

ACHILLION PHARMACEUTICALS INC

Form 424B5

January 22, 2010

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Filed Pursuant to Rule 424(b)(5)
Registration File No. 333-162306

The information in this preliminary prospectus supplement and accompanying prospectus is not complete and may be changed. This prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus dated October 16, 2009) Subject to completion, dated January 22, 2010

Achillion Pharmaceuticals, Inc.

Shares of Common Stock

We are offering shares of our common stock, par value \$.001 per share. Each share will be sold at a negotiated price of \$ per share.

Our common stock trades on the NASDAQ Global Market under the symbol ACHN. On January 20, 2010, the last reported sale price of our common stock on the NASDAQ Global Market was \$2.70 per share.

On January 20, 2010, the aggregate market value of our outstanding common stock held by non-affiliates was \$73,865,056. We have not offered any securities during the past twelve months pursuant to General Instruction I.B.6 of Form S-3.

Investing in our securities involves significant risks. You should read this prospectus supplement and the accompanying prospectus carefully before you make your investment decision. See Risk Factors beginning on page S-5 of this prospectus supplement and page 3 of the accompanying prospectus, as well as the documents we file with the Securities and Exchange Commission that are incorporated by reference therein for more information.

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 supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

Per Share Total

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Public offering price	\$	\$
Underwriting discounts and commissions (1)	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) We have also agreed to reimburse the underwriters for certain out-of-pocket-expenses incurred by them up to an aggregate of \$10,000.

We have granted the underwriters the right to purchase up to an additional [] shares to cover over-allotments, if any.

We estimate the total expenses of this offering payable by us, excluding the underwriting discounts and commissions, will be approximately \$216,000. We anticipate that delivery of the shares will be made on or about January , 2010.

ROTH CAPITAL PARTNERS

NATIONAL SECURITIES

NOBLE FINANCIAL CAPITAL MARKETS

Prospectus Supplement dated January , 2010

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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 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 and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus outside of the United States. This prospectus supplement and the accompanying prospectus do 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 and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference therein, in making your investment decision. You should rely only on the information contained in, or incorporated by reference in, this prospectus supplement and the accompanying prospectus. We have not authorized anyone, and the underwriters have not authorized anyone to provide you with information different from that contained in this prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus may only be used where it is legal to sell these securities. You should not assume that the information that appears in this prospectus supplement, the accompanying prospectus and any document incorporated by reference is accurate as of any date other than their respective dates. Our business, financial condition, results of operations and prospects may have changed since the date of such information. You should also read and consider the information in the documents we have referred you to in the section entitled "Where You Can Find More Information."

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ABOUT THIS PROSPECTUS SUPPLEMENT

On October 2, 2009, we filed with the SEC a registration statement on Form S-3 (File No. 333-162306) utilizing a shelf registration process relating to the securities described in this prospectus supplement, which registration statement was declared effective on October 16, 2009. Under this shelf registration process, we may, from time to time, sell up to \$50 million in the aggregate of common stock, preferred stock, warrants and units.

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of our 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, 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 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 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.

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

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information about us, this offering and information appearing elsewhere in this prospectus supplement and in the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all of the information that you should consider before investing in the securities offered pursuant to this prospectus. After you read this summary, to fully understand this offering and its consequences to you, you should read and consider carefully the more detailed information and financial statements and related notes that we include in and/or incorporate by reference into this prospectus supplement and the accompanying prospectus, especially the section entitled Risk Factors. If you invest in our securities, you are assuming a high degree of risk. Except as otherwise specifically noted, all information in this prospectus supplement assumes the underwriters do not exercise their over-allotment option.

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 ACH-1625, a protease inhibitor for the treatment of chronic hepatitis C currently in phase I clinical testing, and ACH-1095, a NS4A antagonist also for the treatment of chronic hepatitis, which has been developed in collaboration with Gilead Sciences, Inc., or Gilead, and is currently in late-stage preclinical testing. In addition, we have established a pipeline of certain other 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 serious bacterial infections and elvucitabine for the treatment of HIV infection. We believe that there are several business advantages to developing anti-infective drugs as compared to developing drugs in other therapeutic areas. The emergence of drug resistance seen with current antiviral and antibacterial therapy creates a continuing need for new drugs, which we believe provides us with a large and growing business opportunity.

