

IsoRay, Inc.
Form 424B5
July 11, 2018
Table of Contents

Filed pursuant to Rule 424(b)(5)

Registration No. 333-206559

PROSPECTUS SUPPLEMENT

(To Prospectus dated November 23, 2015)

IsoRay, Inc.

11,000,000 Shares of Common Stock

We are offering 11,000,000 shares of our common stock to certain institutional and accredited investors pursuant to this prospectus supplement and the accompanying prospectus. The common stock is being offered at a per share purchase price of \$0.75 per share. In a concurrent private placement, we are also selling to the purchasers of common stock offered by this prospectus supplement warrants to purchase up to 5,500,000 shares of our common stock, which represent fifty percent (50%) of the shares of our common stock being purchased in this offering (the Warrants). The Warrants and the shares of our common stock issuable upon the exercise of the Warrants (the Warrant Shares) are being offered pursuant to the exemption provided in Section 4(a)(2) under the Securities Act of 1933, as amended (the “Securities Act”) and Rule 506(b) promulgated thereunder, and they are not being offered pursuant to this prospectus supplement and the accompanying prospectus. The Warrants being issued in the concurrent private placement are not listed on any securities exchange, and we do not expect to list the Warrants.

Our common stock is listed on the NYSE American stock exchange under the symbol “ISR.” On July 6, 2018, the last reported sale price of our common stock on the NYSE American stock exchange was \$0.44 per share.

As of July 6, 2018, a date within 60 days of the date of this prospectus supplement, the aggregate market value of our outstanding shares of common stock held by non-affiliates, or public float, was \$24,785,705 based on 56,331,147 outstanding shares of common stock, of which 56,139,442 shares are held by non-affiliates, and a per share price of \$0.44, based on the last sale price of our common stock on July 6, 2018. One-third of our public float, calculated in accordance with Instruction I.B.6 of Form S-3 as of May 17, 2018, is equal to \$10,292,231. During the 12 calendar months prior to and including the date of this prospectus supplement, we have sold \$489,853 of common stock pursuant to General Instruction I.B.6 of Form S-3. In no event will we sell securities registered on this

registration statement in a public primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below \$75.0 million pursuant to General Instruction I.B.6 of Form S-3.

Investing in our securities involves a high degree of risk. Before buying any securities, you should read the discussion of material risks of investing in our securities referred to under the heading "Risk Factors" of this prospectus supplement.

	Per share	Total
Offering price	\$0.75	\$8,250,000
Placement agent fees ⁽¹⁾	\$0.045	\$495,000
Proceeds, before expenses, to us	\$0.705	\$7,755,000

(1) We have agreed to reimburse the placement agent for certain of its expenses and to grant warrants to purchase shares of our common stock to the placement agent. See "Plan of Distribution."

We expect the total offering expenses, excluding the placement agent fees, to be approximately \$182,500 for all sales pursuant to this prospectus supplement and accompanying prospectus.

We have entered into a certain letter agreement with H.C. Wainwright & Co., LLC (Wainwright or the placement agent) to act as our exclusive placement agent in connection with the shares of common stock offered by this prospectus supplement and the accompanying prospectus. The placement agent is arranging for the sale of shares of the common stock offered in this prospectus supplement on a "reasonable best efforts" basis. The placement agent is not required to sell any specific number or dollar amount of the securities offered by this prospectus supplement, but will use its reasonable best efforts to sell all such shares up to the maximum of \$8,250,000.

Delivery of the shares of common stock will be made to the purchasers on or about July 11, 2018, subject to customary closing conditions.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

H.C. Wainwright & Co.

The date of this prospectus supplement is July 9, 2018.

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

<u>ABOUT THIS PROSPECTUS SUPPLEMENT</u>	i
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	i
<u>INDUSTRY AND MARKET DATA</u>	ii
<u>TRADEMARKS</u>	ii
<u>Prospectus Supplement Summary</u>	S-1
<u>THE OFFERING</u>	S-4
<u>Risk Factors</u>	S-5
<u>Use of Proceeds</u>	S-6
<u>DETERMINATION OF OFFERING PRICE</u>	S-6
<u>Dilution</u>	S-7
<u>Description of THE SECURITIES WE ARE OFFERING</u>	S-7
<u>PLAN OF DISTRIBUTION</u>	S-8
<u>PRIVATE PLACEMENT OF WARRANTS</u>	S-9
<u>LEGAL MATTERS</u>	S-9
<u>EXPERTS</u>	S-9
<u>Where You Can Find More Information</u>	S-10
<u>Incorporation of Certain Documents by Reference</u>	S-10

