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PROSPECTUS
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23,150,165 SHARES OF COMMON STOCK
AASTROM BIOSCIENCES, INC.

This Prospectus relates to the offer and sale of 23,150,165 shares of common stock being offered by RGC International Investors, LDC. The shares are issuable upon conversion of shares of our 1998 Series I Convertible Preferred Stock, our 1999 Series III Convertible Preferred Stock and upon exercise of warrants issued in connection with the sale of the 1999 Series III Convertible Preferred Stock.

Our common stock is quoted on the Nasdaq National Market under the symbol "ASTM." The selling stockholder will determine the price it may offer or sell shares of our common stock independent of Aastrom. On December 8, 1999, the last sale price of our common stock was $1.188 and 19,479,643 shares were issued and outstanding.

INVESTING IN THE COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD CONSIDER CAREFULLY THE RISK FACTORS BEGINNING ON PAGE 5 OF THIS PROSPECTUS BEFORE MAKING A DECISION TO PURCHASE OUR STOCK.

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NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

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THE DATE OF THIS PROSPECTUS IS DECEMBER 23, 1999.

You should rely only on the information provided or incorporated by reference in this prospectus. We have not authorized anyone to provide you with additional or different information. This document may only be used where it is legal to sell these securities. You should not assume that any information in this prospectus is accurate as of any date other than the date of this prospectus.

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SUMMARY

Because this is a summary, it does not contain all the information about us that may be important to you. You should read the more detailed information and the financial statements and related notes which are incorporated by reference in this Prospectus.

Aastrom

Aastrom develops proprietary process technologies and devices for a range of cell therapy applications. The AastromReplicell(TM) System is our lead product under development, and consists of a clinical cell culture system that operates single-use therapy kits tailored for patient therapy in the emerging cell therapy market. Commercialization of the AastromReplicell(TM) System for use in stem cell therapy has begun in Europe. However, because of funding limitations, we have suspended marketing efforts in Europe until additional funding is obtained. Aastrom believes that the AastromReplicell(TM) System method will be a cost-effective, less invasive and less time consuming alternative, or improvement to, currently available stem cell collection methods and may enhance the clinical utility of umbilical cord blood transplants by expanding the number of cells available for transplant. The AastromReplicell(TM) System is designed as a platform product which implements Aastrom's pioneering stem cell replication technology. Aastrom believes that the AastromReplicell(TM) System can be modified to produce a wide variety of other cell types for selected emerging therapies currently in development.

Stem cell therapy is a form of cell therapy used to restore blood and immune system function to cancer patients following chemotherapy or radiation therapy. Current stem cell collection methods, including bone marrow harvest and peripheral blood progenitor cell mobilization, can be costly, invasive and time-consuming for both medical personnel and patients. Aastrom believes that the AastromReplicell(TM) System will offer significant advantages over traditional stem cell collection methods. The AastromReplicell(TM) System is intended to be used to produce cells used for stem cell therapy from a small starting volume of bone marrow or umbilical cord blood cells. Further, in an evaluation of seven tumor-contaminated bone marrow samples that were expanded with the AastromReplicell(TM) System process, the presence of breast cancer cells in each sample was either substantially reduced or was no longer detectable. Aastrom believes that the combination of passive tumor cell depletion during culture with the lower starting volume cells used for the procedure may result in a procedure that offers a tumor-free or tumor-reduced cell product for transplant. Although Aastrom may not market the AastromReplicell(TM) System in the United States for stem cell therapy unless and until it receives FDA and other necessary regulatory approvals, Aastrom has already completed production-level versions of the AastromReplicell(TM) System and has obtained permission to affix the CE Mark to such versions. This has allowed Aastrom to initiate a limited product launch in Europe.

Aastrom's principal executive offices are located at 24 Frank Lloyd Wright Drive, P.O. Box 376, Ann Arbor, MI 48106. Aastrom's telephone number is (734) 930-5555.

The Offering

Common stock offered by the selling shareholder..... 23,150,165 shares

For purposes of estimating the number of shares of common stock covered by this prospectus Aastrom calculated the number of shares of common stock issuable in connection with the conversion of 1998 Series I Convertible Preferred Shares (the "Series I Shares") and the 1999 Series III Convertible Preferred Shares (the "Series III Shares") (based on a conversion price of $0.475875, which is the lowest

average of the closing bid prices of the common stock reported on the Nasdaq National Market for the lowest five consecutive trading days during the twenty trading days preceding December 8, 1999 multiplied by 94% pursuant to the terms of the Series I Shares and Series III Shares) and added the number of shares issuable upon exercise of the warrants issued in connection with the sale of the Series III Shares and added those shares carried forward from Registration Statement No. 333-81399 and Registration Statement No. 333-60125.

RISK FACTORS

You should carefully consider the following risk factors before purchasing our common stock. The risks and uncertainties described below are not the only ones we face. There may be additional risks and uncertainties that are not known to us or that we do not consider to be material at this time. If the events described in these risks occur, our business, financial condition and results of operations would likely suffer. This prospectus contains forward-looking statements which involve risks and uncertainties. Aastrom's actual results may differ significantly from the results discussed in the forward-looking statements. This section discusses some of the factors that might cause those differences.

We Cannot Be Certain That We Will Be Able to Raise the Required Capital to Conduct Our Operations and Develop Our Products.