We have established our current drug candidate pipeline primarily through our internal discovery capabilities except for elvucitabine, which we in-license. Through both these efforts we have identified and are developing the following drug candidates and programs:

ACH-1625, a Protease Inhibitor for Chronic Hepatitis C Infection. We are evaluating ACH-1625, a protease inhibitor for the treatment of chronic hepatitis C, in a phase I/Ib clinical trial to assess the compound's safety, tolerability, pharmacokinetic properties and efficacy in healthy volunteers and HCV-infected subjects. ACH-1625 has demonstrated strong potency, unique pharmacokinetics and a good safety profile in preclinical studies, even at high doses. In the phase 1a segments of this clinical trial, as well as the two phase 1b segments that we have completed to date, ACH-1625 was demonstrated to be safe and well-tolerated at daily doses ranging from 50mg to 2000mg. Further, ACH-1625 was demonstrated to significantly reduce viral load in HCV patients by 3.94log₁₀ and 4.25log₁₀ at doses of 600 mg twice daily and 500 mg twice daily, respectively.

ACH-1095, a NS4A Antagonist for Chronic Hepatitis C Infection. We are evaluating ACH-1095 for the treatment of chronic hepatitis C. In preclinical and clinical studies, NS4A antagonists studied demonstrate potent inhibition of the replication of HCV, the virus that causes hepatitis C, by targeting a non-structural, or NS, viral protein called 4A. We believe these NS4A antagonists may offer several potential advantages compared to currently available treatments, including greater potency, a novel mechanism of action, lack of cross resistance and the potential for oral administration. We believe these compounds could be used in combination with the current standard of care, or with other therapies in development, to significantly improve treatment outcomes. Since November 2004, we have collaborated with Gilead under an exclusive license and collaboration agreement for the research, development and commercialization of compounds operating by this mechanism of action. In May 2009, Gilead indicated that it did not intend to initiate clinical development of ACH-1095. We believe that the compound should be advanced. Therefore, in September 2009, we entered into an amendment to our license and collaboration agreement with Gilead which allows us to continue to develop ACH-1095 independently, while the parties would jointly continue to advance additional compounds also operating by the NS4A mechanism of action. In November 2009, we requested a pre-IND consultation with the food and drug administration, or FDA, to discuss the most appropriate clinical development path for the compound. We anticipate that the consultation with the FDA will take place in the first quarter of 2010.

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ACH-702 for Drug Resistant Bacterial Infections. ACH-702 is a preclinical candidate with potency against a broad spectrum of bacterial pathogens including methicillin-resistant staphylococcus aureus, or MRSA. We completed a pre-IND consultation with the FDA on the most appropriate clinical development program for ACH-702. While the FDA provided guidance on an appropriate path toward regulatory approval for topical administration for ACH-702, the Division of Anti-Infective and Ophthalmology Products referred our request for additional guidance on systemic administration of ACH-702 to the Division of Special Pathogen and Transplant Products, or the DSPTP. We have assessed our strategic and development options for ACH-702 and are considering pursuing other applications, including dermatologic and ophthalmic use, use in medical biofilms and use against drug resistant tuberculosis. At this time, we do not anticipate moving into clinical development of ACH-702 and we do not expect to invest significantly in the future development of this compound without a collaboration partner or other external funding source.

Elvucitabine for HIV Infection. Elvucitabine is an antiviral we are developing for the treatment of HIV infection. We have evaluated elvucitabine in phase II clinical trials to further explore its safety and efficacy in HIV-infected patients over 48 and 96-weeks of treatment, and the open-label extension of one trial remains on-going through 2010. We currently retain full development and marketing rights to elvucitabine. However, we are currently seeking to enter a collaboration arrangement for elvucitabine and do not plan to advance elvucitabine into phase III clinical trials without a collaboration partner.

