Filed Pursuant to Rule 424(b)(1)
Registration No. 333-66133

1,809,000 Shares

Integrated Surgical Systems, Inc.
Common Stock

The selling securityholders named in this prospectus are offering and selling up to 1,809,000 shares of the common stock of Integrated Surgical Systems, Inc. They may acquire 1,760,000 of those shares upon conversion of 3,520 shares of series A preferred stock and 44,000 shares upon exercise of warrants.

The common stock is quoted on The Nasdaq SmallCap Market under the symbol "RDOC", and is listed on The Pacific Exchange Inc. under the symbol "ROB". The common stock also has been admitted for trading on the European Association of Securities Dealers' Automated Quotation system under the symbol "RDOC".

THE COMMON STOCK IS A SPECULATIVE INVESTMENT AND INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD READ THE DESCRIPTION OF CERTAIN RISKS UNDER THE CAPTION "RISK FACTORS" COMMENCING ON PAGE 2 BEFORE PURCHASING THE COMMON STOCK.

Our executive offices are at 1850 Research Park Drive, Davis, California 95616-4884, and our telephone number is 530-792-2600.

THESE SECURITIES HAVE NOT BEEN APPROVED OR DISAPPROVED BY THE SEC OR ANY STATE SECURITIES COMMISSION NOR HAS THE SEC OR ANY STATE SECURITIES COMMISSION PASSED UPON THE ACCURACY OR ADEQUACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

THE DATE OF THIS PROSPECTUS IS MARCH 17, 1999

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This prospectus is part of a registration statement we filed with the SEC. You should rely only on the information or representations provided in this prospectus. We have not authorized anyone to provide you with different information. The common stock will not be offered in any state where an offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the cover of this prospectus.

RISK FACTORS

OUR POTENTIAL FUTURE SUCCESS AND FINANCIAL PERFORMANCE WILL DEPEND ALMOST ENTIRELY ON OUR ABILITY TO SUCCESSFULLY MARKET THE ROBODOC SYSTEM. For the near term, we expect to derive most of our revenues from sales of the ROBODOC System. Accordingly, our potential future success and financial performance will depend almost entirely on our ability to successfully market the ROBODOC System. To successfully market the ROBODOC System, we must commit substantial marketing efforts, develop an effective sales and marketing organization, and expend significant funds to inform potential customers, including hospitals and physicians, of the distinctive characteristics and advantages of using the ROBODOC System instead of traditional surgical tools and procedures. Since the ROBODOC System employs innovative technology, rather than being an improvement of existing technology, and represents a substantial capital expenditure, we expect to encounter resistance to change, which we must overcome if the ROBODOC System is to achieve significant market acceptance. Furthermore, our ability to market the ROBODOC System in the United States is dependent upon approval by the U.S. Food and Drug Administration. We cannot give you any assurance that we will obtain FDA approval to market the ROBODOC System in the United States, or that the ROBODOC System will achieve significant market acceptance in the United States, Europe and other foreign markets to generate sufficient revenues to become profitable.

ALTERNATIVES TO OUR PRODUCTS MAY AFFECT OUR POTENTIAL FUTURE SUCCESS. The principal competition for the ROBODOC System is manual surgery performed by orthopaedic surgeons, using surgical power tools and manual devices. The providers of these instruments are the major orthopaedic companies, which include Howmedica, Inc. (a subsidiary of Stryker Corporation), located in New York; Zimmer, Inc. (a subsidiary of Bristol-Myers Squibb Company), located in Indiana; Johnson & Johnson Orthopaedics, Inc. (a subsidiary of Johnson & Johnson), located in New Jersey; DePuy, Inc. (a subsidiary of Johnson & Johnson) located in Indiana; Biomet, Inc., located in Indiana; and Osteonics, Inc. (a subsidiary of the Stryker Corporation), located in New Jersey. MAQUET, a manufacturer of operating tables located in Germany, recently entered the market with a device similar to the ROBODOC System. The principal competition for the NeuroMate System are frame-based and frameless navigators, which are manually operated. Approximately twenty navigator models have been introduced, including those by Radionics, Sofamor-Danek and Ohio Medical Surgical products, all located in the United States; Elekta, located in Sweden; and Fischer Leibingher and Brain Lab, both located in Germany. In general, there are companies in the medical products industry capable of developing and marketing computer-controlled robotic systems for surgical applications, many of whom have significantly greater financial, technical, manufacturing, marketing and distribution resources than us, and have established reputations in the medical device industry. Furthermore, we cannot give you any assurance that IBM or the University of California, which developed the technology embodied in the ROBODOC System and hold patents relating thereto, will not enter the market or license the technology to other companies.

