

AS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION ON FEBRUARY 3, 1999

REGISTRATION NO. 333-66133

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

POST-EFFECTIVE AMENDMENT NO. 2

TO

FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

INTEGRATED SURGICAL SYSTEMS, INC.
(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

DELAWARE
(STATE OR OTHER JURISDICTION OF
INCORPORATION OR ORGANIZATION)

1850 RESEARCH PARK DRIVE
DAVIS, CALIFORNIA 95616-4884
TELEPHONE: (530) 792-2600
TELECOPIER: (530) 792-2690

60-0232575
(I.R.S. EMPLOYER IDENTIFICATION NO.)

(ADDRESS AND TELEPHONE NUMBER OF PRINCIPAL EXECUTIVE OFFICES)

DR. RAMESH C. TRIVEDI
CHIEF EXECUTIVE OFFICER AND PRESIDENT
INTEGRATED SURGICAL SYSTEMS, INC.
1850 RESEARCH PARK DRIVE
DAVIS, CALIFORNIA 95616-4884
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(NAME, ADDRESS, INCLUDING ZIP CODE, AND TELEPHONE NUMBER, INCLUDING AREA CODE,
OF AGENT FOR SERVICE)

A COPY OF ALL COMMUNICATIONS, INCLUDING COMMUNICATIONS SENT TO THE AGENT FOR
SERVICE SHOULD BE SENT TO:

JACK BECKER, ESQ.
SNOW BECKER KRAUSS P.C.
605 THIRD AVENUE
NEW YORK, N.Y. 10158-0125
TELEPHONE: (212) 687-3860
TELECOPIER: (212) 949-7052

APPROXIMATE DATE OF PROPOSED SALE TO THE PUBLIC: As soon as practicable
after the effective date of this registration statement.

If the only securities being registered on this form are being offered
pursuant to dividend or interest reinvestment plans, please check the following
box. []

If any of the securities being registered on this form are to be offered or
delayed or continuous basis pursuant to Rule 415 under the Securities Act of
1933, other than securities offered only in connection with dividend or interest
reinvestment plans, check the following box. [X]

If this Form is filed to register additional securities for an offering
pursuant to Rule 462(b) under the Securities Act, please check the following box
and list the Securities Act registration statement number of the earlier
effective registration statement for the same offering. []

If this Form is a post-effective amendment filed pursuant to Rule 462(c)
under the Securities Act, check the following box and list the Securities Act
registration statement number of the earlier effective registration statement
for the same offering. []

If delivery of the prospectus is expected to be made pursuant to Rule 434,
please check the following box. []

THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR
DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL

FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(a) OF THE SECURITIES ACT OF 1933, AS AMENDED, OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE COMMISSION, ACTING PURSUANT TO SAID SECTION 8(a), MAY DETERMINE.

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PRELIMINARY PROSPECTUS, SUBJECT TO COMPLETION, DATED FEBRUARY 3, 1999

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 Calferine 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 _____, 1999

INFORMATION CONTAINED HEREIN IS SUBJECT TO COMPLETION OR AMENDMENT. A REGISTRATION STATEMENT RELATING TO THESE SECURITIES HAS BEEN FILED WITH THE SECURITIES AND EXCHANGE COMMISSION. THESE SECURITIES MAY NOT BE SOLD NOR MAY OFFERS TO BUY BE SOLD NOR MAY OFFERS TO BUY BE ACCEPTED PRIOR TO THE TIME THE REGISTRATION STATEMENT BECOMES EFFECTIVE. THIS PROSPECTUS SHALL NOT CONSTITUTE AN OFFER TO SELL OR THE SOLICITATION OF AN OFFER TO BUY NOR SHALL THERE BE ANY SALE OF THESE SECURITIES IN ANY STATE IN WHICH SUCH OFFER, SOLICITATION OR SALE WOULD BE UNLAWFUL PRIOR TO REGISTRATION OR QUALIFICATION UNDER THE SECURITIES LAWS OF ANY STATE.