We have devoted and are continuing to devote substantially all of our efforts toward product research and development. We have incurred losses of \$185 million from inception through September 30, 2009 and had an accumulated deficit of \$199 million through September 30, 2009. Our net losses were \$19.2 million and \$19.5 million for the nine months ended September 30, 2009 and 2008, respectively. We have funded our operations primarily through:

proceeds from the sale of equity securities, including our initial public offering in October 2006 and a private placement of our common stock in August 2008;

borrowings from debt facilities; and

receipts from up-front and milestone payments, as well as cost-sharing receipts, from our collaboration partner, Gilead.

In July 2009, we entered into a Standby Equity Distribution Agreement, or SEDA, with YA Global Master SPV Ltd., or YA Global, pursuant to which we may, at our option, periodically sell YA Global shares of our common stock for a total purchase price of up to \$15.0 million. For each share of common stock purchased under the SEDA, YA Global will pay us ninety-five percent of the lowest volume weighted average price of the common stock on the NASDAQ Global Market during the five consecutive trading days following our advance notice. As of the date of this prospectus supplement, the full \$15.0 million remains available under the SEDA.

We expect to incur substantial and increasing losses for at least the next several years as we seek to:

continue clinical testing of ACH-1625;

determine the appropriate clinical development path for ACH-1095 and if appropriate, initiate clinical development of this compound; and

progress additional HCV drug candidates.

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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 normal 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 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.

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The Offering

Common stock offered	shares
Common stock to be outstanding after the offering(1)(2)	shares
Use of proceeds	We intend to use the net proceeds from this offering to continue clinical testing of ACH-1625, as well as to progress additional HCV drug candidates and for general corporate expenses. Pending the application of the net proceeds, we intend to invest the net proceeds in investment-grade, interest-bearing securities. See Use of Proceeds.
Risk factors	See Risk Factors beginning on page S-6 for a discussion of factors you should consider carefully before deciding to invest in our common stock.
Market for the common stock	Our common stock is listed on the NASDAQ Global Market under the symbol ACHN.

(1) Based on 26,705,646 shares outstanding as of December 31, 2009, and excludes:

3,319,638 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2009, at a weighted average exercise price of \$4.10 per share;

348 shares of our common stock available for future issuance as of December 31, 2009 under our 2006 stock incentive plan;

68,148 shares of our common stock available for future issuance as of December 31, 2009 under our 2006 employee stock purchase plan; and

2,784,939 shares of common stock issuable upon the exercise of warrants outstanding as of December 31, 2009, at a weighted average exercise price of \$3.74 per share.

(2) Assumes no exercise of the underwriters' over-allotment option.

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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, 2008, and in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2009 which are incorporated by reference herein, before making an investment decision with respect to the securities. 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.

Risks Relating to this Offering

You will experience immediate dilution in the book value per share of the common stock you purchase

Because the price per share of our common stock being offered is substantially higher than the book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. After giving effect to the sale by us of shares of common stock in this offering, and based on a public offering price of \$ per share in this offering and a pro forma net tangible book value per share of our common stock of \$ as of September 30, 2009, if you purchase shares in this offering, you will suffer immediate and substantial dilution of \$ per share in the net tangible book value of the common stock purchased. See Dilution for a more detailed discussion of the dilution you will incur in connection with 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 may 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.

If we do not comply with Nasdaq's listing requirements, our common stock could be delisted from the Nasdaq Global Market, which would negatively impact our liquidity, our stockholders' ability to sell shares and our ability to raise capital.