We will require substantial capital resources in order to conduct our operations and develop our products. Based on our declining level of capital resources and our current financing alternatives, we recently reduced our operations to align the existing resources with our focus on pursuing corporate strategic alternatives, including a possible merger or acquisition. This reduction in our operating activities has negatively impacted our ability to develop our products. Aastrom anticipates that its available cash and expected interest income will only be sufficient to finance its current activities into early 2000. If we can not obtain additional funding, Aastrom will be forced to further substantial reductions in the scope and size of its operations and has only a very limited amount of capital to sustain its operations, even at a reduced scale. This estimate is based on certain assumptions, which could be negatively impacted by the matters discussed under this heading and elsewhere under the caption "Risk Factors." In order to resume our earlier activities, grow and expand our business, and to introduce our product candidates into the marketplace, Aastrom will need to raise additional funds. We will also need additional funds or a collaborative partner to finance the research and development activities of Aastrom's product candidates for the expansion of additional cell types.

Aastrom's future capital requirements will depend upon many factors, including:

- continued scientific progress in its research and development programs;
- costs and timing of conducting clinical trials and seeking regulatory approvals and patent prosecutions;
- competing technological and market developments;
- the ability of Aastrom to establish additional collaborative relationships; and
- effective commercialization activities and facilities expansions if and as required.

Because of our long-term funding requirements, we may attempt to access the public or private equity markets if and whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time. This additional funding may not be available to Aastrom on reasonable terms, or at all. If adequate funds are not available, Aastrom may be required to further delay or terminate research and development programs, curtail capital expenditures, and reduce business development and other operating activities.

If We Cannot Complete Our Product Development Activities Successfully, Our Ability to Operate or Finance Operations Will Be Severely Limited.

Commercialization in the United States of our lead product candidate, the AastromReplicell(TM) Cell Production System ("System"), will require additional research and development by Aastrom as well as substantial clinical trials. While we have commenced initial marketing on a limited basis of the Aastrom Replicell(TM) System in Europe, we believe that the United States will be the principal market for our products. Aastrom may not be able to successfully complete development of the AastromReplicell(TM) System or its other product candidates, or successfully market its technologies or product candidates. Aastrom or its potential collaborators may encounter problems and delays relating to research and development, regulatory approval and intellectual property rights of Aastrom's technologies and product candidates. Aastrom's research and development programs may not be successful, and its cell culture technologies and product candidates may not facilitate the ex vivo production of cells with the expected biological activities in humans. Our technologies and product candidates may not prove to be safe and efficacious in clinical trials, and we may not obtain the intended regulatory approvals for our technologies or product candidates and the cells produced in such products. If any of these events happen, we may not have adequate resources to continue operations for the period required to resolve the issue delaying commercialization and we may not be able to raise capital to finance our continued operation during the period required for resolution of that issue.

We Must Successfully Complete Our Clinical Trials to be Able to Market Our Products.

To be able to market products in the United States, Aastrom must demonstrate, through extensive preclinical studies and clinical trials, the safety and efficacy of its processes and product candidates, together with the cells produced by such processes in such products, for application in the treatment of humans. Aastrom is currently conducting a pivotal clinical trial to demonstrate the safety and biological activity of patient-derived cells produced in the AastromReplicell(TM) System. Contingent upon the availability of resources, we intend to commence two other pivotal clinical trials to demonstrate the safety and biological activity of umbilical cord blood cells produced in the AastromReplicell(TM|) System. If our clinical trials are not successful, our products may not be marketable.

Our ability to complete our clinical trials in a timely manner depends on many factors, including the rate of patient enrollment. Patient enrollment can vary with the size of the patient population, the proximity of suitable patients to clinical sites, perceptions of the utility of stem cell therapy for the treatment of certain diseases and the eligibility criteria for the study. We have experienced delays in patient accrual in our previous and current clinical trials. If we experience future delays in patient accrual, we could experience increased costs and delays associated with clinical trials which would impair our product development programs and our ability to market our products. Furthermore, the FDA monitors the progress of clinical trials and it may suspend or terminate clinical trials at any time due to patient safety or other considerations.

Failure to Obtain and Maintain Required Regulatory Approvals Would Severely Limit Our Ability to Sell Our Products.

We must obtain the approval of the U.S. Food and Drug Administration (the "FDA") before commercial sales of Aastrom's product candidates may commence in the United States, which we believe will be the principal market for our products. We may also be required to obtain additional approvals from foreign regulatory authorities to continue or increase our sales activities in those jurisdictions. If we cannot demonstrate the safety, reliability and efficacy of our product candidates, or

of the cells produced in such products, we may not be able to obtain required regulatory approvals. Many of the patients enrolled in the clinical trials will have previously undergone extensive treatment which will have substantially weakened the patients and may have irreparably damaged the ability of their blood and immune systems to recover. Some patients undergoing the transplant recovery process have died, from causes that were, according to the physicians involved, unrelated to the AastromReplicell(TM) System procedure, and it is possible that other patients may die or suffer severe complications during the course of either the current trials or future trials. In addition, patients receiving cells produced with Aastrom's technologies and product candidates may not demonstrate long-term engraftment in a manner comparable to cells obtained from current stem cell therapy procedures. If we cannot demonstrate the safety or efficacy of our technologies and product candidates, including long-term sustained engraftment, or if one or more patients die or suffer severe complications, the FDA or other regulatory authorities could delay or withhold regulatory approval of our product candidates.

Finally, even if we obtain regulatory approval of a product, that approval may be subject to limitations on the indicated uses for which it may be marketed. Even after granting regulatory approval, the FDA, other regulatory agencies, and governments in other countries continue to review and inspect marketed products, manufacturers and manufacturing facilities. Later discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions on the product or manufacturer, including a withdrawal of the product from the market. Further, governmental regulatory agencies may establish additional regulations which could prevent or delay regulatory approval of our products.

