

ACHILLION PHARMACEUTICALS INC

Form 424B5

August 31, 2012

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Filed Pursuant to Rule 424(b)(5)

Registration No. 333-172594

PROSPECTUS SUPPLEMENT

(to Prospectus dated April 25, 2011)

6,367,853 Shares

Common Stock

We are selling directly to selected investors 6,367,853 shares of our common stock.

Our common stock trades on the NASDAQ Global Select Market under the symbol ACHN. On August 30, 2012, the last reported sale price of our common stock on the NASDAQ Global Select Market was \$6.57 per share.

Investing in our common stock involves risks that are described in the **Risk Factors** section beginning on page S-4 of this prospectus supplement and in our Annual Report on Form 10-K for the annual period ended December 31, 2011 and in our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2012, which have been filed with the Securities and Exchange Commission and are incorporated by reference in this prospectus supplement and the accompanying prospectus.

	Per Share	Total
Offering price	\$ 6.57	\$ 41,836,794

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.

The date of this prospectus supplement is August 30, 2012

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We have not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement or the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us that we have authorized for use in connection with this offering. We have not authorized anyone to provide you with different information. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus prepared by or on behalf of us that we have authorized for use in connection with this offering is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus prepared by or on behalf of us that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents we have referred you to in the sections of this prospectus supplement entitled **Where You Can Find More Information** and **Incorporation of Certain Information by Reference**.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated April 25, 2011, including the documents incorporated by reference therein, provides more general information, some of which may not apply to the securities offered by this prospectus supplement. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. 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 in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before 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 incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

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.

All references in this prospectus supplement and the accompanying prospectus to Achillion, the Company, we, us, our, or similar references refer to Achillion Pharmaceuticals, Inc., unless the context requires otherwise.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read carefully this entire prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering, including the Risk Factors section beginning on page S-4 of this prospectus supplement and our consolidated financial statements and the related notes and the other documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

Achillion Pharmaceuticals, Inc.

We are a biopharmaceutical company that was established to discover, develop and commercialize innovative treatments for infectious diseases. Within the anti-infective market, we are currently concentrating on the development of antivirals for the treatment of chronic hepatitis C infection, or HCV, and the development of antibacterials for the treatment of resistant bacterial infections. We are currently focusing our efforts on developing the following drug candidates for the treatment of HCV:

Sovaprevir, formerly ACH-1625, a NS3 protease inhibitor for the treatment of HCV, currently in phase II clinical development;

ACH-2684, a NS3 protease inhibitor for the treatment of HCV, currently in phase I clinical development;

ACH-2928, a NS5A inhibitor for the treatment of HCV, which recently completed phase I clinical development; and

ACH-3102, a NS5A inhibitor for the treatment of HCV, currently in phase I clinical development.

In addition, we have established a pipeline of certain antibacterial product candidates for which we are currently seeking appropriate collaborative partners, but to which we are not devoting significant resources at this time. These product candidates include ACH-702 for the treatment of dermatologic and ophthalmic infections, and ACH-2881 for the treatment of serious resistant bacterial infections, including methicillin resistant staphylococcus aureus.

Corporate Information

We were incorporated in Delaware in August 1998. Our principal executive office is located at 300 George Street, New Haven, Connecticut 06511, and our telephone number is (203) 624-7000. Our internet address is www.achillion.com. The information on our web site is not incorporated by reference into this prospectus and should not be considered to be a part of this prospectus. Our internet address is included in this prospectus as an inactive technical reference only.

Our trademarks and service marks include, among others, Achillion®. Other service marks, trademarks and trade names appearing in this annual report are the properties of their respective owners.