Our listing on the Nasdaq Global Market is conditioned upon our compliance with the Nasdaq Marketplace Rules. On November 13, 2009, we received notification from the NASDAQ Listings Qualification Department that our stockholders' equity of \$7,214,000, as reported on our Quarterly Report on Form 10-Q for the quarter ended September 30, 2009, does not comply with the minimum stockholders' equity requirement of \$10,000,000 for continued listing on The NASDAQ Global Market. On December 14, 2009, we received notification from the NASDAQ Listings Qualification Department that we had regained compliance for continued listing on The NASDAQ Global Market based on compliance with the market value standard. If the price of our common stock declines and we are unable to raise additional equity, we may once again receive a notification from the NASDAQ Listings Qualification Department that our stockholders' equity does not comply with the minimum stockholders' equity requirement for continued listing on The NASDAQ Global Market. The delisting of our common stock would significantly affect the ability of investors to trade our securities and would significantly negatively affect the value and liquidity of our common stock. In addition, the delisting of our common stock could materially adversely affect our ability to raise capital on terms acceptable to us or at all. Delisting from the NASDAQ Global Market could also have other negative results, including the potential loss of confidence by suppliers and employees, the loss of institutional investor interest and fewer business development opportunities.

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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 . These important factors include the factors that we identify in the documents that we incorporate by reference in this prospectus supplement. 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

We estimate that the net proceeds from the sale of the securities we are offering will be approximately \$ million, after deducting the estimated underwriting discounts and commissions and all other estimated offering expenses that are payable by us. If the underwriters exercise their over-allotment option in full, we estimate that the net proceeds to us will be approximately \$ million.

We currently intend to use the net proceeds from this offering to continue clinical testing of ACH-1625, as well as to progress additional HCV drug candidates and for general corporate expenses.

Pending the application of the net proceeds, we intend to invest the net proceeds in short-term investment-grade, interest-bearing securities.

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Our net tangible book value on September 30, 2009 was approximately \$, or approximately \$ per share of common stock. Net tangible book value is total assets minus the sum of liabilities and intangible assets. Net tangible book value per share is net tangible book value divided by the total number of shares of common stock outstanding.

After giving effect to the sale of shares of common stock offered by us in this offering at a price of \$ per share, less underwriting discounts and commissions and other estimated expenses of this offering payable by us, our adjusted net tangible book value on September 30, 2009 would have been approximately \$, or \$ per share of common stock. This represents an immediate increase in net tangible book value of \$ per share to our existing stockholders and an immediate dilution of \$ per share to anyone who purchases our common stock in the offering. The following table illustrates this calculation on a per share basis, assuming that we sell all of the shares we are offering:

Public offering price per share	\$
Net tangible book value per share as of September 30, 2009	\$
Increase per share attributable to the offering	\$
Adjusted net tangible book value per share as of September 30, 2009 after giving effect to the offering	\$
Dilution per share to new investors	\$

The foregoing table is based on 26,655,445 shares of common stock outstanding at September 30, 2009, which does not take into effect further dilution to new investors that could occur upon the exercise of outstanding options and warrants having a per share exercise price less than the public offering price.

In addition, the calculations in the foregoing table do not take into account, as of September 30, 2009:

2,666,968 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2009, at a weighted average exercise price of \$4.32 per share;

661,793 shares of our common stock available for future issuance as of September 30, 2009 under our 2006 stock incentive plan;

68,148 shares of our common stock available for future issuance as of September 30, 2009 under our 2006 employee stock purchase plan; and

2,933,339 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2009, at a weighted average exercise price of \$3.75 per share.

To the extent that any of our outstanding options or warrants are exercised, we grant additional options under our stock option plans 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 SECURITIES WE ARE OFFERING

In this offering, we are offering up to shares of common stock.

Common Stock

The material terms and provisions of our common stock and each other class of our securities which qualifies or limits our common stock are described under the caption Description of Capital Stock starting on page 5 of the accompanying prospectus.