We cannot give you any assurance that future competition will not have a material adverse effect on our business. The cost of our systems represents a significant capital expenditure for a customer and accordingly may discourage purchases by certain customers.

WE NEED BUT HAVE NOT YET OBTAINED APPROVAL OF THE U.S. FOOD AND DRUG ADMINISTRATION TO MARKET THE ROBODOC SYSTEM IN THE UNITED STATES. Before a new medical device can be introduced into the U.S. market, the manufacturer must obtain FDA permission to market through either the 510(k) pre-market notification process for medical devices which are substantially similar to other approved medical devices or the costlier, lengthier and less certain pre-market approval application process. Following a pre-filing meeting with representatives of the FDA in early 1998, we stated that we intended to file our pre-market approval application to market the ROBODOC System with the FDA in the second quarter of 1998. As a result of further discussions with representatives of the FDA as part of the pre-submission review process (which process is intended to expedite the FDA's formal pre-market approval process), we have deferred the filing of our pre-market approval application with the FDA so that we may incorporate our DigiMatch Single

Surgery System, and possibly other technical developments, as part of our pre-market approval application. We believe, based upon our discussions with representatives of the FDA, that the incorporation of the DigiMatch Single Surgery System will enhance our prospects for obtaining FDA approval. However, we cannot give you any assurance as to when or if the FDA will grant pre-market approval for the ROBODOC System or that such approval, if obtained, will not include unfavorable limitations or restrictions.

In order to obtain FDA clearance or approval, we must demonstrate that the ROBODOC System is safe and effective, and we may be required to show a clinical benefit to patients. We believe that a reduced incidence of intraoperative fractures with the ROBODOC System compared to conventional total hip replacement surgery would offer an important benefit. The number of patients enrolled in our U.S. clinical study is less than the 300 patients (150 ROBODOC System; 150 control group) we initially requested to study in our investigational device exemption application to the FDA. Nonetheless, over 3,300 primary surgeries have been performed with the ROBODOC System in the U.S. clinical trial and the European treatment population without a single reported intraoperative fracture. Since the observed fracture rate in the control group in the U.S. clinical trial was lower than anticipated, the data from this study are not sufficient to establish a statistically significant reduction in intraoperative fractures compared to the control group. Nevertheless, the data from both the U.S. and the European group of patients suggest that the ROBODOC System reduces intraoperative fractures when compared to the fracture rate of approximately 3 to 28 percent for conventional surgery reported in the scientific and medical literature. However, we cannot give you any assurance that the FDA will agree that the ROBODOC System offers a clinically significant reduction in intraoperative fractures, in the absence of a controlled trial demonstrating such a reduction, or that such a reduction is of clinical benefit to patients.

The FDA has advised us that it believes long-term functional assessments are the primary endpoints for evaluating the safety and effectiveness of the ROBODOC System. Our preliminary review of the functional assessment data from the U.S. clinical trial shows equivalence between the ROBODOC System and conventional surgery. We believe that achieving better implant fit and alignment in the femoral cavity are significant factors in the success of cementless total hip replacement surgery, although the FDA has questioned whether fit is an appropriate endpoint and has not addressed alignment.

Our most recent statistical analysis of fit and alignment parameters from 3-month radiographs showed that the ROBODOC System surgeries produced better fit and alignment when compared to conventional surgeries. We believe a more accurate fit of the prosthesis reflects the implant manufacturers' design goals for implant cavity preparation. We also reviewed 24-month radiographs evaluating prosthesis stability. We cannot give you any assurance that the FDA will accept our data that demonstrates the ROBODOC System achieves better implant fit, alignment and stability, or that the FDA will agree that better fit and alignment are significant surgical endpoints. In addition, we cannot give you any assurance that the FDA will agree that the greater surgery time and blood loss associated with the ROBODOC System does not pose a significant safety concern or create an unfavorable risk/benefit ratio. Further, we cannot give you any assurance that the FDA will not require us to obtain additional clinical data from a randomized, controlled trial to resolve any concern about the risk/benefit ratio offered by the ROBODOC System. If we must obtain such additional data, the FDA review process could be prolonged by several years.