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The Offering

Common stock offered by us	6,367,853 shares
Common stock to be outstanding immediately after this offering	78,953,881 shares
Use of proceeds	We intend to use the net proceeds from this offering to continue clinical testing of sovalprevir, formerly, ACH-1625, ACH-2684, and ACH-3102 and for general corporate purposes. Pending the application of the net proceeds, we intend to invest the net proceeds in short-term investment-grade, interest-bearing securities. See Use of Proceeds.
Risk factors	Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page S-4 and other information included and incorporated by reference in this prospectus supplement for a discussion of factors you should carefully consider before deciding to invest in our common stock.
Market for our common stock	Our common stock is listed on the NASDAQ Global Select Market under the symbol ACHN.
The number of shares of our common stock to be outstanding after this offering is based on 72,586,028 shares outstanding as of August 27, 2012. Unless specifically stated otherwise, the information in this prospectus supplement excludes:	

5,768,921 shares of common stock issuable upon the exercise of stock options outstanding as of August 27, 2012, at a weighted average exercise price of \$4.69 per share;

7,208,572 shares of our common stock available for future issuance as of August 27, 2012 under our 2006 stock incentive plan;

207,003 shares of our common stock available for future issuance as of August 27, 2012 under our 2006 employee stock purchase plan; and

6,071,440 shares of common stock issuable upon the exercise of warrants outstanding as of August 27, 2012, at a weighted average exercise price of \$3.21 per share.

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RISK FACTORS

Investing in our securities involves a high degree of risk and uncertainty. You should review carefully the risks and uncertainties described under the heading Risk Factors contained in our Annual Report on Form 10-K for the year ended December 31, 2011 as well as our Quarterly Report on Form 10-Q for the quarter ended June 30, 2012, each of which is incorporated by reference into this prospectus supplement, as well as other information we have provided or incorporated by reference in the accompanying prospectus, before making an investment decision with respect to this offering. 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the documents we incorporate by reference in this prospectus supplement include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. For purposes of these statutes, any statement contained herein or in the documents we incorporate by reference in this prospectus supplement other than a statement of historical fact, may be a forward-looking statement. For example, we may, in some cases, use words such as anticipate, believe, could, estimate, expect, intend, plan, project, should, will, would or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements.

Our actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including the factors referred to above under the heading Risk Factors and the following:

our ability to obtain marketing approvals from the FDA and similar foreign regulatory authorities;

our ability to complete the development of our drug candidates under the timelines we anticipate in current and future clinical trials, if at all;

our ability to obtain patent protection for our drug candidates and freedom to operate under third party intellectual property;

our ability to establish commercial manufacturing arrangements and to identify, enter into and maintain collaboration agreements with appropriate third-parties;

our ability to launch commercial sales of our drug candidates, whether alone or in collaboration with others; and

our ability to achieve profitability and raise the additional capital needed to achieve our business objectives.

If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. You should consider these factors and the other cautionary statements made in this prospectus supplement or the documents we incorporate by reference in this prospectus as being applicable to all related forward-looking statements wherever they appear in this prospectus supplement or the documents incorporated by reference. While we may elect to update forward-looking statements wherever they appear in this prospectus supplement or the documents incorporated by reference, we do not assume, and specifically disclaim, any obligation to do so, whether as a result of new information, future events or otherwise.

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USE OF PROCEEDS

The net proceeds of this offering will be approximately \$41.7 million after deducting estimated expenses related to this offering payable by us.

We intend to use the net proceeds from this offering to continue clinical testing of sovalprevir, formerly ACH-1625, ACH-2684, and ACH-3102 and for general corporate purposes.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. The occurrence of unforeseen events or changed business conditions, however, could result in the application of the net proceeds from this offering in a manner other than as described in this prospectus supplement. As a result, our management will have broad discretion to allocate the net proceeds from this offering.

Pending the uses described above, we plan to invest the net proceeds from this offering in short-term, investment-grade instruments, interest bearing securities.

DILUTION

If you purchase our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock after this offering. We calculate net tangible book value per share by subtracting our total liabilities from our total tangible assets and dividing the difference by the number of outstanding shares of our common stock.

Our net tangible book value at June 30, 2012 was \$53.4 million, or \$0.74 per share. After giving effect to the sale of 6,367,853 shares of common stock by us at the public offering price of \$6.57 per share, less the estimated offering expenses payable by us, our as adjusted net tangible book value at June 30, 2012 would be \$95.1 million, or \$1.21 per share. This represents an immediate increase in net tangible book value of \$0.47 per share to existing stockholders and an immediate dilution of \$5.36 per share to investors in this offering. The following table illustrates this per share dilution:

Public offering price per share	\$ 6.57
Net tangible book value per share as of June 30, 2012	\$ 0.74
Increase per share attributable to new investors purchasing shares in this offering	\$ 0.47
Net tangible book value per share as of June 30, 2012 after giving effect to this offering	\$ 1.21
Dilution per share to new investors	\$ 5.36