Even If We Obtain Regulatory Approvals to Sell Our Products, Lack of Commercial Acceptance Would Impair Our Business.

Aastrom's product development efforts are primarily directed toward obtaining regulatory approval to market the AastromReplicell(TM) System as an alternative to, or as an improvement for, the bone marrow harvest and peripheral blood progenitor cell stem cell collection methods. These stem cell collection methods have been widely practiced for a number of years, and Aastrom's technologies or product candidates may not be accepted by the marketplace as readily as these or other competing processes and methodologies. Additionally, our technologies or product candidates may not be employed in all potential applications being investigated, and any limited applications would limit the market acceptance of our technologies and product candidates and our potential revenues. As a result, even if we obtain all required regulatory approvals, we cannot be certain that our products and processes will be adopted at a level that would allow us to operate profitably.

Failure of Third Parties to Manufacture Component Parts or Provide Limited Source Supplies Would Impair Our New Product Development and Our Sales Activities.

Aastrom relies solely on third parties to manufacture its product candidates and their component parts. Aastrom also relies solely on third party suppliers to provide necessary key mechanical components, as well as growth factors and other materials used in the cell expansion process. We would not be able to obtain alternate sources of supply for many of these items on a short-term basis. If any of our key manufacturers or suppliers fail to perform their respective obligations or if our supply of growth factors, components or other materials is limited or interrupted, we would not be able to conduct clinical trials or market our product candidates on a timely and cost-competitive basis, if at all.

Furthermore, some of the compounds used by Aastrom in its current stem cell expansion processes involve the use of animal-derived products. Suppliers or regulatory authorities may limit or

restrict the availability of such compounds for clinical and commercial use. Any restrictions on these compounds would impose a potential competitive disadvantage for Aastrom's products. If Aastrom was not able to develop or obtain alternative compounds, its product development and commercialization efforts would be harmed.

Finally, Aastrom may not be able to continue its present arrangements with its suppliers, supplement existing relationships, establish new relationships or be able to identify and obtain the ancillary materials that are necessary to develop its product candidates in the future. Aastrom's dependence upon third parties for the supply and manufacture of such items could adversely affect Aastrom's ability to develop and deliver commercially feasible products on a timely and competitive basis.

Our Past Losses and Expected Future Losses Cast Doubt on Our Ability to Operate Profitably.

Aastrom was incorporated in 1989 and has experienced substantial operating losses since inception. As of September 30, 1999, Aastrom has incurred net operating losses totaling approximately $73 million. These losses have resulted principally from costs incurred in the research and development of Aastrom's cell culture technologies and the AastromReplicell(TM) System, general and administrative expenses, and the prosecution of patent applications. Aastrom expects to incur significant operating losses until product sales increase, primarily owing to its research and development programs, including preclinical studies and clinical trials, and the establishment of marketing and distribution capabilities necessary to support commercialization efforts for its products. Aastrom cannot predict with any certainty the amount of future losses. Aastrom's ability to achieve profitability will depend, among other things, on successfully completing the development of its product candidates, obtaining regulatory approvals, establishing manufacturing, sales and marketing arrangements with third parties, and raising sufficient funds to finance its activities. Aastrom may not be able to achieve or sustain profitability.

Given Our Limited Internal Sales and Marketing Capabilities, We Need to Develop Collaborative Relationships to Sell, Market and Distribute Our Products.

While we have commenced initial marketing on a limited basis of the AastromReplicell(TM) System in Europe, we have only limited internal sales, marketing and distribution capabilities. We intend to market our products through collaborative relationships with companies for sales, marketing and distribution capabilities. If we cannot develop and maintain those relationships, we would have only limited abilities to market, sell and distribute our products. Even if we are able to enter into those relationships, they may not succeed or be sustained on a long-term basis, and termination would require us to develop alternate arrangements at a time when we need sales, marketing or distribution capabilities to meet existing demand. For example, in November 1998 Aastrom and COBE BCT terminated their strategic alliance for the worldwide distribution of the AastromReplicell(System for stem cell therapy and related uses and Aastrom is seeking to enter into other arrangements relating to the development and marketing of our product candidates.

Any Changes in the Governmental Regulatory Classifications of Our Products Could Prevent, Limit or Delay Our Ability to Market or Develop Our Products.

The FDA establishes regulatory requirements based on the classification of a product. Although the FDA has indicated it intends to regulate the AastromReplicell(TM) System for stem cell therapy as a Class III medical device, the FDA may ultimately choose to regulate the AastromReplicell(TM) System under another category. Because our product development programs are designed to satisfy the

standards applicable to Class III medical devices, a change in the regulatory classification would affect our ability to obtain FDA approval of our products. Also, the FDA is in the process of developing its requirements with respect to somatic cell therapy and gene cell therapy products. Until the FDA issues definitive regulations covering our product candidates, the regulatory guidelines or requirements for approval of such product candidates will continue to be uncertain.

If We Do Not Keep Pace With Our Competitors and With Technological and Market Changes, Our Products May Become Obsolete and Our Business May Suffer.