WE MAY NOT BE ABLE TO COMPLY WITH QUALITY SYSTEM AND OTHER FDA REPORTING AND INSPECTION REQUIREMENTS. Assuming we obtain the necessary FDA approvals and clearances for our products, in order to maintain such approvals and clearances we must, among other things, register our establishment and list our devices with the FDA and with certain state agencies, maintain extensive records, report any adverse experiences on the use of our products and submit to periodic inspections by the FDA and certain state agencies. The Food, Drug, and Cosmetic Act also requires devices to be manufactured in accordance with the quality system regulation, which sets forth good manufacturing practices requirements with respect to manufacturing and quality assurance activities. The quality system regulation revises the previous good manufacturing practices regulation and imposes certain enhanced requirements that are likely to increase the cost of compliance, including design controls.

WE MAY NOT BE ABLE TO OBTAIN REGULATORY APPROVALS NEEDED TO SELL OUR PRODUCTS IN FOREIGN MARKETS. The introduction of our products in foreign markets has subjected and will continue to subject us to foreign regulatory clearances, which may be unpredictable and uncertain, and which may impose substantial additional costs and burdens. Many countries also impose product standards, packaging requirements, labeling requirements and import restrictions on devices. We cannot give you any assurance that any of our products will receive further approvals or clearances, if required on a timely basis, or at all.

UNCERTAINTY REGARDING PATENTS AND PROTECTION OF PROPRIETARY TECHNOLOGY. Our ability to compete successfully may depend, in part, on our ability to obtain and protect patents, protect trade secrets and operate without infringing the proprietary rights of others. Certain robotic medical technology underlying our products is the subject of a United States patent issued to IBM, which IBM has agreed not to enforce against the manufacture and sale of our products. We have been issued four U.S. patents and filed seven patent applications covering various aspects of our technology.

Our U.S. patents include

- Computer assisted software system for planning and performing hip revision surgery

- Computer assisted system and method for creating cavities in the femur that will accept a prosthesis

- Computer system and method for creating a pre-operative surgical plan for hip replacement surgery

- Method for orienting real patient anatomy to a digital image of the patient's anatomy

We cannot give you any assurance that our pending or future patent applications will mature into issued patents, or that we will continue to develop our own patentable technologies. Further, we cannot give you any assurance that any patents that may be issued to us effectively protect our technology or provide a competitive advantage for our products or will not be challenged, invalidated, or circumvented in the future. In addition, we cannot give you any assurance that competitors, many of which have substantially more resources than us and have made substantial investments in competing technologies, will not obtain patents that will prevent, limit or interfere with our ability to make, use or sell our products either in the United States or internationally.

The medical device industry has been characterized by substantial competition and litigation regarding patent and other proprietary rights. We intend to vigorously protect and defend our patents and other proprietary rights relating to our proprietary technology. Litigation alleging infringement claims against us (with or without merit), or instituted by us to enforce patents and to protect trade secrets or know-how owned by us or to determine the enforceability, scope and validity of the proprietary rights of others, is costly and time consuming. If any relevant claims of third-party patents are upheld as valid and enforceable in any litigation or administrative proceedings, we could be prevented from practicing the subject matter claimed in such patents, or could be required to obtain licenses from the patent owners of each patent, or to redesign our products or processes to avoid infringement. We cannot give you any assurance that such licenses would be available or, if available, would be available on terms acceptable to us or that we would be successful in any attempt to redesign our products or processes to avoid infringement. Accordingly, an adverse determination in a judicial or administrative proceeding or failure to obtain necessary licenses could prevent us from manufacturing and selling our products, which would have a material adverse effect on our business, financial condition and results of operations.

LIMITED PRODUCTION EXPERIENCE. Our success will depends in part on our ability to assemble our products in a timely, cost-effective manner and in compliance with good manufacturing practices, and manufacturing requirements of other countries, including the International Standards Organization 9000 standards and other regulatory requirements. The assembly of our products is a complex operation involving a number of separate processes and components. Our production activities to date have consisted

primarily of assembling limited quantities of systems for use in clinical trials and systems for commercial sale. We do not have experience in assembling our products in larger commercial quantities. Furthermore, as a condition to receipt of pre-market approval, our facilities, procedures and practices will be subject to pre-approval and ongoing good manufacturing practices inspections by the FDA.

