As Filed Pursuant to Rule 424(b)(3)
Registration No. 333-40710

PROSPECTUS

INTEGRATED SURGICAL SYSTEMS, INC.

COMMON STOCK

The selling securityholders named in this prospectus are offering and selling up to 1,863,000 shares of our common stock, including 1,800,000 shares that they may acquire upon conversion of our series G preferred stock.

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 JULY 28, 2000

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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

WE HAVE A HISTORY OF OPERATING LOSSES AND THESE LOSSES MAY CONTINUE.

We have experienced significant losses since we began operations. We incurred net losses of approximately $10.2 million for the year ended December 31, 1999 and approximately $10.3 million for the year ended December 31, 1998 and a net loss of approximately $2.6 million for the three months ended March 31, 2000 as compared to a net loss of approximately $2.3 million for the three months ended March 31, 1999. As a result of these losses, we had an accumulated deficit of approximately $51.1 million as of March 31, 2000. We will continue to incur losses until such time, if ever, as we derive significant revenues from the sale of our products.

THE REPORT OF INDEPENDENT AUDITORS ON OUR DECEMBER 31, 1999 CONSOLIDATED FINANCIAL STATEMENTS INCLUDES AN EXPLANATORY PARAGRAPH CONCERNING OUR ABILITY TO CONTINUE AS A GOING CONCERN.

The report of independent auditors on our December 31, 1999 consolidated financial statements includes an explanatory paragraph which indicates there is substantial doubt about our ability to continue as a going concern because of recurring operating losses and an accumulated deficit of approximately $45,800,000 as of December 31, 1999.

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.

Orto Maquet, a German manufacturer and major supplier of operating tables to hospitals and physicians in Europe, has entered the market with a device intended to compete with the ROBODOC System. Orto Maquet's system incorporates pin-based registration and requires a second surgical procedure to place pins in the patient's thigh bone prior to performing hip replacement surgery. Although Orto Maquet offers a pre-surgical planning station, only our ROBODOC System offers enhancements that allow the surgeon to plan and perform revision hip surgery, the replacement of a previous hip implant. Orto Maquet has relationships with hospitals and physicians throughout Europe as a supplier of operating tables and has greater financial, marketing and distribution resources than us. Several of our potential customers in

Germany have decided to purchase the Orto Maquet system instead of the ROBODOC System due to their preference for doing business with a German company.

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 8,000 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.

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.

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.

OUR PRODUCTION EXPERIENCE IS LIMITED.

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.

WE ARE DEPENDENT ON OUR SUPPLIER OF ROBOTS.

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 believe we can obtain a robot arm 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.

WE ARE DEPENDENT 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.

WE ARE SUBJECT 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 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 is employed pursuant to an employment agreement. The loss of the services of 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.

WE WILL NEED ADDITIONAL FINANCING FOR OUR OPERATIONS BEFORE WE ARE ABLE TO OBTAIN FUNDS UNDER OUR EQUITY LINE OF CREDIT.

We have entered into an equity line of credit agreement for the sale of $12,000,000 of our common stock. Under the terms of the agreement, we may sell shares of common stock over a three-year period to the investors at a price equal to the lowest bid price during the six trading days commencing two trading days prior to the delivery of a put notice to the investors. At each closing, we also will issue to each investor warrants to purchase 14% of the number of shares purchased by the investor at that closing. These warrants will be exercisable at the per share purchase price of the shares purchased at the closing and may

be exercised at any time prior to the first anniversary of the closing. The equity line of credit agreement limits the number of shares that may be issued under the line, including shares that may be acquired upon exercise of warrants, to an aggregate of 3,357,471 shares, representing 19.9% of the shares outstanding on April 17, 2000, the date of the equity line agreement, until stockholders approve the issuance of shares in excess of that number. This limitation is required under the corporate governance rules of the Nasdaq Stock Market, Inc. We may not obtain funds under our equity line until the registration statement for the resale of the shares that may be issued under that line is declared effective by the SEC.

