

Enzon, Inc.

SUPPLEMENT NO. 1
TO PROSPECTUS DATED FEBRUARY 13, 1999
RELATING TO 150,000 SHARES OF COMMON STOCK, \$.01 PAR VALUE

The Prospectus is supplemented by deleting the section entitled "Risk Factors" and replacing such section in its entirety with the following:

RISK FACTORS

Information contained and incorporated by reference in this Prospectus contains "forward-looking statements" which can be identified by the use of forward-looking terminology such as "believes," "expects," "may," "will," "should," or "anticipates" or the negative thereof or other variations thereon or comparable terminology, or by discussions of strategy. No assurance can be given that the future results covered by the forward-looking statements will be achieved. The risk factors set forth below constitute cautionary statements identifying important factors with respect to such forward-looking statements, including certain risks and uncertainties, that could cause actual results to vary materially from the future results indicated in such forward-looking statements. Other factors could also cause actual results to vary materially from the future results indicated in such forward-looking statements.

An investment in the Shares offered hereby involves a high degree of risk. Prospective investors should carefully consider the following risk factors in addition to the other information set forth and incorporated by reference in this Prospectus before making any decision to invest in the Shares.

Accumulated Deficit and Uncertainty of Future Profitability. The Company was originally incorporated in 1981. To date, the Company's sources of cash have been the proceeds from the sale of its stock through public offerings and private placements, sales of its FDA-approved products, ADAGEN(R) and ONCASPAR(R); sales of its products for research purposes; contract research and development fees; technology transfer and license fees; and royalty advances. At Sept. 30, 1998, the Company had an accumulated deficit of approximately \$117,977,000. The Company expects to incur operating losses for the foreseeable future. To date, ADAGEN and ONCASPAR are the only products of the Company which have been approved for marketing in the United States by the FDA, having been approved in March 1990 and February 1994, respectively. In addition, ONCASPAR has been approved for marketing in Canada, Germany and Russia. In order to achieve profitable operations on a continuing basis, the Company, either alone or through its partners, must successfully manufacture, market and sell its ADAGEN and ONCASPAR products and develop, manufacture and market the Company's products which are under development. These products are in various stages of development, and the period necessary to achieve regulatory approval and market acceptance of any individual product is uncertain and typically lengthy, if achievable at all. Potential investors should be aware of the difficulties a biopharmaceutical enterprise such as the Company encounters, especially in view of the intense competition in the pharmaceutical industry in which the Company competes. There can be no assurance that the Company's plans will either materialize or prove successful, that its products under development will be successfully developed or that its products will generate revenues sufficient to enable the Company to achieve profitability.

Raw Materials and Dependence Upon Suppliers. Except for PEG-hemoglobin, the Company purchases the unmodified compounds utilized in its approved products and products under development from outside suppliers. There can be no assurance that the purified bovine hemoglobin used in the manufacture of PEG-hemoglobin can be produced by the Company in the amounts necessary to expand the current clinical trials. The Company may be required to enter into supply contracts with outside suppliers for certain unmodified compounds. The Company does not produce the unmodified adenosine deaminase used in the manufacture of ADAGEN, the unmodified forms of L-asparaginase used in the manufacture of ONCASPAR and the unmodified camptothecin used in the Company's PROTHECAN(TM) product

which is under development and has a supply contract with an outside supplier

for the supply of each of these unmodified compounds. Delays in obtaining or an inability to obtain any unmodified compound, including unmodified adenosine deaminase, unmodified L-asparaginase, unmodified bovine blood, or unmodified camptothecin on reasonable terms, or at all, could have a material adverse effect on the Company's business, financial condition and results of operations. In the event the Company is required to obtain an alternate source for an unmodified compound utilized in a product which is being sold commercially or which is in clinical development, the FDA and relevant foreign regulatory agencies will likely require the Company to perform additional testing, which would cause delays and additional expenses, to demonstrate that the alternate material is biologically and chemically equivalent to the unmodified compound previously used. Such evaluations could include chemical, pre-clinical and clinical studies and could delay development of a product which is in clinical trials, limit commercial sales of an approved product and cause the Company to incur significant additional expenses. If such alternate material is not demonstrated to be chemically and biologically equivalent to the previously used unmodified compound, the Company will likely be required to repeat some or all of the pre-clinical and clinical trials conducted for such compound. The marketing of an FDA-approved drug could be disrupted while such tests are conducted. Even if the alternate material is shown to be chemically and biologically equivalent to the previously used compound, the FDA or relevant foreign regulatory agency may require the Company to conduct additional clinical trials with such alternate material.