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Table of Contents**UNDERWRITING**

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus supplement, Roth Capital Partners, LLC, Noble Financial Capital Markets and National Securities Corporation, as the underwriters, have, severally and not jointly, agreed to purchase, and we have agreed to sell to them, the number of shares of common stock at the public offering price, less the underwriting discounts and commissions, as set forth on the cover page of this prospectus supplement as indicated below:

Name	Number of Shares
Roth Capital Partners, LLC	
Noble Financial Capital Markets	
National Securities Corporation	
Total:	

The underwriters are offering the shares subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the underwriters to pay for and accept delivery of the shares offered by this prospectus supplement are subject to the approval of certain legal matters by its counsel and to other conditions. The underwriters are obligated to take and pay for all of the shares offered by this prospectus supplement if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' over-allotment option described below.

The underwriters initially propose to offer the shares directly to the public at the public offering price listed on the cover page of this prospectus supplement.

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent, including the absence of any material adverse change in our business and the receipt of customary legal opinions, letters and certificates.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to additional shares of common stock at the public offering price listed on the cover page of this prospectus supplement, less estimated underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus supplement and the accompanying prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

Commissions and Discounts

The following table shows the public offering price, underwriting discounts and commissions and proceeds before expenses to us. These amounts are shown assuming no exercise of the underwriters' over-allotment option.

	Per Share	Total
Public offering price	\$	\$
Underwriting discounts and commissions to be paid by us:	\$	\$
Proceeds, before expenses, to us	\$	\$

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The expenses of the offering, not including underwriting discounts and commissions, are estimated to be \$[] and are payable by us. We may also reimburse the underwriters for certain fees and legal expenses incurred by them in connection with this offering. In no event will the total amount of compensation paid to the underwriters and other securities brokers and dealers exceed 8.0% of the gross proceeds of the offering.

Quotation on the NASDAQ Global Market

Our common stock is listed on the NASDAQ Capital Market under the symbol ACHN.

No Sales of Similar Securities

We, and each of our executive officers and directors, have agreed with the underwriters, subject to certain exceptions, not to dispose of or hedge any of our shares of common stock or securities convertible into or exercisable or exchangeable for common stock for [] days after the date of this prospectus without first obtaining the written consent of the underwriters. The []-day lock-up period during which we and our executive officers and directors are restricted from engaging in transactions in our common stock or securities convertible into or exercisable or exchangeable for common stock is subject to extension such that, in the event that either (i) during the last 17 days of the lock-up period, we issue an earnings or financial results release or material news or a material event relating to us occurs, or (ii) prior to the expiration of the lock-up period, we announce that we will release earnings or financial results during the 16-day period beginning on the last day of the lock-up period, then in either case the expiration of the lock-up period will be extended until the expiration of the 18-day period beginning on the issuance of the earnings or financial results release or the occurrence of the material news or material event, as applicable, unless the underwriters waive, in writing, such an extension.

Price Stabilization, Short Positions

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters can close out a covered short sale by exercising the over-allotment option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. These transactions may be effected on The Nasdaq Global Market, in the over-the-counter market or otherwise. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933, as amended, and liabilities arising from breaches of representations and warranties contained in the underwriting agreement. We have also agreed to contribute to payments the underwriters may be required to make in respect of such liabilities.

A prospectus in electronic format may be made available on websites maintained by the underwriters. The underwriters may agree to allocate a number of shares to their online brokerage account holders. Internet distributions will be allocated by the underwriters on the same basis as other allocations.

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VALIDITY OF SECURITIES

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, Waltham, Massachusetts. Lowenstein Sandler PC, Roseland, New Jersey is acting as counsel for the underwriters in connection with various matters related to this offering.

EXPERTS

The financial statements incorporated in this prospectus supplement by reference to Achillion's Annual Report on Form 10-K for the year ended December 31, 2008 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given upon the authority of said firm as experts in auditing and accounting..

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and accompanying prospectus constitute a part of a registration statement on Form S-3 that we filed on October 2, 2009 with the SEC under the Securities Act. We refer you to this registration statement for further information about us and the common stock offered hereby.

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.