The market for our product is very competitive and is subject to rapid technological changes. Many of Aastrom's competitors have significantly greater resources, more product candidates and have developed product candidates and processes that directly compete with Aastrom's products. Aastrom's competitors may have developed, or could in the future develop, new technologies that compete with our products or even render our products obsolete. In addition, some recently published studies have suggested that stem cell therapy, which is the current principal market for our products, may have limited clinical benefit in the treatment of breast cancer, which is a significant portion of the current overall stem cell transplant market. Our products are designed to improve upon traditional stem cell collection methods, but even if we are able to demonstrate improved or equivalent results, practitioners may not switch to our new processes. Given the experience and expertise associated with traditional methods, if we can not develop our cell production procedure to lead to a less expensive and quicker recovery time than seen with the traditional methods, we will suffer a competitive disadvantage. Finally, to the extent that others develop new technologies that address the diseases and health conditions we have targeted, our business will suffer.

If Our Patents and Proprietary Rights Do Not Provide Substantial Protection, Our Business and Competitive Position Will Suffer.

Our success depends in large part on our ability to develop or license and protect proprietary products and technologies. However, we cannot assure you that patents will be granted on any of our pending or future patent applications. We also cannot be assured that the scope of any of our issued patents will be sufficiently broad to offer meaningful protection. In addition, our issued patents or patents licensed to us could be successfully challenged, invalidated or circumvented so that our patent rights would not create an effective competitive barrier. Furthermore, Aastrom relies on licenses granted by the University of Michigan for certain of its patent rights. If Aastrom breaches such agreements or otherwise fails to comply with such agreements, or if such agreements expire or are otherwise terminated, Aastrom may lose its rights under the patents held by the University of Michigan. Aastrom also relies on trade secrets and unpatentable know-how which it seeks to protect, in part, by confidentiality agreements with its employees, consultants, suppliers and licensees. These agreements may be breached, and Aastrom might not have adequate remedies for any breach. If this were to occur, or business and competitive position would suffer.

Intellectual Property Litigation Could Harm Our Business.

Aastrom's success will also depend in part on its ability to develop commercially viable products without infringing the proprietary rights of others. Although Aastrom has not been subject to any filed infringement claims, other patents could exist or could be filed which would prohibit or limit our ability to market our products or maintain our competitive position. In the event of an intellectual property dispute, Aastrom may be forced to litigate. Intellectual property litigation would divert management's attention from developing our products and would force Aastrom to incur substantial costs regardless of

whether we are successful. An adverse outcome could subject Aastrom to significant liabilities to third parties, and force Aastrom to curtail or cease its development and sale of its products and processes.

The Market for Our Products Will Be Heavily Dependent on Third Party Reimbursement Policies.

Aastrom's ability to successfully commercialize its product candidates will depend on the extent to which government healthcare programs, such as Medicare and Medicaid, as well as private health insurers, health maintenance organizations and other third party payors will pay for our products and related treatments. Reimbursement by third-party payors depends on a number of factors, including the payor's determination that use of the product is safe and effective, not experimental or investigational, medically necessary, appropriate for the specific patient and cost-effective. Reimbursement in the United States or foreign countries may not be available or maintained for any of Aastrom's product candidates. If we do not obtain approvals for adequate third-party reimbursements, we may not be able to establish or maintain price levels sufficient to realize an appropriate return on our investment in product development. Any limits on reimbursement available from third-party payors may reduce the demand for, or negatively affect the price of, our products.

Potential Products Liability Claims Could Effect Our Earnings and Financial Condition.

Aastrom faces an inherent business risk of exposure to product liability claims in the event that the use of the AastromReplicell(TM) System during research and development efforts, including clinical trials, or after commercialization results in adverse effects. As a result, Aastrom may incur significant product liability exposure, which could exceed existing insurance coverage. We may not be able to maintain adequate levels of insurance at reasonable cost and/or reasonable terms. Excessive insurance costs or uninsured claims would increase our operating loss and affect our financial condition.

If We Cannot Attract and Retain Key Personnel, Our Business Will Suffer.

Our success depends in large part upon our ability to attract and retain highly qualified scientific and management personnel. We face competition for such personnel from other companies, research and academic institutions and other entities. For example, since our initial public offering in February 1997 three of the six executive officers who were with Aastrom at the time have since left for positions with other organizations and Aastrom has hired two new executive officers to assume their responsibilities. We may not be successful in hiring or retaining key personnel.

The 1998 Series I Preferred Shares and the 1999 Series III Preferred Shares Have the Potential for Substantial Dilution.

As of December 8, 1999, there are 4,000 shares of Series I Shares, and 1,850 shares of Series III Shares outstanding (together, the "Preferred Shares"). The Preferred Shares are each convertible into a number of shares of common stock that increases as the current market price of the common stock decreases. If the selling shareholder was able to and did convert all of its Preferred Shares as of December 8, 1999, the selling shareholder would have received approximately 13.1 million shares of common stock. This number of shares could become significantly greater in the event of a decrease in the trading price of the common stock. Purchasers of common stock could therefore experience substantial dilution of their investment upon conversion of the Preferred Shares. The Preferred Shares are not registered and may be sold only if registered under the Securities Act or sold in accordance with an applicable exemption from registration, such as Rule 144. The shares of common stock into which the Preferred Shares may be converted are being registered pursuant to this Registration Statement.

Our Stock Price Has Been Volatile and Future Sales of Substantial Numbers of Our Shares Could Have an Adverse Effect on the Market Price of Our Shares.

The market price of shares of our common stock has been volatile. The price of our common stock may continue to fluctuate in response to a number of events and factors, such as:

- clinical trial results;
- the amount of our cash resources and our ability to obtain additional funding;
- announcements of research activities, business developments, technological innovations or new products by us or our competitors;
- changes in government regulation;
- disputes concerning patents or proprietary rights;
- changes in our revenues or expense levels;
- public concern regarding the safety, efficacy or other aspects of the products or methodologies we are developing; and
- changes in recommendations by securities analysts.