We will need additional financing prior to the date the registration statement for the resale of the shares issued under the equity line is declared effective by the SEC since we are experiencing severe short-term liquidity difficulties due to lower than anticipated revenues from sales of our ROBODOC systems. We have only sold one ROBODOC system since the termination of the distribution agreement which granted Spark 1st Vision GmbH KG the exclusive right to distribute our products in Europe, the principal market for our products. We are in the process of reestablishing our marketing and sales operations in Europe. We are engaged in discussions with potential investors for additional financing to alleviate our liquidity difficulties until we are able to sell shares of our common stock under our equity line of credit agreement and generate meaningful cash flow from the sale of our products. If we are unable to obtain additional financing in an amount sufficient to cover our operating and administrative costs, we may have to delay payments to trade creditors and other vendors, and curtail certain research and development activities.

We may issue common stock or debt or equity securities convertible into shares of common stock to obtain additional financing, if required. Any additional financing may result in substantial dilution to current holders of our common stock.

CONVERSION OF OUR PREFERRED STOCK AND SUBSEQUENT PUBLIC SALE OF OUR COMMON STOCK WHILE ITS MARKET PRICE IS DECLINING MAY RESULT IN FURTHER DECREASES IN ITS PRICE.

As of June 1, 2000, we had outstanding 2,534 shares of convertible preferred stock. Each share of preferred stock has a stated value of $1,000 per share and is convertible into common stock at a conversion price equal to 85% of the lowest sale price of the common stock on the Nasdaq SmallCap Market over the five trading days preceding the date of conversion. The number of shares of common stock that may be acquired upon conversion is determined by dividing the stated value of the number of shares of preferred stock to be converted by the conversion price, subject to a maximum conversion price of $1.22 as to 734 shares and $1.63 as to the remaining 1,800 shares. Since there is no minimum conversion price, there is no limit on the number of shares of common stock that holders of preferred stock may acquire upon conversion. For additional information concerning our outstanding preferred stock, see "Preferred Stock Financings." Holders of our preferred stock may sell at market price the shares of common stock they have acquired upon conversion at a 15% discount to prevailing market prices concurrently with, or shortly after, conversion, realizing a profit equal to the difference between the market price and the discounted conversion price. The holders of the preferred stock also could engage in short sales of our common stock, after delivering a notice of conversion to us, which could contribute to a decline in the market price of the common stock and give them the opportunity to profit from that decrease by covering their short position with shares acquired upon conversion at a 15% discount to the prevailing market price. The conversion of the preferred stock and subsequent sale of a large number of shares of common stock acquired upon conversion during periods when the market price of the common stock declines, or the possibility of such conversions and sales, may exacerbate the decline or impede increases in the market price of the common stock.

OTHER ISSUANCES OF PREFERRED STOCK COULD ADVERSELY AFFECT EXISTING HOLDERS OF OUR COMMON STOCK.

Under our certificate of incorporation, our Board of Directors may, without further stockholder approval, issue up to an additional 985,930 shares of preferred stock with dividend, liquidation, conversion, voting or other rights that could adversely affect the voting power or other rights of the holders of common stock. We could use new classes of preferred stock as a method of discouraging, delaying or preventing a change

in persons that control us. In particular, the terms of the preferred stock could effectively restrict our ability to consummate a merger, reorganization, sale of all or substantially all of our assets, liquidation or other extraordinary corporate transaction without the approval of the holders of the preferred stock. We could also create a class of preferred stock with rights and preferences similar to those of our outstanding convertible preferred stock, which could result in substantial dilution to holders of our common stock or adversely affect its market price.

CONVERSION OF OUR OUTSTANDING PREFERRED STOCK, THE ISSUANCE OF SHARES AND WARRANTS UNDER OUR EQUITY LINE OF CREDIT AND THE EXERCISE OF OUR OUTSTANDING WARRANTS AND STOCK OPTIONS AND SUBSEQUENT PUBLIC SALE OF OUR COMMON STOCK WILL RESULT IN SUBSTANTIAL DILUTION TO EXISTING STOCKHOLDERS.

As of June 1, 2000, we had outstanding 16,925,864 shares of common stock. In addition,

- an indeterminate number of shares may be acquired upon conversion of our outstanding preferred stock since there is no minimum conversion price. At an assumed conversion price of $1.00 per share, holders of preferred stock could acquire 2,534,000 shares of common stock, or approximately 15% of the 16,925,864 shares outstanding as of June 1, 2000.