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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 supplement. Statements contained in documents that we file with the SEC and that are incorporated by reference in this prospectus supplement will automatically update and supersede information contained in this prospectus supplement, including information in previously filed documents or reports that have been incorporated by reference in this prospectus supplement, 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, 2008, as filed with the SEC on March 27, 2009;

Our Proxy Statement on Form DEF 14A, as filed with the SEC on April 24, 2009;

Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2009, June 30, 2009 and September 30, 2009, as filed with the SEC on May 15, 2009, August 3, 2009 and November 6, 2009, respectively;

Our Current Reports on Form 8-K, as filed with the SEC on January 8, 2009, February 9, 2009, July 6, 2009, September 4, 2009, November 17, 2009, December 15, 2009 and December 22, 2009.

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. A statement contained in a document incorporated by reference into this prospectus supplement 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 in any other subsequently filed document which is also incorporated in this prospectus supplement 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 supplement.

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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Subject to Completion, dated October 2, 2009

\$50,000,000

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 \$50,000,000. We may sell these securities to or through underwriters, directly to investors or through agents. This prospectus describes the general manner in which 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 September 30, 2009 was \$1.60 per share. We have not offered any securities during the past twelve months pursuant to General Instruction I.B.6 of Form S-3.

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 October 16, 2009.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

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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 \$50,000,000. 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 ACH-1625, a protease inhibitor for the treatment of chronic hepatitis C currently in phase I clinical testing, and ACH-1095, a NS4A antagonist also for the treatment of chronic hepatitis C, which has been developed in collaboration with Gilead Sciences, Inc., or Gilead, and is currently in late stage preclinical testing. Gilead maintains certain rights to ACH-1095 under an existing license and collaboration agreement. In addition, we have established a pipeline of certain other 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 serious bacterial infections and elvucitabine for the treatment of HIV infection.

We have devoted and are continuing to devote substantially all of our efforts toward product research and development. We have funded our operations primarily through:

proceeds from the sale of equity securities, including our initial public offering in October 2006 and a private placement of our common stock in August 2008;

borrowings from debt facilities; and

receipts from up-front and milestone payments, as well as cost-sharing receipts, from our collaboration partner, Gilead.

In addition, in July 2009, we entered into a Standby Equity Distribution Agreement whereby we have the option, at our sole discretion, to sell up to \$15.0 million of common stock to YA Global.

We expect to incur substantial and increasing losses for at least the next several years as we seek to:

continue clinical testing of ACH-1625;

determine the appropriate clinical path for ACH-1095 and continue clinical development of this compound; and

progress additional HCV drug candidates.

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 normal 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 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.

We believe that there are several business advantages to developing anti-infective drugs as compared to developing drugs in other therapeutic areas. The emergence of drug resistance seen with current antiviral and antibacterial therapy creates a continuing need for new drugs, which we believe provides us with a large and growing business opportunity.

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, 2008 and in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2009 on file with the SEC, which are 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. We 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.

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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 \$50,000,000.

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

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 September 30, 2009 there were 26,655,445 shares of our common stock outstanding and 71 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 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.

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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.

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.

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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 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, 2008 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.

Fletcher Spaght, Inc. has consented to reference in this Registration Statement on Form S-3, and any further amendments or supplements thereto, filed by Achillion Pharmaceuticals, Inc. and to the incorporation by reference therein to Achillion Pharmaceutical Inc.'s Annual Report on Form 10-K for the year ended December 31, 2008, as well as the references to and summary of our valuation report included therein.

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.

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, 2008, as filed with the SEC on March 27, 2009;

Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2009 and June 30, 2009, as filed with the SEC on May 15, 2009 and August 3, 2009, respectively;

Our Current Reports on Form 8-K, as filed with the SEC on January 8, 2009, February 9, 2009, March 26, 2009, July 6, 2009, July 30, 2009 and September 4, 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

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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.

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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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Shares of Common Stock

Achillion Pharmaceuticals, Inc.

PROSPECTUS SUPPLEMENT

ROTH CAPITAL MARKETS

NATIONAL SECURITIES

NOBLE FINANCIAL CAPITAL MARKETS

January , 2010