The above discussion and table are based on 72,373,257 shares outstanding as of June 30, 2012 and exclude:

5,975,292 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2012, at a weighted average exercise price of \$4.61 per share;

7,214,972 shares of our common stock available for future issuance as of June 30, 2012 under our 2006 stock incentive plan;

207,003 shares of our common stock available for future issuance as of June 30, 2012 under our 2006 employee stock purchase plan; and

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6,071,440 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2012, at a weighted average exercise price of \$3.21 per share.

To the extent that any of our outstanding options or warrants are exercised, we grant additional options or other awards under our stock incentive plan or issue additional warrants, or we issue additional shares of common stock in the future, there may be further dilution.

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DESCRIPTION OF THE SECURITIES WE ARE OFFERING

The shares of common stock being offered in this offering will be issued pursuant to a subscription agreement.

Common Stock

The material terms and provisions of our common stock are described under the caption Description of Capital Stock Common Stock beginning on page 5 of the accompanying prospectus.

PLAN OF DISTRIBUTION

We entered into a subscription agreement directly with the investors in connection with this offering. Subject to the terms and conditions of the subscription agreement, the investors agreed to purchase, and we agreed to sell, an aggregate of 6,367,853 shares of our common stock, as provided on the cover page of this prospectus supplement.

The shares of common stock sold in this offering will be listed on the NASDAQ Global Select Market. The shares of common stock will be delivered only in book-entry form through The Depository Trust Company, New York, New York on or about September 4, 2012.

The expenses directly related to this offering are estimated to be approximately \$150,000 and will be paid by us. Expenses of the offering include our legal and accounting fees, printing expenses, transfer agent fees, NASDAQ Global Select Market listing fees and miscellaneous fees.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this Prospectus Supplement by reference to the Annual Report on Form 10-K for the year ended December 31, 2011 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Exchange Act and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's website at <http://www.sec.gov>. Our common stock is listed on The NASDAQ Global Select Market, and you can read and inspect our filings at the offices of the Financial Industry Regulatory Authority located at 1735 K Street, N.W., Washington, D.C. 20006.

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This prospectus supplement and the accompanying prospectus are only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act and therefore omits certain information contained in the registration statement. We have also filed exhibits with the registration statement that are excluded from this prospectus supplement and the accompanying prospectus, and you should refer to the applicable exhibit for a complete description of any statement referring to any contract or other document. You may inspect a copy of the registration statement, including the exhibits, without charge, at the public reference room or obtain a copy from the SEC upon payment of the fees prescribed by the SEC.

The reports, proxy statements and other information that we file with the SEC are available to you free of charge through the Investors page of our website, www.achillion.com, as soon as reasonably practicable after they have been electronically filed with, or furnished to, the SEC. We have included our website address as a factual reference and do not intend it as an active link to our website. The information contained, or accessible through, our website is not a part of this prospectus supplement or the accompanying prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate into this prospectus supplement information that we file with the SEC in other documents. This means that we can disclose important information to you by referring to other documents that contain that information. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information that we file with the SEC in the future and incorporate by reference in this prospectus supplement and the accompanying prospectus automatically updates and supersedes previously filed information as applicable. The following documents filed with the SEC pursuant to the Exchange Act are incorporated herein by reference (other than, in each case, documents or information deemed to have been furnished and not filed in accordance with SEC rules):

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2011, as filed with the SEC on March 8, 2012;

Our Quarterly Reports on Forms 10-Q for the quarters ended March 31, 2012, as filed with the SEC on May 9, 2012, and June 30, 2012, as filed with the SEC on August 8, 2012;

Our Current Reports on Forms 8-K, as filed with the SEC on January 17, 2012, June 6, 2012, June 11, 2012, and June 28, 2012;

All documents filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement and before the termination or completion of this offering of common stock shall be deemed to be incorporated by reference in this prospectus supplement and to be a part of it from the filing dates of such documents, except in each case for information contained in any such filing where we indicate that such information is being furnished and is not to be considered filed under the Exchange Act; and

The description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on October 18, 2006.