Manufacturers often encounter difficulties in scaling up manufacturing of new products, including problems involving product yields, quality control and assurance, component and service availability, adequacy of control policies and procedures, lack of qualified personnel, compliance with FDA regulations, and the need for further FDA approval of new manufacturing processes and facilities. We cannot give you any assurance that production yields, costs or quality will not be adversely affected as we seek to increase production, and any such adverse effect could have a material adverse effect on our business, financial condition and results of operations.

DEPENDENCE ON SUPPLIER FOR ROBOT. Although we have multiple sources for most of our components, parts and assemblies used in the ROBODOC and NeuroMate Systems, we are dependent on Sankyo Seiki of Japan for the ROBODOC System robot arm and Audemars-Piguet of Switzerland for the supply of the customized NeuroMate robot. Although we can obtain the robot for either the ROBODOC System or the NeuroMate System from other suppliers, with appropriate modifications and engineering effort, we cannot give you any assurance that delays resulting from the required modifications or engineering effort to adapt alternative components would not have a material adverse effect on our business, financial condition and results of operations.

RELIANCE ON FOREIGN SALES. Since we commenced operations, substantially all of our sales have been to customers in Germany, Austria, France and Japan. We believe that until such time, if ever, as we receive approval from the FDA to market the ROBODOC System in the United States, substantially all of our sales for the ROBODOC System will be derived from customers in foreign markets. Foreign sales are subject to certain risks, including economic or political instability, shipping delays, fluctuations in foreign currency exchange rates, changes in regulatory requirements, custom duties and export quotas and other trade restrictions, any of which could have a material adverse effect on our business. To date, payment for substantially all ROBODOC Systems in Europe has been fixed in U.S. Dollars. However, we cannot give you any assurance that in the future customers will be willing to make payment for our products in U.S. Dollars. If the U.S. Dollar strengthens substantially against the foreign currency of a country in which we sell our products, the cost of purchasing our products in U.S. Dollars would increase and may inhibit purchases of our products by customers in that country. We are unable to predict the nature of future changes in foreign markets or the effect, if any, they might have on us.

LENGTHY SALES CYCLE MAY CAUSE US TO RECOGNIZE THE SALES PRICE OF A SYSTEM IN A SUBSEQUENT FISCAL QUARTER TO THE FISCAL QUARTER IN WHICH WE INCURRED RELATED MARKETING AND SALES EXPENSES. Since the purchase of a ROBODOC System or NeuroMate System represents a significant capital expenditure for a customer, the placement of orders may be delayed due to customers' internal procedures to approve large capital expenditures. We anticipate that the period between initial contact of a customer for a system and submission of a purchase order by that customer could be as long as 9 to 12 months. Furthermore, the current lead time required by the supplier of the robot for either the ROBODOC System or the NeuroMate System is approximately four months after receipt of the order. We may be required to expend significant cash resources to fund our operations until the purchase price is paid. Accordingly, we may not recognize the sales price of a system until a fiscal quarter subsequent to the fiscal quarter in which we incurred marketing and sales expenses associated with an order.

NEED FOR ADDITIONAL FINANCING. Depending upon our ability to generate sufficient sales, collect outstanding accounts receivable and the timing of required expenditures, we may require additional financing. We cannot give you any assurance that such financing, if required, will be available on acceptable terms, if at all. If we are unable to obtain such additional financing on favorable terms, we may have to reduce or curtail certain activities.

EXPOSURE TO PRODUCT LIABILITY CLAIMS. The manufacture and sale of medical products exposes us to the risk of significant damages from product liability claims. Although we maintain product liability insurance against product liability claims in the amount of $5 million per occurrence and $5 million in aggregate, we cannot give you any assurance that the coverage limits of our insurance policies will be adequate or that such insurance can be maintained at acceptable costs. Although we have not experienced any product liability claims to date, a successful claim brought against us in excess of our insurance coverage could have a materially adverse effect on our business, financial condition and results of operations.