Any of these events may cause the price of our shares to fall, which may adversely affect our business and financing opportunities. In addition, the stock market in general and the market prices for biotechnology companies in particular have experience significant volatility that often has been unrelated to the operating performance or financial conditions of such companies. These broad market and industry fluctuations may adversely affect the trading price of our shares, regardless of our operating performance or prospects. For example, within the last year, our stock price has experienced a day where it traded at approximately twice the previous day's closing price and another day when it dropped by approximately 40% from the previous day's closing price.

In addition, sales, or the possibility of sales, of substantial numbers of shares of common stock in the public market could adversely affect prevailing market prices of shares of common stock. Our employees hold a significant number of options to purchase shares, many of which are presently exercisable. Employees may exercise their options and sell shares shortly after such options become exercisable, particularly if they need to raise funds to pay for the exercise of such options or to satisfy tax liabilities that they may incur in connection with exercising their options. Additionally, beginning January 1, 2001, COBE BCT will be able to sell all of its approximately 2.4 million shares of our common stock without restriction.

Our Corporate Documents and Michigan Law Contain Provisions That May Make It More Difficult For Us to Be Acquired.

Our board of directors has the authority, without shareholder approval, to issue additional shares of preferred stock and to fix the rights, preferences, privileges and restrictions of these shares without any further vote or action by our shareholders. This authority, together with certain provisions of our charter documents, may have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire, control of our company. This effect could occur even if our shareholders consider the change in control to be in their best interest.

We May Be Required to Redeem a Portion of the Series I or Series III Shares, Which Would Significantly Reduce Our Limited Cash Resources.

The holders of Series I Shares or Series III Shares may require us to redeem some or all of those shares. These redemption rights would be triggered if we fail to issue shares of common stock on conversion of the Series I Shares or Series III Shares, if we fail to maintain the effectiveness of a registration statement for the resale of those shares of common stock, if we are subject to bankruptcy or insolvency proceedings, or if we fail to maintain our listing on the Nasdaq stock market. Any redemption would reduce our available cash resources, which are already very limited.

Our Stock May Be Delisted From Nasdaq, Which Could Affect its Market Price and Liquidity.

We are required to meet certain financial tests (including a minimum bid price of our common stock of $1.00 and $5 million in tangible net-worth) to maintain the listing of our common stock on the Nasdaq National Market. As a result of recent price fluctuations, our common stock price has fallen below the minimum level and we have been notified that our common stock will be delisted if the Company does not regain compliance with the minimum listing requirements prior to February 16, 2000, unless an exemption is granted. If that happened the market price and liquidity of our Common Stock would be impaired.

Absence of Dividends Could Reduce Our Attractiveness to Investors.

Some investors favor companies that pay dividends, particularly in market downturns. Aastrom has never paid cash dividends on its common stock and does not anticipate paying any cash dividends on its common stock in the foreseeable future. Therefore, your return on this investment will depend on your ability to sell our stock at a profit.

Year 2000 Issues May Adversely Affect Our Computer Systems and Our Business.

Many currently installed computer systems and software products cannot distinguish 20/th/ century dates from 21/st/ century dates. As a result, some computer systems and/or software will experience operating difficulties unless they are modified or upgraded to adequately process information involving, related to, or dependent upon the century change. In light of the potentially broad effects of the year 2000 on a wide range of business systems, we may be affected. We utilize and are dependent upon data processing computer hardware and software to conduct our business. We have completed an assessment of our own computer systems and based upon this assessment, we believe our computer systems are substantially "Year 2000 compliant;" that is, our computer systems are capable of adequately distinguishing 21/st/ century dates from 20/th/ century dates. However, we may not have identified all significant Year 2000 problems in our computer systems, and therefore may be subject to unknown risk and expense. Based on our internal assessment, we believe that the most likely worst case scenario would involve our suppliers and manufacturers. We have not determined the extent, or completed activities to minimize the risk of the computer systems of our suppliers and manufacturers being not Year 2000 compliant, or not becoming compliant on a timely basis. We expect to make inquires with these suppliers through the end of 1999. Year 2000 problems could prevent any of our suppliers from timely delivery of products or services that we need. We currently believe that our costs to address the Year 2000 issue relating to our suppliers will not be material, and that these costs will be funded from our operating cash flows. To the extent practical, we intend to identify alternative suppliers and manufacturers in the event our preferred suppliers cannot deliver products or services that we need on a timely basis. Our expectations of Year 2000 costs relating to our suppliers and manufacturers are only

estimates, which were derived from numerous assumptions of future events, including the continued availability of resources and third-party remediation plans with regard to year 2000 issues. These estimates may not be correct and actual results could differ materially from these estimates.

Forward-Looking Statements

This prospectus contains certain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act. These forward-looking statements include statements regarding:

- uncertainties related to potential strategic collaborations with others;
- future capital needs and uncertainty of additional funding;
- uncertainties related to product development and marketability;
- uncertainties related to clinical trials;
- manufacturing and supply uncertainties and dependence on third parties;
- anticipation of future losses;
- limited sales and marketing capabilities;
- uncertainty of regulatory approval and extensive government regulation;
- competition and technological change;
- uncertainty regarding patents and proprietary rights;
- no assurance of third party reimbursement;
- hazardous materials; and
- potential product liability and availability of insurance.