You may request a copy of these documents, which will be provided to you at no cost, by writing or telephoning us using the following contact information:

300 George Street

New Haven, CT 06511-6624

Phone: (203) 624-7000

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\$100,000,000

Achillion Pharmaceuticals, Inc.

Common Stock

Preferred Stock

Warrants

We may from time to time sell common stock, preferred stock and/or warrants in one or more offerings, for an aggregate initial offering price of \$100,000,000. We may sell these securities to or through underwriters, directly to investors or through agents. This prospectus describes the general manner in which our securities may be offered using this prospectus. We will provide you with specific terms of the offerings in one or more supplements to this prospectus.

Our common stock is listed on the NASDAQ Global Market and traded under the symbol ACHN. The last reported sale price of our common stock on the NASDAQ Global Market on April 25, 2011 was \$6.43 per share.

Investing in our securities involves significant risks. See Risk Factors beginning on page 3.

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

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

Prospectus dated April 25, 2011.

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You should rely only on the information contained in this prospectus and the documents incorporated by reference in this prospectus or to which we have referred you. We have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus does not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. You should not assume that the information contained in this prospectus or any document incorporated by reference is accurate as of any date other than the date on the front cover of the applicable document. Neither the delivery of this prospectus nor any distribution of securities pursuant to this prospectus shall, under any circumstances, create any implication that there has been no change in the information set forth or incorporated by reference into this prospectus or in our affairs since the date of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. Under this shelf registration process, we may from time to time sell common stock, preferred stock and/or warrants to purchase common stock or preferred stock, in one or more offerings, up to a total dollar amount of \$100,000,000. We have provided to you in this prospectus a description of the general manner in which these securities may be offered by this prospectus. Each time we sell securities under this shelf registration process, we will provide a prospectus supplement that will contain specific information about the terms of the offering. We may also add, update or change in the prospectus supplement, or any free writing prospectus we may authorize to be delivered to you, any of the information contained in this prospectus. To the extent there is a conflict between the information contained in this prospectus and the prospectus supplement or any free writing prospectus we may authorize to be delivered to you, you should rely on the information in the prospectus supplement or free writing prospectus, as the case may be, 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. This prospectus, together with the applicable prospectus supplements and any free writing prospectus we may authorize to be delivered to you, includes all material information relating to this offering.

As permitted by the rules and regulations of the SEC, the registration statement, of which this prospectus forms a part, includes additional information not contained in this prospectus. You may read the registration statement and the other reports we file with the SEC at the SEC's web site or at the SEC's offices, each as further described below under the heading Where You Can Find Additional Information.

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SUMMARY

Achillion Pharmaceuticals, Inc.

We are a biopharmaceutical company focused on the discovery, development and commercialization of innovative treatments for infectious diseases. Within the anti-infective market, we are currently concentrating on the development of antivirals for the treatment of chronic hepatitis C and the development of antibacterials for the treatment of resistant bacterial infections. We are currently focusing our efforts on developing three drug candidates for the treatment of chronic hepatitis C (HCV): ACH-1625, a protease inhibitor for the treatment of chronic hepatitis C, currently being tested in an on-going phase IIa clinical trial, ACH-2684, a pangenotypic protease inhibitor for which we have completed preclinical testing, and ACH-2928, a NS5A inhibitor for which we have completed preclinical testing. We also have developed ACH-1095, a NS4A antagonist for the treatment of chronic hepatitis C, to which Gilead Sciences, Inc., or Gilead, retains certain future development rights. We are not devoting significant resources at this time to the further development of ACH-1095. In addition, we have established a pipeline of certain product candidates for which we are currently seeking appropriate collaborative partners, but to which we are not devoting significant resources at this time. These product candidates include ACH-702 for the treatment of dermatologic and ophthalmic infections, ACH-2881 for the treatment of serious resistant bacterial infections, including methicillin-resistant staphylococcus aureus, and elvucitabine for the treatment of HIV infection.

We will need substantial additional financing to obtain regulatory approvals, fund operating losses, and, if deemed appropriate, establish manufacturing and sales and marketing capabilities, which we will seek to raise through public or private equity or debt financings, collaborative or other arrangements with third parties or through other sources of financing. There can be no assurance that such funds will be available on terms favorable to us, if at all.