- an indeterminate number of shares may be acquired under our $12,000,000 equity line of credit which has no minimum purchase price. Assuming a purchase price of $1.00 per share, we will issue 12,000,000 shares under the line, together with warrants to purchase an additional 1,680,000 shares at an exercise price of $1.00 per share. The issuance of those shares and exercise of those warrants would result in the issuance of a total of 13,680,000 shares, representing approximately 81% of the shares outstanding as of June 1, 2000.

- 13,518,277 shares may be acquired upon exercise of outstanding warrants.

- 1,864,098 shares may be acquired upon exercise of outstanding stock options.

Existing stockholders will experience substantial dilution in their percentage ownership of our common stock if the preferred stock is converted, shares of common stock and warrants are issued under our equity line of credit and warrants and stock options are exercised. If all of the outstanding preferred stock is converted at an assumed conversion price of $1.00 per share, $12,000,000 of shares of common stock, together with warrants to purchase 14% of the number of shares purchased, are issued under our equity line of credit at an assumed purchase price of $1.00 per share and those warrants are exercised at $1.00 per share, and all outstanding warrants and stock options are exercised, the number of outstanding shares of common stock will increase by 31,596,375, representing approximately 187% of the outstanding common stock as of June 1, 2000.

SALES OF SUBSTANTIAL AMOUNTS OF OUR COMMON STOCK, OR THE POSSIBILITY OF SUCH SALES, MAY HAVE AN ADVERSE EFFECT ON THE MARKET PRICE OF OUR COMMON STOCK AND IMPAIR OUR ABILITY TO RAISE CAPITAL THROUGH AN OFFERING OF EQUITY SECURITIES IN THE FUTURE.

As of June 1, 2000, there were 16,925,864 shares of common stock outstanding. Except for 4,028,820 shares of common stock (representing approximately 24% of the outstanding common stock), substantially all of the outstanding shares of common stock are transferable without restriction under the Securities Act. In addition,

- an indeterminate number of shares may be acquired upon conversion of our outstanding preferred stock since there is no minimum conversion price. At an assumed conversion price of $1.00 per share, holders of our outstanding preferred stock could acquire 2,534,000 shares of common stock. The number of shares that may be acquired upon conversion will increase if the market price of the common stock declines below the assumed conversion price.

- an indeterminate number of shares may be acquired under our $12,000,000 equity line of credit, which has no minimum purchase price. At an assumed purchase price of $1.00 per share, we will issue 12,000,000 shares of our common stock and warrants to purchase an additional 1,680,000 shares at an exercise price of $1.00 per share.

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

- 4,123,389 shares may be acquired upon exercise of warrants issued in our initial public offering at an exercise price of $2.79.

- 6,000,000 shares may be acquired upon exercise of warrants at an exercise price of $1.027.

- 1,120,822 shares may be acquired upon exercise of warrants having exercise prices ranging from $1.88 to $4.39 per share.

- 1,864,098 shares may be acquired upon exercise of stock options granted pursuant to our stock option plans at exercise prices ranging from $.07 to $8.62 per share.

Substantially all of such shares, when issued, may be immediately resold in the public market pursuant to effective registration statements under the Securities Act or pursuant to Rule 144.

We have granted registration rights to:

- ILTAG International Licensing Holding S.A.L., Bernd Herrmann, Urs Wettstein, IBM, EJ Financial Investments V,L.P. and certain other institutional investors owning or having the right to acquire 12,538,861 shares of common stock.

- holders of warrants to purchase 353,506 shares of common stock issued in connection with our European offering in November 1997 for those shares.

- holders of warrants to purchase 57,441 shares of common stock have piggyback registration rights for those shares.

- the investor under our $12,000,000 equity line of credit.

If our securityholders sell publicly a substantial number of shares they own or may acquire under our equity line of credit, upon exercise of outstanding options and warrants or upon conversion of our preferred stock, then the market price of our common stock may decline. Public perception that those sales will occur may also exert downward pressure on our common stock. A decline in the price of our common stock may also impair our ability to raise capital through the sale of equity securities.