Prospectus

<u>ABOUT THIS PROSPECTUS</u>	1
<u>ABOUT ISORAY</u>	1
<u>RISK FACTORS</u>	3
<u>NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	3
<u>USE OF PROCEEDS</u>	4
<u>GENERAL DESCRIPTION OF SECURITIES</u>	4
<u>DESCRIPTION OF CAPITAL STOCK</u>	5
<u>DESCRIPTION OF PREFERRED STOCK</u>	8
<u>DESCRIPTION OF WARRANTS</u>	10
<u>DESCRIPTION OF UNITS</u>	11
<u>PLAN OF DISTRIBUTION</u>	11
<u>LEGAL MATTERS</u>	13
<u>EXPERTS</u>	13
<u>INTERESTS OF NAMED EXPERTS AND COUNSEL</u>	13
<u>MATERIAL CHANGES</u>	14
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	14
<u>INCORPORATION BY REFERENCE</u>	14
<u>COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES</u>	15

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

A registration statement on Form S-3 (File No. 333-206559) utilizing a shelf registration process relating to the securities described in this prospectus supplement has been filed with the Securities and Exchange Commission (SEC), and was declared effective on November 23, 2015. Under this shelf registration process, of which this offering is a part, we may, from time to time, sell up to 11 million shares of common stock.

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of our common stock and also adds, updates and changes information contained in the accompanying prospectus and the documents incorporated by reference. The second part is the accompanying base prospectus, which gives more general information, some of which may not apply to this offering. To the extent the information contained in this prospectus supplement differs or varies from the information contained in the accompanying prospectus or any document filed prior to the date of this prospectus supplement and incorporated by reference, the information in this prospectus supplement will control. Generally, when we refer to this “prospectus,” we are referring to both documents combined, together with any free writing prospectus that we have authorized for use in connection with this offering.

You should rely only on the information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus. We have not, and Wainwright has not, authorized anyone to provide you with information that is different. This prospectus supplement is not an offer to sell or solicitation of an offer to buy these securities in any circumstances under which the offer or solicitation is unlawful. You should not assume that the information we have included in this prospectus supplement or the accompanying prospectus is accurate as of any date other than the date of this prospectus supplement or the accompanying prospectus, respectively, or that any information we have incorporated by reference is accurate as of any date other than the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement or of any of our securities. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents we have referred you to in “Incorporation of Certain Documents by Reference” and “Where You Can Find More Information” in this prospectus supplement.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

All statements contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, other than statements of historical facts, that address future activities, events or developments are forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act. These statements often contain the words “may,” “will,” “believe,” “expect,” “anticipate,” “intends,” “estimate,” “forecast,” “project,” and similar expressions, although not all forward-looking statements contain these words. All statements other than statements of historical fact are statements that could be deemed forward-looking

statements, including statements relating but not limited to:

projections of earnings, revenues or other financial items;

plans and objectives of management for future operations;

proposed new products or services;

future operations, plans, regulatory filings or approvals;

proposed new products or services, any statements regarding pending or future mergers or acquisitions; and

future economic conditions or performance, and any statement of assumptions underlying any of the foregoing.

Table of Contents

These statements are based on certain assumptions and analyses made by us in light of our experience and our assessment of historical trends, current conditions and expected future developments, as well as other factors we believe are appropriate under the circumstances. However, whether actual results will conform to the expectations and predictions of management is subject to a number of risks and uncertainties that may cause actual results to differ materially.

You should not place undue reliance on our forward-looking statements because the matters they describe are subject to known and unknown risks, uncertainties and other unpredictable factors, many of which are beyond our control. Our forward-looking statements are based on the information currently available to us and speak only as of the date of this prospectus supplement, the date on the cover of the accompanying prospectus, or, in the case of forward-looking statements incorporated by reference, as of the date of the filing that includes the statement. New risks and uncertainties arise from time to time, and it is impossible for us to predict these matters or how they may affect us. Over time, our actual results, performance or achievements will likely differ from the anticipated results, performance or achievements that are expressed or implied by our forward-looking statements, and such difference might be significant and materially adverse to our security holders. We do not undertake and specifically decline any obligation to update any forward-looking statements or to publicly announce the results of any revisions to any statements to reflect new information or future events or developments.