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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

ABILITY TO OPERATE PROFITABLY. We have incurred losses since we commenced operations in 1990. We incurred a net loss of approximately \$4,478,000 (on net sales of approximately \$4,934,000) for the fiscal year ended December 31, 1997 and a net loss of approximately \$3,449,000 (on net sales of approximately \$2,280,000) for the fiscal year ended December 31, 1996. We incurred a net loss of approximately \$7,454,000 (on net sales of approximately \$4,188,000) for the nine months ended September 30, 1998, as compared to a net loss of approximately \$2,851,000 (on net sales of approximately \$2,818,000) for the nine months ended September 30, 1997. As a result of continuing losses, our accumulated deficit was approximately \$31,049,000 at September 30, 1998. We expect to continue to incur operating losses until such time, if ever, as we derive significant revenues from the sale of our products. Our ability to operate profitably depends upon market acceptance of our orthopaedic and neurosurgical products, our development of an effective sales and marketing organization, and our development of new products and improvements to existing products. Our ability to market the ROBODOC System in the United States is dependent upon approval by the Food and Drug Administration. See "Risk Factors -- Need to Obtain Approval of U.S. Food and Drug Administration to Market ROBODOC System in the United States." We cannot give you any assurance that we will obtain FDA approval to market the ROBODOC System in the United States or that our products will achieve market acceptance in the United States, Europe and other foreign markets to generate sufficient revenues to become profitable.

DEPENDENCE ON PRINCIPAL PRODUCT. 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. If we are unable to obtain the requisite regulatory approvals or to achieve commercial acceptance of the ROBODOC System, our business, financial condition and results of operations will be materially and adversely affected. We have not obtained, and we cannot give you any assurance that we will obtain, clearance or approval to market the ROBODOC System in the United States. See "Risk Factors -- Need to Obtain Approval of U.S. Food and Drug Administration to Market ROBODOC System in the United States."

UNCERTAINTY OF MARKET ACCEPTANCE. To successfully commercialize our systems we must commit substantial marketing efforts and expend significant funds to inform potential customers, including hospitals and physicians, of the distinctive characteristics and advantages of using our systems instead of traditional surgical tools and procedures. Since our systems employ innovative technology, rather than being an improvement of existing technology, and represent a substantial capital expenditure, we expect to encounter resistance to change, which we must overcome to successfully market our products. If our systems do not achieve significant market acceptance, our business, financial condition and results of operations would be materially and adversely affected.

ALTERNATIVES TO OUR PRODUCTS. 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, has announced that it intends to market 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 Leibinger 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.

NEED TO OBTAIN APPROVAL OF U.S. FOOD AND DRUG ADMINISTRATION TO MARKET 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.

ABILITY 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.

NEED TO OBTAIN FOREIGN REGULATORY APPROVALS. 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 depend 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.

UNCERTAINTY CONCERNING THIRD PARTY REIMBURSEMENT. We expect that our ability to successfully commercialize our products will depend significantly on the availability of reimbursement for surgical procedures using our products from third-party payors, such as governmental programs, private insurance and private health plans. Reimbursement is a significant factor considered by hospitals in determining whether to acquire new equipment. Notwithstanding FDA approval, if granted, third-party payors may deny reimbursement if the payor determines that a therapeutic medical device is unnecessary, inappropriate, not cost-effective or experimental or is used for a nonapproved indication. Although we are not aware of any potential customer that has declined to purchase the ROBODOC System based upon third party reimbursement policies, cost control measures adopted by third-party payors may have a significant effect on surgeries performed with the ROBODOC System or as to the levels of reimbursement. We cannot give you any assurance that levels of reimbursement, if any, will not be decreased in the future, or that future legislation, regulation, or reimbursement policies of third-party payors will not otherwise adversely affect the demand for our products or our ability to sell our products on a profitable basis. Fundamental reforms in the healthcare industry in the United States and Europe that could affect the availability of third-party reimbursement continue to be proposed, and we cannot predict the timing or effect of any such proposal. If third-party payor coverage or reimbursement is unavailable or inadequate, our business, financial condition and results of operation could be materially and adversely affected.

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.