In addition to the risks associated with early-stage companies, there can be no assurance that we will successfully complete our research and development, obtain adequate patent protection for our technology, obtain necessary government regulatory approval for drug candidates we develop, find and maintain appropriate collaboration partners or that any approved drug candidates will be commercially viable. In addition, we may not be profitable even if we succeed in commercializing any of our drug candidates.

Corporate Information

We were incorporated in Delaware in August 1998. Our principal executive office is located at 300 George Street, New Haven, Connecticut 06511, and our telephone number is (203) 624-7000. Our internet address is www.achillion.com. The information on our web site is not incorporated by reference into this prospectus and should not be considered to be a part of this prospectus. Our internet address is included in this prospectus as an inactive technical reference only.

Unless otherwise stated, all references to us, our, Achillion, we, the Company and similar designations refer to Achillion Pharmaceuticals, Inc. Our logo, trademarks and service marks are the property of Achillion. Other trademarks or service marks appearing in this prospectus are the property of their respective holders.

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RISK FACTORS

Investing in our securities involves significant risks. Please see the risk factors under the heading "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2010 on file with the SEC, which is incorporated by reference in this prospectus. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus and any prospectus supplement. 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and the documents we incorporate by reference in this prospectus include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. For purposes of these statutes, any statement contained herein, in any prospectus supplement or in the documents we incorporate by reference in this prospectus other than a statement of historical fact, may be a forward-looking statement. For example, we may, in some cases, use words such as "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "plan," "project," "should," "will," "would" or other words that convey uncertainty of future events to identify these forward-looking statements. Our actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including the factors referred to above under the heading "Risk Factors." These important factors include the factors that we identify in the documents that we incorporate by reference in this prospectus. If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. You should consider these factors and the other cautionary statements made in this prospectus, any prospectus supplement or the documents we incorporate by reference in this prospectus as being applicable to all related forward-looking statements wherever they appear in this prospectus, any prospectus supplement or the documents incorporated by reference. While we may elect to update forward-looking statements wherever they appear in this prospectus, any prospectus supplement or the documents incorporated by reference, we do not assume, and specifically disclaim, any obligation to do so, whether as a result of new information, future events or otherwise.

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USE OF PROCEEDS

Unless otherwise provided in the applicable prospectus supplement, we intend to use the net proceeds from the sale of securities under this prospectus for general corporate purposes, research and development expenses, including clinical trial costs, general and administrative expenses and products and technologies that complement our business. We will set forth in the prospectus supplement our intended use for the net proceeds received from the sale of securities. Pending the application of the net proceeds, we intend to invest the net proceeds in investment-grade, interest-bearing securities.

THE SECURITIES WE MAY OFFER

The descriptions of the securities contained in this prospectus, together with the applicable prospectus supplements, 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 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 U.S. 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:

common stock;

preferred stock;

warrants to purchase common stock or preferred stock; or

any combination of the foregoing securities.

In this prospectus, we refer to the common stock, preferred stock and warrants collectively as securities. The total dollar amount of all securities that we may issue under this prospectus will not exceed \$100,000,000.

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

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DESCRIPTION OF CAPITAL STOCK

The following describes our common stock and provisions of our certificate of incorporation and bylaws. Copies of these documents are filed with the Securities and Exchange Commission as exhibits to our registration statement, of which this prospectus forms a part.

Our authorized capital stock consists of 100,000,000 shares of our common stock, par value \$0.001 per share, and 5,000,000 shares of preferred stock, par value \$0.01 per share.

Common Stock

As of February 28, 2011 there were 58,390,498 shares of our common stock outstanding and 63 holders of record.

Holders of common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Accordingly, holders of a majority of the shares of common stock entitled to vote in any election of directors may elect all of the directors standing for election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock. Upon our liquidation, dissolution or winding up, the holders of common stock are entitled to receive proportionately our net assets available after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are, and the shares offered by us in this offering will be, when issued and paid for, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our certificate of incorporation, our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible future financings, future acquisitions and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. The effects of issuing preferred stock could also include one or more of the following:

restricting dividends on the common stock;

diluting the voting power of the common stock; or

impairing the liquidation rights of the common stock.

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DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, 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 indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement that includes this prospectus.