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.

The conversion of our convertible preferred stock may have consequences that could cause Nasdaq to delist our common stock. The conversion of our preferred stock and resale of the common stock acquired upon conversion, or the possibility of the conversion of our preferred stock and resale of our common stock, may depress or inhibit increases in the market price of our common stock. As a result, the minimum bid price for our common stock may decline below $1.00. Nasdaq also may delist our common stock if it deems it necessary to protect investors and the public interest. If Nasdaq determines that the returns on our convertible preferred stock are excessive compared with the returns received by the holders of our common stock, and those excess returns were egregious, Nasdaq could delist our common stock.

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.

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 securityholder as of June 1, 2000, 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 this offering, assuming all of the shares offered are sold. None of the selling securityholder 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 number of shares listed below as beneficially owned before the offering by each selling securityholder owning series G preferred stock has been computed, without giving effect to the terms of the certificate of designations for the series G preferred stock, which provides that the number of shares that the selling securityholders may acquire upon conversion may not exceed that number which would render a selling securityholder the beneficial owner of more than five percent of the then issued and outstanding shares of common stock, or result in the issuance of more than an aggregate of 3,370,043 shares upon conversion of the series G preferred stock, representing 19.9% of the shares outstanding, on the date that series of preferred stock was issued, until stockholders approve the issuance of shares in excess of that number.

On June 1, 2000, we had 16,925,864 shares of common stock outstanding. For purposes of computing the number and percentage of shares beneficially owned by a selling securityholder on June 1, 2000, 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.

NAME AND ADDRESS OF SELLING SECURITYHOLDER	SHARES OF COMMON STOCK OWNED BEFORE OFFERING(1)		SHARES OF COMMON STOCK OFFERED IN THE OFFERING(2)	SHARES OF COMMON STOCK BENEFICIALLY OWNED AFTER OFFERING	
	NUMBER	PERCENT		NUMBER	PERCENT
Holder of series G preferred stock and warrants:					
AMRO International, S.A.(3)..... c/o UltraFinanz, Grossmunster Platz 6 Switzerland Zurich CH 8022	646,625	3.7%	621,000	25,625(4)	*
Esquire Trade & Finance, Inc.(5)..... Trident Chambers, P.O. Box 146 Road Town, Tortola, B.V.I.	319,874	1.9%	310,500	9,374(4)	*
Celeste Trust Reg.(6)..... c/o Trevisa-Treuhand-Anstalt Landstrasse 8 9496 Furstentum Balzers, Liechtenstein	319,875(7)	1.9%	310,500	9,375(7)	*
Shmuli Margulies..... The Endeavour Capital Fund S.A. c/o Endeavour Advisory, Ltd. P.O.B. 57116 Jerusalem 91570 46/21 Yirmeyahu Street Jerusalem 94467 Israel	1,418,125(8)	7.7%	621,000	797,125	4.5%

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* Less than one percent (1%).

(1) The information presented in the table does not give effect to the terms of the certificate of designations for the preferred stock and the warrants that limit the number of shares that a holder may acquire upon conversion or exercise of these securities to 5% of the then issued and outstanding shares of common stock.

(2) Represents the number of shares that the selling securityholder may acquire upon exercise of warrants to purchase common stock and conversion of the series G preferred stock at an assumed conversion price of $1.00 per share. The actual conversion price is 85% of the lowest sale price of a share of common stock for the five trading days preceding the date of conversion. The number of shares of common stock that the selling securityholder may acquire upon conversion is equal to the number of shares of preferred stock to be converted times $1,000, the stated value of each share of preferred stock, divided by the conversion price. The maximum conversion price of the series G preferred stock is $1.63. Since there is no minimum conversion price, if the market price of the common stock declines below the assumed conversion price, the number of shares that the selling securityholder may acquire upon conversion will increase. If following a sustained increase in the market price of the common stock sufficient to offset the 15% discount used in computing the conversion price the conversion price is higher than the assumed conversion price, the number of shares that the selling securityholder may acquire will decrease.