ABILITY TO MANAGE GROWTH. We plan to expand our sales and marketing, research and development and technical personnel to increase and support sales of systems and to develop additional surgical applications for our orthopaedic and neurosurgical systems. Our anticipated growth will likely result in new and increased responsibilities for management personnel and place significant strain upon our management, operating and financial systems and resources. To accommodate such growth and compete effectively, we must continue to implement and improve our operational, financial, management and information systems, procedures and controls, and to expand, train, motivate and manage our personnel. We cannot give you any assurance that our personnel, systems, procedures and controls will be adequate to support our future operations. If we fail to implement and improve our operational, financial, management and information systems, procedures or controls, or to expand, train, motivate or manage our employees, our business, financial condition and results of operations could be materially and adversely affected.

NEED FOR ADDITIONAL FINANCING. Although we believe that we have sufficient funding to finance our operations through 1999, we cannot give you any assurance that additional financing will not be needed at an earlier date. This will depend upon our ability to generate sufficient sales of our products and the timing of required expenditures. We cannot give you any assurance that if we need additional financing in the future, such financing will be available on acceptable terms, if at all.

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.

DEPENDENCE ON KEY PERSONNEL. 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.

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 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.

NAME AND ADDRESS OF SELLING SECURITYHOLDER	SHARES OF COMMON STOCK BENEFICIALLY OWNED BEFORE OFFERING (1)		SHARES OF COMMON STOCK OFFERED IN THE OFFERING (1)	SHARES OF COMMON STOCK BENEFICIALLY OWNED AFTER OFFERING	
	NUMBER	PERCENT (2)		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	--

* Less than one percent (1%).

(1) Unless otherwise indicated, each person has sole investment and voting power with respect to the shares indicated.

(2) 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.

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. at December 31, 1997 and for the years ended December 31, 1996 and 1997, appearing in our Annual Report (on 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 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.

PART II

INFORMATION NOT REQUIRED IN THE PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

The expenses payable by the Registrant in connection with the issuance and distribution of the securities being registered are estimated below:

SEC registration fee.....	\$ 1,445.85
Listing fees.....	15,000.00
Legal fees and expenses.....	10,000.00
Printing expenses.....	5,000.00
Accounting fees.....	3,500.00
Miscellaneous.....	54.15

Total.....	\$35,000.00
	=====

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.

Article VI of the Registrant's by-laws provides that a director or officer shall be indemnified against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement (provided such settlement is approved in advance by the Registrant) in connection with certain actions, suits or proceedings, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation -- a "derivative action") if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful. A similar standard of care is applicable in the case of derivative actions, except that indemnification only extends to expenses (including attorneys' fees) incurred in connection with the defense or settlement of such an action, except that no person who has been adjudged to be liable to the Registrant shall be entitled to indemnification unless a court determines that despite such adjudication of liability but in view of all of the circumstances of the case, the person seeking indemnification is fairly and reasonably entitled to be indemnified for such expenses as the court deems proper.

Article 6.5 of the Registrant's by-laws further provides that directors and officers are entitled to be paid by the Registrant the expenses incurred in defending the proceedings specified above in advance of their final disposition. provided that such payment will only be made upon delivery to the Registrant by the indemnified party of an undertaking to repay all amounts so advanced if it is ultimately determined that the person receiving such payments is not entitled to be indemnified.

Article 6.4 of the Registrant's by-laws provides that a person indemnified under Article VI of the by-laws may contest any determination that a director, officer, employee or agent has not met the applicable standard of conduct set forth in the by-laws by petitioning a court of competent jurisdiction.

Article 6.6 of the Registrant's by-laws provides that the right to indemnification and the payment of expenses incurred in defending a proceeding in advance of its final disposition conferred in the Article will not be exclusive of any other right which any person may have or acquire under the by-laws, or any statute or agreement. or otherwise.

Finally, Article 6.7 of the Registrant's by-laws provides that the Registrant may maintain insurance, at its expense, to reimburse itself and directors and officers of the Registrant and of its direct and

indirect subsidiaries against any expense, liability or loss, whether or not the Registrant would have the power to indemnify such persons against such expense, liability or loss under the provisions of Article VI of the by-laws. The Registrant maintains and has in effect such insurance.