WE MAY NOT BE ABLE TO RETAIN OUR KEY PERSONNEL OR HIRE THE ADDITIONAL PERSONNEL WE NEED TO SUCCEED. Our business and marketing plan was formulated by, and is to be implemented under the direction of, Dr. Ramesh C. Trivedi, Chief Executive Officer and President. Dr. Trivedi is employed pursuant to an employment agreement that may be terminated by either Dr. Trivedi or us at any time. If we terminate Dr. Trivedi's employment other than for cause, we must pay him his monthly salary (currently, $23,320) for a period of 18 months following the date of termination. We maintain key-man insurance on the life of Dr. Trivedi. Our growth and future success also will depend in large part on the continued contributions of key technical and senior management personnel, as well as our ability to attract, motivate and retain highly qualified personnel generally and, in particular, trained and experienced professionals capable of developing, selling and installing the Systems and training surgeons in their use. Competition for such personnel is intense, and we cannot give you any assurance that we will be successful in hiring, motivating or retaining such qualified personnel. None of our executive or key technical personnel, other than Dr. Trivedi, is employed pursuant to an employment agreement. The loss of the services of Dr. Trivedi or other senior management or key technical personnel, or the inability to hire or retain qualified personnel, could have a material adverse effect on our business, financial condition and results of operations.

IF WE CANNOT SATISFY NASDAQ'S MAINTENANCE REQUIREMENTS, IT MAY DELIST OUR COMMON STOCK FROM ITS SMALLCAP MARKET. Our common stock is quoted on the Nasdaq SmallCap Market. To continue to be listed, we are required to maintain net tangible assets of $2,000,000 and our common stock must maintain a minimum bid price of $1.00 per share. We may not be able to continue to satisfy those requirements. If we are unable to satisfy Nasdaq's maintenance requirements, our common stock may be delisted. If we are delisted and we are not then listed or do not qualify for a listing on a stock exchange, our common stock would be traded in the over-the-counter market and quoted in the NASD's "Electronic Bulletin Board" or the "pink sheets." Consequently, it may be more difficult for an investor to obtain price quotations for our common stock or to sell it.

IF OUR COMMON STOCK IS DELISTED, IT MAY BECOME SUBJECT TO THE SEC'S "PENNY STOCK" RULES AND MORE DIFFICULT TO SELL. SEC rules require brokers to provide information to purchasers of securities traded at less than $5.00 and not traded on a national securities exchange or quoted on the Nasdaq Stock Market. If our common stock becomes a "penny stock" that is not exempt from the SEC rules, these disclosure requirements may have the effect of reducing trading activity in our common stock and make it more difficult for investors to sell. The rules require a broker-dealer to deliver a standardized risk disclosure document prepared by the SEC that provides information about penny stocks and the nature and level of risks in the penny market. The broker must also give bid and offer quotations and broker and salesperson compensation information to the customer orally or in writing before or with his confirmation. The SEC rules also require a broker to make a special written determination that the penny stock is a suitable investment for the purchaser and receive the purchaser's written agreement to the transaction before a transaction in a penny stock.

POSSIBLE ADVERSE EFFECT OF FUTURE SALES OF COMMON STOCK ON THE MARKET PRICE OF OUR COMMON STOCK. Sales of substantial amounts of common stock, or the possibility of such sales, could adversely affect the market price of our common stock and also impair our ability to raise capital through an offering of equity securities in the future. As of December 1, 1998, there were 5,643,372 shares of common stock outstanding. Except for 1,039,792 shares of common stock (representing approximately 18.4% of the outstanding common stock) owned by EJ Financial Investments V, L.P., which may be sold in accordance with the volume limitations of Rule 144, substantially all of the outstanding shares of common stock are transferable without restriction under the Securities Act. An additional

- 1,760,000 shares are issuable upon conversion of the Series A preferred stock, at an assumed conversion price of $2.00 per share. The actual conversion price is computed by reference to 85% of the lowest sale price of one share of common stock for the five trading days preceding the date of conversion.

- 2,274,066 shares are issuable upon exercise of warrants owned by IBM at exercise prices ranging from $.01 to $.07.

- 2,091,986 shares are issuable upon exercise of warrants issued in our initial public offering at an exercise price of $5.47 per share.

- 1,321,058 shares are issuable upon exercise of stock options granted pursuant to our employee stock option plans at exercise prices ranging from $.07 to $8.63 per share.

- 408,155 shares are issuable upon exercise of warrants having exercise prices ranging from $4.31 to $7.42 per share.