These statements are subject to risks and uncertainties, including those set forth in this Risk Factors section, and actual results could differ materially from those expressed or implied in these statements. All forward-looking statements included in this prospectus are made as of the date hereof. Aastrom assumes no obligation to update any such forward-looking statement or reason why actual results might differ.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's public reference rooms located at Room 1024, 450 Fifth Street, N.W., Washington, D.C. 20549, at The Citicorp Center, 500 West Madison Street, Suite 1400, Chicago, Illinois 60661, and at Seven World Trade Center, Suite 1300, New York, New York 10048. Please call the SEC at 1800SEC0330 for further information on the public reference rooms. Our filings with the SEC are also available to the public on the SEC's Internet web site at http://www.sec.gov.

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we file with the SEC later will automatically update and supersede the information in this Prospectus or incorporated by reference. The following documents filed by us and any future filings made by us with the SEC under Sections 13(a), 13(c) 14 or 15(d) of the Securities Exchange Act of 1934, until the selling shareholder sells all of the common stock offered hereby, are incorporated by reference in this Prospectus:

(a) the Company's Annual Report on Form 10K for the year ended June 30, 1999 (Commission File No.: 000-22025), but specifically excluding The Report of the Independent Accountants thereto which is superceded by the Company's current report on Form 8-K filed on December 10, 1999 (Commission File No. 000-22025);

(b) the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 1999 (Commission File No. 000-22025);

(c) the Company's current report of Form 8-K filed with the Commission on October 27, 1999 (Commission File No.: 000-22025);

(d) the Company's current report of Form 8-K filed with the Commission on December 10, 1999 (Commission File No.: 000-22025); and

(e) the Company's Registration Statement on Form 8-A (Commission File No.: 000-22025).

YOU MAY REQUEST A COPY OF THESE FILINGS, AT NO COST, BY WRITING OR TELEPHONING US AT AASTROM BIOSCIENCES, INC., 24 FRANK LLOYD WRIGHT DRIVE, P.O. BOX 376, ANN ARBOR, MICHIGAN 48106, TELEPHONE NUMBER (734) 930-5555, ATTENTION: CHIEF FINANCIAL OFFICER.

SELLING SHAREHOLDER

This prospectus relates to the offering by RGC International Investors, LDC for resale of up to 23,150,165 shares of common stock. The selling shareholder will acquire the shares upon (a) conversion, from time to time, of the Series I Shares that it acquired in July 1998 or the Series III Shares that it acquired in May 1999, and (b) exercise, from time to time, of the warrants that it holds. The table below sets forth the following information with respect to the selling shareholder as of December 8, 1999:

- the name and position or other relationship with Aastrom within the past three years, if any, of the selling shareholder,
- the number of Aastrom's outstanding shares of common stock beneficially owned by the selling shareholder (including shares obtainable under options exercisable within sixty days of such date) prior to the offering hereby,
- the number of such shares being offered hereby,
- the number and percentage of Aastrom's outstanding shares of common stock to be beneficially owned by the selling shareholder after completion of the sale of common stock being offered hereby.

The number of shares reported as being beneficially owned after the offering represents shares of common stock issuable upon conversion of another outstanding series of preferred stock and exercise of the warrants. These shares of common stock have been registered for sale and they may be sold before or after the shares that may be sold pursuant to this prospectus. We cannot assume that the selling shareholder will convert any Series I Shares or Series III Shares or exercise any of the warrants or sell any or all of the shares offered hereby.

Selling Shareholder	Number of Shares Beneficially Owned Prior to the Offering	Number of Such Shares Being Offered	Number of Shares Beneficially Owned After the Offering	Percentage of Aastrom Stock Owned After the Offering
RGC International Investors, LDC	13,371,069	23,150,165	0	0

The number of shares set forth in the table represents an estimate of the number of shares of common stock to be offered by the selling shareholder. Based on a conversion price of $0.475875 on December 8, 1999, the selling shareholder would receive 13,371,069 shares of common stock upon conversion of the Series I Shares, Series III Shares and exercise of the warrants. This prospectus covers the sale of 23,150,165 of the shares of common stock we expect to be issued to the selling shareholder based on the current conversion price less 7,958,729 shares which is the number of shares previously registered by Registration Statement No. 333-81399 and Registration Statement No. 333-60125. If the conversion price decreases 10% to $0.4282875, the number of shares issuable upon conversion of the Series I Shares and Series III Shares would increase to 14,523,410, which would dilute the ownership

interests of existing shareholders by approximately 4.4%. The actual number of shares of common stock issuable upon conversion of Series I Shares and Series III Shares is indeterminate and is subject to adjustment. Therefore, the actual number of shares could be materially less or more than this estimate depending on several unpredictable factors, principally the timing of any future conversions and the market prices of the common stock shortly before the conversion. The actual number of shares of common stock offered hereby, and included in the Registration Statement of which this Prospectus is a part, also includes an additional number of shares of common stock that may be issued or issuable upon conversion of the Series I Shares and Series III Shares by reason of any stock split, stock dividend or similar transaction involving the common stock, in order to prevent dilution, in accordance with Rule 416 under the Securities Act.