Article 11 of the Registrant's certificate of incorporation eliminates the personal liability of the Registrant's directors to the Registrant or its stockholders for monetary damages for breach of their fiduciary duties as a director to the fullest extent provided by Delaware law. Section 102(b) (7) of the DGCL provides for the elimination of such personal liability, except for liability (i) for any breach of the director's duty of loyalty to the Registrant or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the DGCL or (iv) for any transaction from which the director derived any improper personal benefit.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 (the "Securities Act") may be permitted to directors, officers or persons controlling the Registrant pursuant to the foregoing provisions, the Registrant has been informed 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.

ITEM 16. EXHIBITS

EXHIBIT NO.	DESCRIPTION
4.1	-- Preferred Stock Purchase Agreement, as amended.*
4.2	-- Certificate of Designations for Series A Convertible Preferred Stock.*
4.3	-- Form of Warrant.*
4.4	-- Form of Registration Rights Agreement.*
5.1	-- Opinion of Snow Becker Krauss.*
23.1	-- Consent of Snow Becker Krauss P.C. (included in Exhibit 5.1)
23.2	-- Consent of Ernst & Young LLP, independent auditors.

* Previously filed.

ITEM 17. UNDERTAKINGS.

(a) RULE 415 OFFERING

The undersigned small business issuer hereby undertakes that it will:

- (1) File, during any period in which it offers or sells securities, a post-effective amendment to this registration statement to:
 - (i) Include any prospectus required by section 10(a) (3) of the Securities Act.
 - (ii) Reflect in the prospectus any facts or events which, individually or in the aggregate, represent a fundamental change in the information set forth in the registrant 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) 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.

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

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

(e) REQUEST FOR ACCELERATION OF EFFECTIVE DATE

Insofar as indemnification for liabilities arising under the Securities Act of 1933 (the "Securities Act") may be permitted to directors, officers and controlling persons of the small business issuer pursuant to the foregoing provisions, or otherwise, the small business issuer 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 small business issuer of the expenses incurred or paid by a director, officer, or controlling person of the small business issuer 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 small business issuer 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.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Post-Effective Amendment to the Registration Statement to be signed on its behalf by the undersigned, hereunto duly authorized, in the City of Davis, State of California, on February , 1999.

INTEGRATED SURGICAL SYSTEMS, INC.

By /s/ RAMESH C. TRIVEDI

By: /s/ MARK W. WINN

Ramesh C. Trivedi
Chief Financial Officer
and President (Principal
Executive Officer)

Mark W. Winn
Chief Financial Officer
(Principal Financial and
Accounting Officer)

Pursuant to the requirements of the Securities Act of 1933, this Post-Effective Amendment to the Registration Statement has been signed by the following persons in the capacities indicated on February , 1999.

SIGNATURES

TITLE

/s/ RAMESH C. TRIVEDI

Chief Executive Officer,
President and Director
(Principal Executive Officer)

Ramesh C. Trivedi

/s/ MARK W. WINN

Chief Financial Officer
(Principal Financial and
Accounting Officer)

Mark W. Winn

*

James C. McGroddy

Chairman of the Board of
Directors

*

John N. Kapoor

Director

*

Paul A. H. Pankow

Director

*

Gerald D. Knudson

Director

Patrick G. Hays

Director

*By /s/ RAMESH C. TRIVEDI

Ramesh C. Trivedi
Attorney-in-fact

EXHIBIT INDEX

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* Previously filed

CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the reference to our firm under the caption "Experts" in Post-Effective Amendment No. 2 to the Registration Statement (Form S-3 No. 333-66133) and related Prospectus of Integrated Surgical Systems, Inc. for the registration of 1,809,000 shares of its common stock and to the incorporation by reference therein of our report dated February 26, 1998, with respect to the consolidated financial statements of Integrated Surgical Systems, Inc. included in its Annual Report (Form 10-KSB) for the year ended December 31, 1997, filed with the Securities and Exchange Commission.

ERNST & YOUNG LLP

Sacramento, California
February, 1999