Substantially all of such shares (other than the shares issuable upon exercise of the warrants owned by IBM), when issued, may be immediately resold in the public market pursuant to effective registration statements under the Securities Act or pursuant to Rule 144. In April 1998, we amended the warrants owned by IBM to permit IBM to exercise them without the payment of cash for a lesser number of shares, based upon the difference between the market price of the common stock at the time of exercise and the exercise price, in which case such shares could be sold immediately under Rule 144 since under applicable SEC interpretations, the holding period under Rule 144 for shares acquired in this manner includes the period for which the selling shareholder owned the warrants.

Certain securityholders have agreed to limit the number of shares they may sell:

- IBM has agreed to limit sales of shares acquired upon exercise of its warrants to the volume limitations of Rule 144, whether or not applicable, and has granted us or our designee a right of first refusal with respect to such sales.

- Former securityholders of Innovative Medical Machines International, S.A., which we acquired in September 1997 in exchange for shares of common stock, have agreed to limit future sales of shares under a currently effective registration statement to the volume limitations of Rule 144, except that during the period from December 6, 1998 through March 5, 1999, they may sell an aggregate of 100,000 shares plus 1% of the total number of shares of common stock traded on Nasdaq during the preceding three month period.

We have granted registration rights to:

- The selling securityholders with respect to the shares of common stock covered by this prospectus.

- IBM, EJ Financial Investments V,L.P and certain other institutional investors owning or having the right to acquire 4,030,649 shares of common stock. These investors have agreed that they will not exercise these registration rights prior to May 21, 1999.

- Holders of warrants to purchase 166,837 shares of common stock issued in connection with our European offering in November 1997 have demand and piggyback registration rights for those shares.

- The holder of warrants to purchase 27,706 shares of common stock has piggyback registration rights for those shares, fully subordinated to the registration rights of our other securityholders.

FORWARD LOOKING STATEMENTS

Some of the information in this prospectus and the documents we incorporate by reference may contain forward-looking statements. Such statements can be identified by the use of forward-looking terminology such as "may," "will," "expect," "believe," "intend," "anticipate," "estimate," "continue" or similar words. These statements discuss future expectations, estimate the happening of future events or our financial condition or state other "forward-looking" information. When considering such forward-looking statements, you should keep in mind the risk factors and other cautionary statements in this prospectus and the documents that we incorporate by reference. The risk factors discussed in this prospectus and other factors noted throughout this prospectus, including certain risks and uncertainties, could cause our actual results to differ materially from those contained in any forward-looking statement.

SELLING SECURITYHOLDERS

The table below sets forth the name and address of each selling securityholder, the number of shares of common stock beneficially owned by each selling securityholder as of December 1, 1998, the number of shares that each selling securityholder may offer, and the number of shares of common stock beneficially owned by each selling securityholder upon completion of the Offering, assuming all of the shares offered are sold. None of the selling securityholders has, or within the past three years has had, any position, office or other material relationship with us or any of our predecessors or affiliates.

The selling securityholders are offering up to 1,809,000 by this prospectus.

- - 1,760,000 shares may be acquired upon conversion of the series A preferred stock, based upon an assumed conversion price of $2.00 per share. The conversion price is computed by reference to 85% of the lowest sale price of one share of common stock for the five trading days preceding the date of conversion.

- - 44,000 shares may be acquired upon exercise of warrants.

- - 5,000 shares were acquired by one of the selling securityholders as a finder's fee in connection with the sale of the series A preferred stock and warrants to the other selling securityholders.

The number of shares listed below as beneficially owned before the offering by each selling securityholder owning series A preferred stock has been computed, in part, based upon the terms of the series A preferred stock, which provides that the number of shares that the selling securityholders may acquire upon conversion may not exceed that number which (1) would render a selling securityholder the beneficial owner of more than five percent of the then issued and outstanding shares of common stock, or (2) result in the issuance of more than an aggregate of 1,127,674 shares, representing 20% of the number of shares of common stock issued and outstanding on September 10, 1998, the date upon which the series A preferred stock was issued, until stockholders approve the issuance of more than 1,127,674 shares upon conversion. For purposes of computing the number and percentage of shares beneficially owned by a selling securityholder on December 1, 1998, any shares which such person has the right to acquire within 60 days after such date are deemed to be outstanding, but those shares are not deemed to be outstanding for the purpose of computing the percentage ownership of any other selling securityholder. On December 1, 1998, we had 5,643,372 shares of common stock outstanding.