The Company's quality assurance department has observed increased levels of particulates in certain batches of ONCASPAR, which were manufactured by the Company. These batches were not shipped and the Company's recent rejection rate for the manufacture of this product is significantly higher than it has been historically. The Company is currently engaged in an extensive review of its manufacturing procedures for this product and believes that the problem may be related to certain materials which are used in the filing process, although this has not yet been determined. The Company has been in discussions with the FDA regarding this problem. The Company and the FDA have agreed to temporary labeling and distribution modifications for ONCASPAR, until the current manufacturing problem is resolved. The Company, rather than RPR, will temporarily distribute ONCASPAR directly to patients, on an as needed basis, in order to institute the additional inspection and labeling procedures prior to distribution. Upon resolution of the existing manufacturing problem, it is expected that RPR will resume the normal distribution of ONCASPAR. This manufacturing problem is isolated to ONCASPAR only.

Patents and Proprietary Technology. The Company has licensed, and been issued, a number of patents in the United States and other countries and has other patent applications pending to protect its proprietary technology. Although the Company believes that its patents provide certain protection from competition, there can be no assurance that such patents will be of substantial protection or commercial benefit to the Company, will afford the Company adequate protection from competing products, will not be challenged or declared invalid, or that additional United States patents or foreign patent equivalents will be issued to the Company. The scope of patent claims for biotechnological inventions is uncertain and the Company's patents and patent applications are subject to this uncertainty. The Company is aware of certain issued patents and patent applications belonging to third parties, and there may be other patents and patent applications, containing subject matter which the Company or its licensees or collaborators may require in order to research, develop or commercialize at least some of the Company's products. There can be no assurance that licenses under such patents and patent applications will be available on acceptable terms or at all. If the Company does not obtain such licenses, it or its partners could encounter delays in product market introductions while it attempts to design around such patents or could find that the development, manufacture or sale of products requiring such licenses could be foreclosed. If the Company does obtain such licenses it will in all likelihood be required to make royalty and other payments to the licensors, thus reducing the profits realized by the Company from the products covered by such licenses. In certain cases, the Company has obtained opinions of patent counsel that certain of such patents, including patents relevant to PEG-hemoglobin held by Biopure Inc. and patents relevant to PEG-Intron A held by Hoffman La Roche, are not infringed by the products of the Company or its collaborators or would not be held to be valid if litigated. Such opinions have been relied upon by the Company and its collaborators in continuing to pursue development of the subject product. Such opinions are not binding on any court and there can be no assurance that such opinions will prove to be correct and that a court would find any of the claims of such patents to be invalid or that the Company or its collaborators does not infringe such patents. The Company is aware that certain organizations are engaging in activities that infringe certain of the Company's PEG technology and

SCA patents. The Company expects that there may be

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significant litigation in the industry regarding patents and other proprietary rights and, such litigation, it could consume a substantial amount of the Company's resources. In addition, the Company relies heavily on its proprietary technologies for which pending patent applications have been filed and on unpatented know-how developed by the Company. Insofar as the Company relies on trade secrets and unpatented know-how to maintain its competitive technological position, there can be no assurance that others may not independently develop the same or similar technologies. Although the Company has taken steps to protect its trade secrets and unpatented know-how, third-parties nonetheless may gain access to such information. The Company has two research and license agreements with The Green Cross Corporation ("Green Cross") regarding rHSA. The Company and Yoshitomi Pharmaceutical Industries, Ltd. ("Yoshitomi"), the successor to Green Cross' business, are currently in arbitration to resolve the amount of royalties that will be due the Company, if any. Yoshitomi has filed documents in such arbitration seeking a declaratory judgment that under its agreement with the Company no royalties are payable. Any adverse decision from such an arbitration proceeding could result in a material adverse effect to the Company's future business, financial condition and results of operations. Research Corporation Technologies, Inc. ("Research Corporation") held the original patent upon which the PEG Process is based and had granted the Company a license under such patent. Research Corporation's patent for the PEG Process in the United States and its corresponding foreign patents have expired. Although the Company has obtained several improvement patents in connection with the PEG Process, there can be no assurance that any of these patents will enable the Company to prevent infringement or that competitors will not develop competitive products outside the protection that may be afforded by these patents. The Company is aware that others have also filed patent applications and have been granted patents in the United States and other countries with respect to the application of PEG to proteins and other compounds. Based upon the expiration of the Research Corporation patent, other parties will be permitted to make, use, or sell products covered by the claims of the Research Corporation patent, subject to other patents, including those held by the Company. There can be no assurance that the expiration of the Research Corporation patent will not have a material adverse effect on the business, financial condition and results of operations of the Company.

