section 203 of the General Corporation Law of Delaware. Section 203 prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. A business combination includes mergers, asset sales and other transactions resulting in a financial benefit to the interested stockholder. Subject to specified exceptions, an interested stockholder is a person who, together with affiliates and associates, owns, or within three years did own, 15% or more of the corporation's voting stock.

Warrants

The following description, together with the additional information we may include in any applicable prospectus supplement, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we so indicate in a prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms we describe below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement.

We may offer warrants to purchase common stock. We may offer warrants separately or together with common stock or a combination of those securities in the form of units, as described in the applicable prospectus supplement. If we offer warrants as part of a unit, the accompanying prospectus supplement will specify whether those warrants may be separated from the common stock in the unit prior to the expiration date of the warrants.

We will describe in the applicable prospectus supplement the following terms of any warrants:

the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;

the currency or currency units in which the offering price, if any, and the exercise price are payable;

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the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;

whether the warrants are to be sold separately or with common stock as parts of units;

whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and the common stock included in that unit;

any applicable material U.S. federal income tax consequences;

the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;

the proposed listing, if any, of the warrants or the common stock purchasable upon exercise of the warrants on any securities exchange;

if applicable, the designation and terms of the common stock with which the warrants are issued and, the number of warrants issued with each security;

if applicable, the date from and after which any warrants and common stock issued as part of a unit will be separately transferable;

the number of shares of common stock purchasable upon exercise of a warrant and the price at which those shares may be purchased;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

information with respect to book-entry procedures, if any;

the antidilution provisions of, and other provisions for changes to or adjustment in the exercise price of, the warrants, if any;

any redemption or call provisions; and

any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

PLAN OF DISTRIBUTION

We may sell the securities being offered hereby:

through underwriters;

through dealers;

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through agents;

directly to purchasers; and

through a combination of any of these methods of sale.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act, and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. Agents, dealers and underwriters may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

The distribution of the securities may be effected from time to time in one or more transactions:

at a fixed price, or prices, which may be changed from time to time;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; and

at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

the name of any agents or any underwriters;

the public offering or purchase price;

any discounts and commissions to be allowed or paid to the agent or underwriters;

all other items constituting underwriting compensation;

any discounts and commissions to be allowed or paid to dealers; and

any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to

such offering the names of the underwriters or agents and the terms of the related agreement with them.

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If a dealer is utilized in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

Remarketing firms, agents, underwriters and dealers may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and

if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain of the underwriters and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for, us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallocate in connection with the offering, creating a short position for their own accounts. In addition, to cover overallocations or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

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The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

VALIDITY OF SECURITIES

The validity of the securities offered hereby will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts.

EXPERTS

The financial statements of Idera Pharmaceuticals, Inc. appearing in Idera Pharmaceuticals, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2009 and the effectiveness of Idera Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2009, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file reports, proxy statements and other documents with the SEC. You may read and copy any document we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room.

The SEC also maintains an Internet site, the address of which is www.sec.gov. That site contains our annual, quarterly and current reports, proxy statements, information statements and other information.

We have filed this prospectus with the SEC as part of a registration statement on Form S-3 under the Securities Act. This prospectus does not contain all of the information set forth in the registration statement because some parts of the registration statement are omitted in accordance with the rules and regulations of the SEC. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's Internet site.

We also maintain an Internet site at www.iderapharma.com, through which you can access our SEC filings. The information set forth on our Internet site is not part of this prospectus.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this

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prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below (File No. 001-31918) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) after the date of the initial registration statement and prior to effectiveness of the registration statement and until the offering of the securities under the registration statement is terminated or completed:

Our Annual Report on Form 10-K for the year ended December 31, 2009, as filed with the SEC on March 10, 2010;

Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2010, as filed with the SEC on May 4, 2010;

Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2010, as filed with the SEC on August 5, 2010;

Our Current Reports on Form 8-K, as filed with the SEC on January 27, 2010, April 7, 2010, June 21, 2010 and August 3, 2010; and

The description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on December 4, 2003, as amended by Amendment No. 1 to Form 8-A on Form 8-A/A filed with the SEC on August 17, 2007 and Amendment No. 2 to Form 8-A on Form 8-A/A filed with the SEC on December 7, 2007.

We will provide a copy of any or all of the documents we incorporate by reference, at no cost, to any person who receives this prospectus. To request a copy of any or all of these documents, you should write us at 167 Sidney Street, Cambridge, Massachusetts 02139, Attention: Investor Relations, or telephone us at (617) 679-5500.

The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing

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provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

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\$10,000,000

Common Stock

PROSPECTUS SUPPLEMENT

Cowen and Company, LLC

April 12, 2012