The number of shares of common stock set forth above as beneficially owned by the selling shareholder is based on a conversion price of $0.475875. The conversion price reflects the average of the closing bid prices of the common stock for the lowest five consecutive trading days during the twenty trading days preceding December 8, 1999, multiplied by 94% pursuant to the terms of the Series I Shares and Series III Shares. Pursuant to our charter documents and the warrants, the Series I Shares and Series III Shares are convertible and the warrants held by the holder of the Series III Shares to purchase 300,000 shares of common stock are exercisable by any holder only to the extent that the number of shares of common stock owned by such holder and its affiliates (but not including shares of common stock underlying unconverted Series I Shares and Series III Shares) after such conversion or exercise would not exceed 4.9% of the then outstanding common stock as determined in accordance with Section 13(d) of the Securities Exchange Act. Accordingly, the number of shares of common stock set forth in the table for the selling shareholder exceeds the number of shares of common stock that the selling shareholder could own beneficially at any given time through its ownership of Series I Shares or Series III Shares. In that regard, beneficial ownership of the selling shareholder set forth in the table is not determined in accordance with Rule 13d-3 under the Exchange Act.

The selling shareholder, RGC International Investors, LDC, is a party to an investment management agreement with Rose Glen Capital Management, L.P., a limited partnership of which the general partner is RGC General Partner Corp. Messrs. Wayne Bloch, Gary Kaminsky and Steve Katznelson own all of the outstanding capital stock of RGC General Partner Corp., are the sole officers and directors of RGC General Partner Corp. and are parties to a shareholders' agreement pursuant to which they collectively control RGC General Partner Corp. Through RGC General Partner Corp., these individuals control Rose Glen Capital Management, L.P. These individuals disclaim beneficial ownership of Aastrom's Common Stock owned by the selling shareholder.

PLAN OF DISTRIBUTION

The shares of common stock may be offered for sale from time to time after conversion of the Series I Shares, Series III Shares or exercise of the Warrants by or on behalf of the holder of those shares. The actual number of shares that may be offered will vary based on the market price of our common stock, and the 13,071,069 shares covered by this prospectus is based on an assumed conversion price of $0.475875. Because the actual number of shares issued upon conversion of the Series I Shares and Series III Shares may vary, we have registered up to 19,906,604 shares pursuant to a Registration Statement that includes this Prospectus.

The shares of common stock being offered by the selling shareholder or its permitted donees, pledgees, transferees, or other successors in interest, will be sold in one or more transactions (which may

involve block transactions) on the Nasdaq National Market or on such other market on which the common stock may from time to time be trading:

- in privately-negotiated transactions
- through the writing of options on the shares
- short sales or
- any combination of these transactions.

The shares may also be sold pursuant to Rule 144.

The sale price may be:

- the market price prevailing at the time of sale
- a price related to the prevailing market price or
- such other price as the selling shareholder determines from time to time.

The selling shareholder may not accept any purchase offer or make any sale of shares if it considers the purchase price to be unsatisfactory at any particular time.

The selling shareholder or its permitted donees, pledgees, transferees, or other successors in interest, may also sell the shares directly to market makers acting as principals and/or broker-dealers acting as agents for themselves or their customers. Brokers acting as agents for the selling shareholder will receive usual and customary commissions for brokerage transactions, and market makers and block purchasers purchasing the shares will do so for their own account and at their own risk. The selling shareholder may attempt to sell shares of common stock in block transactions to market makers or other purchasers at a price per share which may be below the then current market price. There can be no assurance that all or any of the shares offered hereby will be issued to, or sold by, the selling shareholder.

Alternatively, the selling shareholder may sell all or any part of the shares through an underwriter. The selling shareholder has not entered into any agreement with a prospective underwriter and may not do so. If the selling shareholder enters into such an agreement or agreements, Aastrom will supplement or revise this prospectus.

The selling shareholder and any other persons participating in a distribution of the shares will be subject to applicable provisions of the Securities Exchange Act and the rules and regulations thereunder, including Regulation M, which may restrict certain activities of, and limit the timing of purchases and sales of the shares by the selling shareholder and other persons participating in a distribution of the shares. Furthermore, under Regulation M, persons engaged in a distribution of the shares are prohibited from simultaneously engaging in market making and certain other activities with respect to the shares for a specified period of time prior to the commencement of such distributions subject to specified exceptions or exemptions. All of the foregoing may affect the marketability of the shares offered hereby.

Aastrom has agreed to indemnify the selling shareholder, or certain transferees or assignees, against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the selling shareholder, or certain transferees or assignees, may be required to make in respect thereof. The selling shareholder has agreed to indemnify Aastrom against certain liabilities, including liabilities under the Securities Act, or to contribute to payments Aastrom may be required to make in respect thereof.

USE OF PROCEEDS

Aastrom will not receive any proceeds from sales of the shares or from any conversions of the Series I Shares or Series III Shares.

LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for Aastrom by Pepper Hamilton LLP, Detroit, Michigan. Gray Cary Ware & Freidenrich LLP, San Diego, California, has acted as special counsel to Aastrom in connection with this offering.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Report on Form 8-K filed with the Commission on December 10, 1999 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, independent accountants, given on the authority of said firm as experts in auditing and accounting.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

Other expenses in connection with the registration of the common stock hereunder will be substantially as follows (all expenses other than the SEC Registration Fee are estimates):

Item	Company Expense
SEC Registration Fee.....	$ 5,140
Printing and engraving expenses.....	$ 2,000
Legal fees and expenses.....	$10,000
Accounting fees and expenses.....	$ 5,000
Miscellaneous.....	$ 2,860
Total.....	$25,000

Item 15. Indemnification of Directors and Officers.