Limited Sales and Marketing Experience; Dependence on Marketing Partners. Other than ADAGEN, which the Company markets on a worldwide basis to a small patient population, the Company does not engage in the direct commercial marketing of any of its products and therefore does not have significant sales and marketing experience. For certain of its products, the Company has provided exclusive marketing rights to its corporate partners in return for royalties to be received on sales. With respect to ONCASPAR, the Company has granted exclusive marketing rights in North America and the Pacific Rim to RPR. As discussed above in " - Raw Materials and Dependence Upon Suppliers", currently, the Company, rather than RPR, will temporarily distribute ONCASPAR directly to patients, on an as needed basis, in order to institute additional inspection and labeling procedures prior to distribution. Upon resolution of the existing manufacturing problem, it is expected that RPR will resume the normal distribution of ONCASPAR. This manufacturing problem is isolated to ONCASPAR only. The Company has also granted exclusive marketing rights in Europe and Russia to Medac GmbH and in Israel to Tzamal Pharma Ltd. The Company expects to retain marketing partners to market ONCASPAR in other foreign markets, principally South America, and is currently pursuing arrangements in this regard. There can be no assurance that such efforts will result in the Company concluding such arrangements. Regarding the marketing of certain of the Company's other future products, the Company expects

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to evaluate whether to create a sales force to market certain products in the United States or to continue to enter into license and marketing agreements with others for United States and foreign markets. These agreements generally provide that all or a significant portion of the marketing of these products will be

conducted by the Company's licensees or marketing partners. In addition, under certain of these agreements, the Company's licensees or marketing partners may have all or a significant portion of the development and regulatory approval responsibilities. There can be no assurance that the Company will be able to control the amount and timing of resources that any licensee or marketing partner may devote to the Company's products or prevent any licensee or marketing partner from pursuing alternative technologies or products that could result in the development of products that compete with the Company's products and the withdrawal of support for the Company's products. Should the licensee or marketing partner fail to develop a marketable product (to the extent it is responsible for product development) or fail to market a product successfully, if it is developed, the Company's business, financial condition and results of operations may be adversely affected. There can be no assurance that the Company's marketing strategy will be successful. Under the Company's marketing and license agreements, the Company's marketing partners and licensees may have the right to terminate the agreements and abandon the applicable products at any time for any reason without significant payments. The Company is aware that certain of its marketing partners are pursuing parallel development of products on their own and with other collaborative partners which may compete with the licensed products and there can be no assurance that the Company's other current or future marketing partners will not also pursue such parallel courses.

Reimbursement from Third-Party Payors. Sales of the Company's products will be dependent in part on the availability of reimbursement from third-party payors, such as governmental health administration authorities, private health insurers and other organizations. Government and other third-party payors are increasingly sensitive to the containment of health care costs and are limiting both coverage and levels of reimbursement for new therapeutic products approved for marketing, and are refusing, in some cases, to provide any coverage for indications for which the FDA and other national health regulatory authorities have not granted marketing approval. There can be no assurance that such third-party payor reimbursement will be available or will permit the Company to sell its products at price levels sufficient for it to realize an appropriate return on its investment in product development. Since patients who receive ADAGEN will be required to do so for their entire lives (unless a cure or another treatment is developed), lifetime limits on benefits which are included in most private health insurance policies could permit insurers to cease reimbursement for ADAGEN. Lack of or inadequate reimbursement by government and other third party payors for the Company's products would have a material adverse effect on the Company's business, financial condition and results of operations.