	SHARES OF COMMON STOCK BENEFICIALLY OWNED BEFORE OFFERING		SHARES OF COMMON STOCK OFFERED IN THE OFFERING	SHARES OF COMMON STOCK BENEFICIALLY OWNED AFTER OFFERING	
NAME AND ADDRESS OF SELLING SECURITYHOLDER	NUMBER	PERCENT	NUMBER	NUMBER	PERCENT
The Shaar Fund Ltd. Citro Building, Wickhams Cay, P.O. Box 662, Road Town, Tortola, B.V.I.	297,020	5.0%	1,291,500	0	--
AMRO International, S.A. c/o Ultrafinance, Grossmunster Platz 26, Zurich CH 8022	297,020	5.0%	512,500	0	--
Trinity Capital Advisors, Inc. 211 Sutter Street, Suite 2000, San Francisco, California 94104	5,000	*	5,000	0	--

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* Less than one percent (1%).

We are registering the shares for resale by the selling securityholders in accordance with registration rights granted to the selling securityholders. We will pay the registration and filing fees, printing expenses, listing fees, blue sky fees, if any, and fees and disbursements of our counsel in connection with this offering, but the selling securityholders will pay any underwriting discounts, selling commissions and similar expenses

relating to the sale of the shares, as well as the fees and expenses of their counsel. In addition, we have agreed to indemnify the selling securityholders, underwriters who may be selected by the selling securityholders and certain affiliated parties, against certain liabilities, including liabilities under the Securities Act, in connection with the offering. The selling securityholders may agree to indemnify any agent, dealer or broker-dealer that participates in transactions involving sales of the shares against certain liabilities, including liabilities under the Securities Act. The selling securityholders have agreed to indemnify us and our directors and officers, as well as any person controlling the company, against certain liabilities, including liabilities under the Securities Act. Insofar as indemnification for liabilities under the Securities Act may be permitted to our directors or officers, or persons controlling the company, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

PLAN OF DISTRIBUTION

The selling securityholders (or, subject to applicable law, their pledgees, donees, distributees, transferees or other successors in interest)may sell shares from time to time in public transactions, on or off The Nasdaq SmallCap Market, or private transactions, at prevailing market prices or at privately negotiated prices, including but not limited to the following types of transactions:

- ordinary brokerage transactions and transactions in which the broker solicits purchasers;

- a block trade in which the broker-dealer so engaged will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

- purchases by a broker or dealer as principal and resale by such broker or dealer for its account pursuant to this prospectus; and

- face-to-face transactions between sellers and purchasers without a broker-dealer.

The selling securityholders also may sell shares that qualify under Section 4(1) of the Securities Act or Rule 144.

In effecting sales, brokers or dealers engaged by the selling securityholders may arrange for other brokers or dealers to participate in the resales. The selling securityholders may enter into hedging transactions with broker-dealers, and in connection with those transactions, broker-dealers may engage in short sales of the shares. The selling securityholders also may sell shares short and deliver the shares to close out such short positions, except that the selling securityholders have agreed that they will not enter into any put option or short position with respect to the common stock prior to the date of the delivery of a conversion notice. The selling securityholders also may enter into option or other transactions with broker-dealers which require the delivery to the broker-dealer of the shares, which the broker-dealer may resell pursuant to this prospectus. The selling securityholders also may pledge the shares to a broker or dealer and upon a default, the broker or dealer may effect sales of the pledged shares pursuant to this prospectus.

Brokers, dealers or agents may receive compensation in the form of commissions, discounts or concessions from selling securityholders in amounts to be negotiated in connection with the sale. The selling securityholders and any participating brokers or dealers may be deemed to be "underwriters" within the meaning of the Securities Act in connection with such sales and any such commission, discount or concession may be deemed to be underwriting compensation.

Information as to whether underwriters who may be selected by the selling securityholders, or any other broker-dealer, is acting as principal or agent for the selling securityholders, the compensation to be received by underwriters who may be selected by the selling securityholders, or any broker-dealer, acting as principal or agent for the selling securityholders and the compensation to be received by other broker-dealers, in the event the compensation of such other broker-dealers is in excess of usual and customary commissions, will, to the extent required, be set forth in a supplement to this prospectus. Any dealer or

broker participating in any distribution of the shares may be required to deliver a copy of this prospectus, including a prospectus supplement, if any, to any person who purchases any of the shares from or through such dealer or broker.