General

We may issue warrants for the purchase of common stock or preferred stock in one or more series. We may issue warrants independently or together with common stock or preferred stock, and the warrants may be attached to or separate from these securities. We will issue warrants under one or more warrant agreements between us and a warrant agent that we will name in the prospectus supplement.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Additional Information

We will describe in the applicable prospectus supplement the terms of the warrants, including:

the offering price and aggregate number of warrants offered;

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;

if applicable, the date on and after which the warrants and the related securities will be separately transferable;

the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;

the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;

the terms of any rights to redeem or call the warrants;

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreement and warrants may be modified;

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a discussion on any material or special United States federal income tax consequences of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

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Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to 5 p.m., Eastern time, on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Anti-Takeover Provisions of Delaware Law, our Certificate of Incorporation and our Bylaws

We are subject to the provisions of Section 203 of the General Corporation Law of Delaware. Subject to certain exceptions, 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 person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or the business combination is approved in a prescribed manner. A business combination includes, among other things, a merger or consolidation involving us and the interested stockholder and the sale of more than 10% of our assets. In general, an interested stockholder is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Our certificate of incorporation and our bylaws divide our board of directors into three classes with staggered three-year terms. In addition, our certificate of incorporation provides that directors may be removed only for cause by the affirmative vote of the holders of 75% of our shares of capital stock entitled to vote. Under our certificate of incorporation, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may only be filled by vote of a majority of our directors then in office. The classification of our board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from acquiring, control of us.

Our certificate of incorporation and our bylaws also provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before the meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws further provide that, except as otherwise required by law, special meetings of the stockholders may only be called by the chairman of the board, chief executive officer or our board of directors. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions may also discourage a third party from making a tender offer for our common stock, because even if it

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acquired a majority of our outstanding voting securities, the third party would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders' meeting, and not by written consent.

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 bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our certificate of incorporation and bylaws 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 two paragraphs.

Limitation of Liability and 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 violation of law. Further, our certificate of incorporation contains provisions to indemnify our directors and officers to the fullest extent permitted by the General Corporation Law of Delaware.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare, with offices at 250 Royall Street, Canton, Massachusetts 02021.

NASDAQ Global Market

Our common stock is traded on the Nasdaq Global Market under the symbol ACHN.

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PLAN OF DISTRIBUTION

We may sell the securities being offered through underwriters or dealers, through agents, or directly to one or more purchasers. The prospectus supplement will describe the terms of the offering of the securities, including:

the number of securities we are offering;

the name or names of any agents or underwriters;

any securities exchange or market on which the securities may be listed;

the purchase price of the securities being offered and the proceeds we will receive from the sale;

any over-allotment options pursuant to which underwriters may purchase additional securities from us;

any underwriting discounts or agency fees and other items constituting underwriters' or agents' compensation; and

any discounts or concessions allowed or reallocated or paid to dealers.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of the sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all the securities offered by the prospectus supplement. We may change from time to time the public offering price and any discounts or concessions allowed or reallocated or paid to dealers.

We may sell the securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of the securities, and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may provide underwriters and agents with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act, or contribution with respect to payments that the underwriters or agents may make with respect to these liabilities. Underwriters and agents may engage in transactions with, or perform services for, us in the ordinary course of business. We will describe such relationships in the prospectus supplement naming the underwriter and the nature of any such relationship.

Rules of the Securities and Exchange Commission may limit the ability of any underwriters to bid for or purchase securities before the distribution of the shares of common stock is completed. However, underwriters may engage in the following activities in accordance with the rules:

Stabilizing transactions Underwriters may make bids or purchases for the purpose of pegging, fixing or maintaining the price of the shares, so long as stabilizing bids do not exceed a specified maximum.

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Over-allotments and syndicate covering transactions Underwriters may sell more securities than the number of securities that they have committed to purchase in any underwritten offering. This over-allotment creates a short position for the underwriters. This short position may involve either covered short sales or naked short sales. Covered short sales are short sales made in an amount not greater than the underwriters' over-allotment option to purchase additional securities in any underwritten offering. The underwriters may close out any covered short position either by exercising their over-allotment option or by purchasing shares in the open market. To determine how they will close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market, as compared to the price at which they may purchase shares through

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the over-allotment option. Naked short sales are short sales in excess of the over-allotment option. The underwriters must close out any naked position by purchasing securities in the open market. A naked short position is more likely to be created if the underwriters are concerned that, in the open market after pricing, there may be downward pressure on the price of the shares that could adversely affect investors who purchase shares in the offering.