Government Regulation. The manufacturing and marketing of pharmaceutical products in the United States and abroad is subject to stringent governmental regulation and the sale of any of the Company's products for use in humans in the United States will require the prior approval of the FDA. Similar approvals by comparable agencies are required in most foreign countries. The FDA has established mandatory procedures and safety standards which apply to the clinical testing, manufacture and marketing of pharmaceutical products. Pharmaceutical manufacturing facilities are also regulated by state, local and other authorities. Obtaining FDA approval for a new therapeutic may take several years and involve substantial expenditures. ADAGEN was approved by the FDA in March 1990. ONCASPAR was approved by the FDA in February 1994, in Germany in November 1994 and in Canada in 1997 in each case for patients with acute lymphoblastic leukemia who are hypersensitive to native forms of L-asparaginase. ONCASPAR was approved in Russia for therapeutic use in a broad range of cancers. Except for these approvals, none of the Company's other products have been approved for sale and use in humans in the United States or elsewhere. There can be no assurance that the Company will be able to obtain FDA approval for any of its other products. In addition, any approved products are subject to continuing regulation, and noncompliance by the Company with applicable requirements can result in criminal penalties, civil penalties, fines, recall or seizure, injunctions requiring suspension of production, orders requiring ongoing supervision by the FDA or refusal by the government to approve marketing or export applications or to allow the Company to enter into supply contracts. Failure to obtain or maintain requisite governmental approvals or failure to obtain or maintain approvals of the scope requested, will delay or preclude the Company or its licensees or marketing partners from marketing their products, or limit the commercial use of the products, and thereby may have a material adverse affect on the Company's business, financial condition and results of operations.

Intense Competition and Risk of Technological Obsolescence. Many established biotechnology and pharmaceutical companies with resources greater than those of the Company are engaged in activities that are competitive with the Company's and may develop products or technologies which compete with those of the Company. The Company is aware that other companies are engaged in utilizing PEG technology in developing drug products. There can be no assurance that the Company's competitors will not successfully develop, manufacture and market competing products utilizing PEG technology or otherwise. Other drugs or treatment modalities which are currently available or that may be developed in the future, and which treat the same diseases as those which the Company's products are designed to treat, may be competitive with the Company's products. There can be no assurance that the Company will be able to compete successfully against current or future competitors or that such competition will not have a material adverse effect on the Company's business, financial condition and results of operations. Rapid technological development by others may result in the Company's products becoming obsolete before the Company recovers a significant portion of the research, development and commercialization expenses incurred with respect to those products. The Company's success, in large part, depends upon developing and maintaining a competitive position in the development of products and technologies in its area of focus. There can be no assurance that the Company's competitors will not succeed in developing technologies or products that are more effective than any which are being sold or developed by the Company or which would render the Company's technologies or products obsolete or noncompetitive. The Company's failure to develop and maintain a competitive position with respect to its products and/or technologies would have a material adverse effect on its business, financial condition and results of operations.

Uncertainty of Market Acceptance. The Company's products, ONCASPAR and ADAGEN, have been approved by the FDA to treat patients with acute lymphoblastic leukemia and a rare form of severe combined immunodeficiency disease, respectively. Neither product has become widely used due to the small patient population and limited indications approved by the FDA. The Company's current research and development efforts are directed towards developing new technologies to aid in drug delivery. Assuming that the Company is able to develop such technologies and secure the requisite FDA approvals, the market acceptance of any such products will depend upon the acceptance by the medical community of the use of such technologies. There can be no assurance that any additional products will be approved by the FDA or that, if approved, the medical community will use them. In addition, the use of any such new products will depend upon the extent of third party medical reimbursement, increased awareness of the effectiveness of such technologies and sales efforts by the Company or any marketing partner. The Company's proprietary PEG technology has received only limited market acceptance to date. Failure of the Company to develop new FDA-approved products and to achieve market acceptance for such products would have a material adverse effect on the Company's business, financial condition and results of operation.

Potential Product Liability. The use of the Company's products during testing or after regulatory approval entails an inherent risk of adverse effects which could expose the Company to product liability claims. The Company maintains product liability insurance coverage in the total amount of \$10 million for claims arising from the use of its products in clinical trials prior to FDA approval and for claims arising from the use of its products after FDA approval. There can be no assurance that the Company will be able to maintain its existing insurance coverage or obtain coverage for the use of its other products in the future. There can be no assurance that such insurance coverage and the resources of the Company would be sufficient to satisfy any liability resulting from product liability claims or that a product liability claim would not have a material adverse effect on the Company's business, financial condition or results of operations.