We have advised the selling securityholders that during such time as they may be engaged in a distribution of the shares they are required to comply with Regulation M promulgated under the Securities Exchange Act. With certain exceptions, Regulation M precludes any selling securityholder, any affiliated purchasers and any broker-dealer or other person who participates in such distribution from bidding for or purchasing, or attempting to induce any person to bid for or purchase any security which is the subject of the distribution until the entire distribution is complete. Regulation M also prohibits any bids or purchases made in order to stabilize the price of a security in connection with the distribution of that security. All of the foregoing may affect the marketability of the common stock.

INFORMATION ABOUT THE COMPANY

At Integrated Surgical Systems, Inc., we develop, assemble, market and service image-directed, computer-controlled robotic products for orthopaedic and neurosurgical applications. Our principal orthopaedic product is the ROBODOC(R) Surgical Assistant System, consisting of a computer-controlled surgical robot and our ORTHODOC(R) Presurgical Planner, and our principal neurosurgical product is the NeuroMate System.(TM)

We file reports, proxy statements and other information with the SEC. You may read and copy any document we file at the Public Reference Room of the SEC at Judiciary Plaza, 450 Fifth Street, N.W., Washington, D.C. 20549 and at the Regional Offices of the SEC at Seven World Trade Center, Suite 1300, New York, New York 10048 and at 500 West Madison Street, Suite 1400, Chicago, Illinois 60661-2511. Please call 1-800-SEC-0330 for further information concerning the Public Reference Room. Our filings also are available to the public from the SEC's website at www.sec.gov. We distribute to our stockholders annual reports containing audited financial statements.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring to those documents. The information incorporated by reference is considered to be part of this prospectus, and information we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act until the offering is completed:

1. Annual Report on Form 10-KSB for the fiscal year ended December 31, 1997.

2. Proxy Statement dated March 26, 1998.

3. Quarterly Reports on Form 10-QSB for the fiscal quarters ended March 31, 1998, June 30, 1998 and September 30, 1998.

4. The description of the common stock contained in our Registration Statement on Form 8-A (File No. 1-12471) under Section 12 of the Securities Exchange Act.

You may request a copy of these filings, at no cost, by writing or calling us at:

INTEGRATED SURGICAL SYSTEMS
1850 Research Park Drive
Davis, California 95616-4884
Attention: Corporate Secretary
Telephone: (530) 792-2600

RECENT DEVELOPMENT

We have developed and commenced marketing to our customers in Europe our DigiMatch Single Surgery System, that, in most cases, eliminates the need for an initial surgery to place registration pins in a patient's femur before using the ROBODOC System in total hip replacement surgery. More than 150 patient surgeries have been successfully performed at a clinic in Frankfurt, Germany with our DigiMatch Single Surgery System.

We plan to amend our investigational device exemption under the Food, Drug and Cosmetic Act, which allowed us to conduct clinical trials for the ROBODOC System in the United States, to permit us to perform a relatively small clinical study showing a correlation between the ROBODOC System using the DigiMatch technology and the three pin system that we used in our initial clinical

evaluations. We have deferred the filing of our pre-market approval application to market the ROBODOC System in the United States so that we may incorporate our DigiMatch Single Surgery System, and possibly other technical developments, as part of our pre-market approval application. We believe, based upon our discussions with representatives of the FDA, that the incorporation of the DigiMatch Single Surgery System will enhance our prospects for obtaining FDA approval. However, we cannot give you any assurance as to when or if the FDA will approve our pre-market approval application to market the ROBODOC System or that such approval, if obtained, will not include unfavorable limitations or restrictions. See "Risk Factors -- Need to Obtain Approval of U.S. Food and Drug Administration to Market the ROBODOC System in the United States."

LEGAL MATTERS

The validity of the shares of common stock offered hereby has been passed upon by Snow Becker Krauss P.C., 605 Third Avenue, New York, New York 10158.

EXPERTS

The consolidated financial statements of Integrated Surgical Systems, Inc. appearing in Integrated Surgical Systems, Inc. Annual Report (Form 10-KSB) for the year ended December 31, 1997 have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon incorporated by reference therein and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given upon the authority of such firm as experts in accounting and auditing.