(3) Hans Ulrich Bachofen and Michael Klee share voting and dispositive power with respect to shares owned by AMRO International, S.A.

(4) Represents warrants to purchase common stock.

(5) Gisela Kindla has sole voting and dispositive power with respect to shares owned by Esquire Trade and Finance, Inc.

(6) Thomas Hackl has voting and dispositive power with respect to shares owned by Celeste Trust Reg.

(7) Includes 9,375 shares that may be acquired upon exercise of warrants, by Austinvest Anstalt Balzers, an affiliate of Celeste Trust Reg-, as to which Walter Grill has voting and dispositive power.

(8) Includes 734,000 shares that may be acquired by Endeavour Management, Inc. upon conversion of our series F convertible preferred stock at an assumed conversion price of $1.00 per share.

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 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. They may sell their shares in 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. As used in this prospectus, selling securityholders include donees, pledgees, distributees, transferees and other successors-in-interest of the selling securityholders named in this prospectus.

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 under 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 under 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 them, and the compensation to be received by other broker-dealers, in the event such compensation 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.

INFORMATION ABOUT 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)

RECENT DEVELOPMENTS

EQUITY LINE FINANCING

We have entered into an equity line of credit agreement for the sale of $12,000,000 of our common stock. Under the terms of the agreement, we may sell shares of common stock over a three-year period to the investors at a price equal to the lowest bid price during the six trading days commencing two trading days prior to the delivery of a put notice to the investor. The number and dollar amount of shares that may be purchased on each closing date is based upon a formula that varies with the market price and trading volume of the common stock, subject to a minimum of $100,000. We may not sell shares of common stock under the agreement more often than once every fifteen days. At each closing, we also will issue to each investor warrants to purchase 14% of the number of shares purchased by the investor at that closing. These warrants will be exercisable at the per share purchase price of the shares purchased at the closing and may be exercised at any time prior to the first anniversary of the closing. We also will issue warrants to purchase 35,000 shares of common stock to the investors at the initial closing. This warrant will be exercisable at $1.88 per share during the period commencing October 17, 2000 and ending on April 16, 2003.

In addition, we will issue to a financial advisor 12,000 shares of common stock for each one million dollars of shares sold to the investor. We issued 5,000 shares to the advisor upon signing the agreement. We also will pay the financial advisor 3% of the gross proceeds from the sale of shares purchased at each closing, plus an advisory fee of $20,000 at each of the first six closings.

We will file a registration statement for the resale of the shares issued under the equity line. No shares will be sold under the equity line until the registration statement is declared effective by the SEC.

TERMINATION OF DISTRIBUTION AGREEMENT

On May 9, 2000, we entered into an agreement with Spark 1st Vision GmbH & Co. KG terminating the agreement that granted Spark 1st Vision exclusive distribution rights for our products in Europe, the Middle East and Africa. We received approximately $1,000,000 from Spark 1st Vision in connection with the termination in settlement of its obligations under the distribution agreement.

EUROPEAN INVESTORS

ILTAG International Licensing Holding S.A.L., Bernd Herrmann and Urs Wettstein, who purchased an aggregate of 2,922,396 shares of our common stock and warrants to purchase an additional 11,700,000 shares of common stock in December 1999 for a purchase price of $4,000,000 have agreed to surrender an aggregate of 5,700,000 warrants. In addition, they have agreed to exercise an aggregate of 2,000,000 of the remaining 6,000,000 warrants as follows: 500,000 warrants by each of September 5, October 5, November 5 and December 5, 2000, provided the market price of one share of our common stock is not less than $1.03, the exercise price of the warrants. These 2,000,000 warrants will expire if they are not exercised by those dates. The remaining 4,000,000 warrants are exercisable until December 14, 2002.

Messrs. Wettstein and Herrmann have resigned from our Board of Directors.

PREFERRED STOCK FINANCINGS

Since September 1998, we have received aggregate net proceeds of approximately $13.1 million from the sale of seven series of our convertible preferred stock. Information concerning these preferred stock financings is set forth below.