Future Capital Needs; Uncertainty of Additional Financing. The Company's current sources of liquidity are its cash reserves, and interest earned on such cash reserves, sales of ADAGEN and ONCASPAR, sales of its products for research purposes, and license fees. There can be no assurance as to the level of sales of the Company's FDA-approved product, ADAGEN and ONCASPAR, or the amount of royalties realized from the commercial sale of ONCASPAR pursuant to the Company's licensing agreements. Total cash reserves, including short term investments, as of September 30, 1998, were approximately \$23,033,000. Based upon its currently planned research and development activities and related costs and its current sources of liquidity, the Company anticipates its current cash

reserves will be sufficient to meet its capital and operational requirements for the foreseeable future. The Company's future needs and the adequacy of available funds will depend on numerous factors, including without limitation, the successful commercialization of

its products, progress in its product development efforts, the magnitude and scope of such efforts, progress with preclinical studies and clinical trials, progress with regulatory affairs activities, the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights, competing technological and market developments, and the development of strategic alliances for the marketing of its products. There can be no assurance that the Company will not require additional financing for its currently planned capital and operational requirements. In addition, the Company may seek to acquire additional technology, enter into strategic alliances and engage in additional research and development programs, which may require additional financing. The Company does not have any committed sources of additional financing, and there can be no assurance that additional funding, if necessary, will be available on acceptable terms, if at all. To the extent the Company is unable to obtain financing, it may be required to curtail its activities or sell additional securities. There can be no assurance that any of the foregoing fund raising activities will successfully meet the Company's anticipated cash needs. If adequate funds are not available, the Company's business, financial condition and results of operations will be materially and adversely affected.

Dividend Policy and Restrictions. The Company has paid no dividends on its Common Stock since its inception and does not plan to pay dividends on its Common Stock in the foreseeable future. Except as may be utilized to pay the dividends payable on the Company's Series A Cumulative Convertible Preferred Stock (the "Series A Preferred Stock"), any earnings which the Company may realize will be retained to finance the growth of the Company. In addition, the terms of the Series A Preferred Stock restrict the payment of dividends on other classes and series of stock.

Possible Volatility of Stock Price. Historically, the market price of the Company's Common Stock has fluctuated over a wide range and it is likely that the price of the Common Stock will fluctuate in the future. Announcements regarding technical innovations, the development of new products, the status of corporate collaborations and supply arrangements, regulatory approvals, patent or proprietary rights or other developments by the Company or its competitors could have a significant impact on the market price of the Common Stock. In addition, due to one or more of the foregoing factors, in one or more future quarters, the Company's results of operations may fall below the expectations of securities analysts and investors. In that event, the market price of the Company's Common Stock could be materially and adversely affected.

Shares Eligible for Future Sale. As of December 8, 1998, the Company had approximately 35,955,000 shares of Common Stock outstanding and after giving effect to the offering of 112,500 shares of Common Stock issuable upon exercise of the Warrants described in "Selling Stockholders" which are offered hereby, but assuming no additional shares are issued pursuant to outstanding options, warrants or convertible securities, would have had approximately 36,068,000 shares of Common Stock outstanding. The 112,500 shares offered hereby are "restricted securities," as that term is defined in Rule 144 under the Securities Act, which when sold pursuant to the Registration Statement will be freely transferrable without restrictions under the Securities Act, assuming such Shares are held by non-affiliates of the Company. Of the other shares of Common Stock outstanding, approximately 28,189,953 shares will be immediately available for sale without restriction in the public market and approximately 1,654,240 and 2,398,114 shares will be eligible for sale under Rule 144 and Rule 144(k) of the Securities Act, respectively. In addition, the approximately 243,000 shares of Common Stock issuable upon conversion of the Series A Preferred Stock will be immediately available for sale without restriction in the public market when issued. Certain holders of the Company's securities are entitled to registration rights with respect to an aggregate of approximately 8,179,000 shares of Common Stock, including approximately 1,201,000 shares underlying outstanding warrants. Of such shares, approximately 7,044,000 shares are registered currently on Form S-3 registration statements which includes the registration statement of which this Prospectus forms a part. The approximately 4,015,000 shares of Common Stock underlying outstanding options which are held

by employees, directors and consultants are registered on Form S-8 registration statements. Sales of substantial amounts of such shares in the public market or the prospect of such sales could adversely affect the market price of the Common Stock.

Anti-takeover Considerations. The Company has the authority to issue up to 3,000,000 shares of Preferred Stock of the Company in one or more series and to fix the powers, designations, preferences and relative rights thereof without any further vote of shareholders. The issuance of such Preferred Stock could dilute the voting powers of holders of Common Stock and could have the effect of delaying, deferring or preventing a change in control of the Company.

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Certain provisions of the Company's Articles of Incorporation and By-laws, including those providing for a staggered Board of Directors, as well as Delaware law, may operate in a manner that could discourage or render more difficult a takeover of the Company or the removal of management or may limit the price certain investors may be willing to pay for shares of Common Stock.

The Date of this Supplement is January 14, 1999.

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