Penalty bids If underwriters purchase securities in the open market in a stabilizing transaction or syndicate covering transaction, they may reclaim a selling concession from other underwriters and selling group members who sold those securities as part of the offering.

Similar to other purchase transactions, an underwriter's purchases to cover the syndicate short sales or to stabilize the market price of our securities may have the effect of raising or maintaining the market price of our common stock or preventing or mitigating a decline in the market price of our securities. As a result, the price of the shares of our securities may be higher than the price that might otherwise exist in the open market. The imposition of a penalty bid might also have an effect on the price of shares if it discourages the resale of the securities.

If commenced, the underwriters may discontinue any of these activities at any time.

Our common stock is quoted on the NASDAQ Global Market. One or more underwriters may make a market in our securities, but the underwriters will not be obligated to do so and may discontinue market making at any time without notice. We cannot give any assurance as to liquidity of the trading market for our securities.

Any underwriters who are qualified market makers on the NASDAQ Global Market may engage in passive market making transactions in the securities on the NASDAQ Global Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

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LEGAL MATTERS

The validity of the issuance of the securities offered by this prospectus will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP.

EXPERTS

The financial statements incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2010 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file reports, proxy statements and other information with the SEC as required by the Exchange Act. You can find, copy and inspect information we file at the SEC's public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can call the SEC at 1-800-SEC-0330 for further information about the public reference room. You can review our electronically filed reports, proxy and information statements on the SEC's web site at <http://www.sec.gov> or on our web site at <http://www.achillion.com>. Information included on our web site is not a part of this prospectus or any prospectus supplement.

This prospectus 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 exhibits and schedules. You can obtain a copy of the registration statement from the SEC at any address listed above or from the SEC's web site.

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INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

We are incorporating by reference certain documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information in the documents incorporated by reference is considered to be part of this prospectus. Statements contained in documents that we file with the SEC and that are incorporated by reference in this prospectus will automatically update and supersede information contained in this prospectus, including information in previously filed documents or reports that have been incorporated by reference in this prospectus, to the extent the new information differs from or is inconsistent with the old information. Except as set forth below, the SEC file number for the documents incorporated by reference in this prospectus is 001-33095.

We have filed or may file the following documents with the SEC and they are incorporated herein by reference as of their respective dates of filing:

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2010, as filed with the SEC on March 3, 2011;

Definitive Proxy Statement on Schedule 14A, filed on April 22, 2010 (excluding those portions that are not incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2009).

All documents filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act (1) after the date of the filing of this registration statement and prior to its effectiveness and (2) until all of the common stock to which this prospectus relates has been sold or the offering is otherwise terminated, except in each case for information contained in any such filing where we indicate that such information is being furnished and is not to be considered filed under the Exchange Act, will be deemed to be incorporated by reference in this prospectus and the accompanying prospectus supplement and to be a part hereof from the date of filing of such documents; and

The description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on October 18, 2006. A statement contained in a document incorporated by reference into this prospectus shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus, any prospectus supplement or in any other subsequently filed document which is also incorporated in this prospectus modifies or replaces such statement. Any statements so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You may request a copy of these documents, which will be provided to you at no cost, by writing or telephoning us using the following contact information:

300 George Street

New Haven, CT 06511-6624

Phone: (203) 624-7000

You should rely only on the information contained in this prospectus, including information incorporated by reference as described above, or any prospectus supplement or that we have specifically referred you to. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of those documents or that any document incorporated by reference is accurate as of any date other than its filing date. You should not consider this prospectus to be an offer or solicitation relating to the securities in any jurisdiction in which such an offer or solicitation relating to the securities is not authorized. Furthermore, you should not consider this prospectus to be an offer or solicitation relating to the securities if the person making the offer or solicitation is not qualified to do so, or if it is unlawful for you to receive such an offer or solicitation.

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6,367,853 Shares

Common Stock

PROSPECTUS SUPPLEMENT