SERIES	DATE OF SALE	SHARES OF PREFERRED STOCK SOLD	WARRANTS ISSUED	GROSS PROCEEDS
A	September 10, 1998	3,520	44,000	$3,520,000
B	March 26, 1999	1,000	12,500	1,000,000
C	June 10, 1999	750	9,375	750,000
D	June 30, 1999	2,000	25,000	2,000,000
E	July 30, 1999	3,000	37,500	3,000,000
F	February 8, 2000	2,000	125,000	2,000,000
G	May 30, 2000	1,800	63,000	1,800,000

Each series of preferred stock has a stated value of $1,000 per share and is convertible into common stock at a conversion price equal to 85% of the lowest sale price of the common stock on the Nasdaq SmallCap Market over the five trading days preceding the date of conversion subject to a maximum conversion price. The number of shares of common stock that may be acquired upon conversion is determined by dividing the stated value of the number of shares of preferred stock to be converted by the conversion price. As of June 1, 2000, 734 shares of series F preferred stock and 1,800 shares of series G preferred stock were outstanding. No other shares of preferred stock are outstanding. On February 7, 2000 we redeemed the 1,085 shares of series E preferred stock outstanding for a total redemption price of $1,085,000, or $1,000 per share, the stated value of a share of series E preferred stock.

The maximum conversion price for the series F preferred stock is $1.22 per share and the maximum conversion price of the series G preferred stock is $1.63.

There is no minimum conversion price for any series of preferred stock. Consequently, there is no limit on the number of shares of common stock that may be issued upon conversion, except that the terms of each series, set forth in the certificate of designations for that series, limit:

- - The number of shares of common stock that a holder of preferred stock may acquire upon conversion, together with shares beneficially owned by the holder and its affiliates, to five percent (5%) of the total outstanding shares of common stock.

- - The number of shares of common stock that the holders of a series of preferred stock may acquire upon conversion to that number of shares representing 19.9% of the shares outstanding on the date upon which that series was issued, until stockholders approve the issuance upon conversion of shares in excess of that number of shares. This limitation is required by the rules of The Nasdaq Stock Market, Inc.

The number of shares of common stock issued upon conversion of each series of preferred stock as of June 1, 2000 was as follows: series A -- 2,867,135; series B -- 459,831; series C -- 563,497; series D -- 1,605,203; series E -- 1,490,101; series F: 1,038,078 series G: none. The average actual conversion price for shares of each series of preferred stock converted into shares of common stock as of June 1, 2000 was as follows: series A -- $1.23; Series B -- $2.17; Series C -- $1.33; Series D -- $1.25; Series E -- $1.22.; and series F -- $1.22.

The number of shares of common stock that may be acquired upon conversion of the outstanding shares of preferred stock as of June 1, 2000, based upon an assumed conversion prices of $1.00, the maximum conversion price, is as follows: Series F -- 734,000; and series G -- 1,800,000.

The market price of the common stock on the date of issue of each series of preferred stock was as follows: series A -- $3.56; series B -- $1.97; series C -- $1.81; series D -- $2.97; series E -- $3.50; series F -- $2.38; and series G -- $1.38.

The conversion price of each series of preferred stock on the date of issue would have been as follows: series A -- $2.76; series B -- $1.49; series C -- $1.41; series D -- $2.23; series E -- $2.87; series F -- $1.22; and series G -- $1.06. The number of shares of common stock into which the preferred stock would have been convertible on the date of issue would have been as follows: series A -- 1,274,000; series B -- 672,000; series C -- 533,000; series D -- 896,000; series E -- 1,046,000; series F -- 1,639,345; and series G -- 1,694,118.

WHERE YOU CAN FIND MORE INFORMATION

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 and Form 10-KSB/A (Amendment No. 1) for the fiscal year ended December 31, 1999, including any amendments to that report.

2. Quarterly Report on Form 10-QSB for the fiscal quarter ended March 31, 2000, including any amendments to that report.

3. 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

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

Ernst & Young LLP, independent auditors, have audited our consolidated financial statements included in our Annual Report on Form 10-KSB and Form 10-KSB/A (Amendment No. 1) for the year ended December 31, 1999, as set forth in their report (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the consoliated financial statements), which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.