Sections 1561 through 1565 of the Michigan Business Corporation Act (the "MBCA") authorize a corporation to grant or a court to award indemnity to directors, officers, employees and agents in terms sufficiently broad to permit such indemnification under certain circumstances for liabilities (including reimbursement for expenses incurred) arising under the Securities Act of 1933.

The Bylaws of the Registrant, provide that the Registrant shall, to the fullest extent authorized or permitted by the MBCA, or other applicable law, indemnify a director or officer who was or is a party or is threatened to be made a party to any proceeding by or in the right of the Registrant to procure a judgment in its favor by reason of the fact that such person is or was a director, officer, employee or agent of the Registrant, against expenses, including actual and reasonable attorneys' fees, and amounts paid in settlement incurred in connection with the action or suit, if the indemnitee acted in good faith and in a manner the person reasonably believed to be in, or not opposed to, the best interests of the Registrant or its shareholders. This section also authorizes the Registrant to advance expenses incurred by any agent of the Registrant in defending any proceeding prior to the final disposition of such proceeding upon receipt of an undertaking by or on behalf of the agent to repay such amount unless it shall be determined ultimately that the agent is entitled to be indemnified.

The Bylaws also authorize the Registrant to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the Registrant against any liability asserted against or incurred by such person in such capacity or arising out of such person's status as such, regardless of whether the Registrant would have the power to indemnify such person against such liability under the provisions of the MBCA.

The Registrant has entered into an indemnification agreement with certain of its directors, officers and other key personnel, which contains provisions that may in some respects be broader than the specific indemnification provisions contained under applicable law. The indemnification agreement may require the Registrant, among other things, to indemnify such directors, officers and key personnel

against certain liabilities that may arise by reason of their status or service as directors, officers or employees of the Registrant, to advance the expenses incurred by such parties as a result of any threatened claims or proceedings brought against them as to which they could be indemnified and, to the maximum extent that insurance coverage of such directors, officers and key employees under the Registrant's directors' and officers' liability insurance policies is maintained.

Section 1209 of the MBCA permits a Michigan corporation to include in its Articles of Incorporation a provision eliminating or limiting a director's liability to a corporation or its shareholders for monetary damages for breaches of fiduciary duty. The enabling statute provides, however, that liability for breaches of the duty of loyalty, acts or omissions not in good faith or involving intentional misconduct or knowing violation of the law, or the receipt of improper personal benefits cannot be eliminated or limited in this manner. The Registrant's Restated Articles of Incorporation include a provision which eliminates, to the fullest extent permitted by the MBCA, director liability for monetary damages for breaches of fiduciary duty.

Item 16. Exhibits.

Exhibit Number	Description of Document
4.1	Restated Articles of Incorporation
4.1	Bylaws, as amended
5.1	Consent and Opinion of Pepper Hamilton LLP
23.1	Consent of PricewaterhouseCoopers LLP, independent accountants
23.2	Consent of Gray Cary Ware & Freidenrich LLP
23.3	Consent of Pepper Hamilton LLP (included in Exhibit 5.1)
24.1	Power of Attorney

A. The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933 (the "Securities Act");

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement; provided, however, that paragraphs (a)(1)(i) and (a)(1)(ii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

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

C. The undersigned Registrant hereby undertakes to deliver or cause to be delivered with the prospectus, to each person to whom the prospectus is sent or given, the latest annual report to security holders that is incorporated by reference in the prospectus and furnished pursuant to and meeting the requirements of Rule 14a-3 or Rule 14c-3 under the Securities Exchange Act of 1934; and, where interim financial information required to be presented by Article 3 of Regulation S-X are not set forth in the prospectus, to deliver, or cause to be delivered to each person to whom the prospectus is sent or given, the latest quarterly report that is specifically incorporated by reference in the prospectus to provide such interim financial information.

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

E. The undersigned Registrant hereby undertakes that:

(1) For the purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1)

or (4) or 497(h) under the Securities Act shall be deemed to be part of the registration statement as of the time it was declared effective.

(2) For the purposes of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements of filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized in the City of Ann Arbor, State of Michigan, on December 10, 1999.

AASTROM BIOSCIENCES, INC.

By: /s/ R. DOUGLAS ARMSTRONG

R. Douglas Armstrong, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL MEN BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints R. Douglas Armstrong and Todd E. Simpson, or either of them, as his or her attorney-in-fact, each with full power of substitution for him or her in any and all capacities, to sign any and all amendments to this registration statement, including, but not limited to, post-effective amendments and any and all new registration statements filed pursuant to Rule 462 under the Securities Act of 1933 in connection with or related to the offer contemplated by this registration statement, as amended, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorney to said registration statement and any and all amendment thereto.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed below by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ R. DOUGLAS ARMSTRONG R. Douglas Armstrong, Ph.D.	President, Chief Executive Officer and Chairman of the Board of Directors (Principal Executive Officer)	December 13, 1999
/s/ TODD E. SIMPSON Todd E. Simpson	Vice President, Finance and Administration, Chief Financial Officer, Secretary and Treasurer (Principal Financial and Accounting Officer)	December 13, 1999
/s/ ROBERT J. KUNZE Robert J. Kunze	Director	December 13, 1999
/s/ MARY L. CAMPBELL Mary L. Campbell	Director	December 13, 1999
/s/ STEPHEN G. EMERSON Stephen G. Emerson, M.D., Ph.D.	Director	December 13, 1999

/s/ ARTHUR F. STAUBITZ Arthur F. Staubitz	Director	December 13, 1999
/s/ JOSEPH A. TAYLOR Joseph A. Taylor	Director	December 13, 1999