We have identified some of the important factors that could cause future events to differ from our current expectations and they are described in this prospectus supplement and the accompanying prospectus under the caption “Risk Factors” as well as in our most recent Annual Report on Form 10-K, including without limitation under the captions “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and in other documents that we may file with the SEC, all of which you should review carefully. Please consider our forward-looking statements in light of those risks as you read this prospectus supplement and the accompanying prospectus.

INDUSTRY AND MARKET DATA

This prospectus supplement and the accompanying prospectus contain and incorporate by reference market data, industry statistics and other data that have been obtained from, or compiled from, information made available by third parties. Although we believe these third-party sources are reliable, we have not independently verified the information. Except as may otherwise be noted, none of the sources cited in this prospectus supplement or the accompanying prospectus has consented to the inclusion of any data from its reports, nor have we sought their consent. In addition, some data are based on our good faith estimates. Such estimates are derived from publicly available information released by independent industry analysts and third-party sources, as well as our own management’s experience in the industry, and are based on assumptions made by us based on such data and our knowledge of such industry and markets, which we believe to be reasonable. However, none of our estimates have been verified by any independent source. See “Special Note Regarding Forward-Looking Statements” above.

TRADEMARKS

Proxcelan, the IsoRay logo, and IsoRay are our registered trademarks. These trademarks are important to our business. Although we may have omitted the “®” or “TM” trademark designation for such trademarks in this prospectus supplement, all rights to such trademarks are nevertheless reserved. Unless otherwise noted, other trademarks used in this prospectus supplement are the property of their respective holders.

Table of Contents

Prospectus Supplement Summary

This summary highlights selected information appearing elsewhere or incorporated by reference in this prospectus supplement and accompanying prospectus and may not contain all of the information that is important to you. This prospectus supplement and the accompanying prospectus include or incorporate by reference information about the shares of common stock we are offering as well as information regarding our business and detailed financial data. After you read this summary, you should read this prospectus supplement and the accompanying prospectus in their entirety, including the information incorporated by reference in this prospectus supplement and the accompanying prospectus, especially the section entitled “Risk Factors.” If you invest in our securities, you are assuming a high degree of risk.

Unless the context requires otherwise, in this prospectus, the terms “IsoRay,” the “Company,” “we,” “us,” “our” and similar terms refer to IsoRay, Inc. and its operating subsidiary IsoRay Medical, Inc., and, to the extent applicable, its non-operating subsidiary, IsoRay International LLC.

Business Overview

In 2003, IsoRay obtained clearance from the Food and Drug Administration (FDA) for the use of Cesium-131 (Cs-131) radioisotope in the treatment of all malignant tumors. As of the date of this report, such applications include prostate cancer, brain cancer, breast cancer, colorectal cancer, gynecological cancer, lung cancer, liver cancer, ocular melanoma and pancreatic cancer. The brachytherapy seed form (a sealed source) of Cs-131 may be used in surface, interstitial and intra-cavity applications for tumors with known radio-sensitivity. Management believes the combination of a short half-life and relatively high-energy of Cs-131 will allow it to become a leader in the brachytherapy market, and Cs-131 represents the first major advancement in brachytherapy technology in approximately 30 years with attributes that could make it the long-term “seed of choice” for internal radiation therapy procedures.

Brachytherapy seeds are small devices containing a therapeutic dose of radiation used in an interstitial radiation procedure. The procedure has become one of the primary treatments for prostate cancer. The brachytherapy procedure places radioactive seeds as close as possible to (in or near) the cancerous tumor (the word “brachytherapy” is derived from Greek and means close therapy). A primary advantage of seed brachytherapy is the ability of the seeds to deliver therapeutic radiation thereby killing the cancerous tumor cells while minimizing exposure (damage) to adjacent healthy tissue. This procedure allows doctors to administer a higher dose of radiation directly to the tumor. A seed contains a radioisotope sealed within a titanium capsule. When brachytherapy is the only treatment (monotherapy) used in the prostate, approximately 70 to 120 seeds are permanently implanted in the prostate during an outpatient procedure. The number of seeds used varies based on the size of the prostate gland, the isotope used, and the activity level specified by the physician. When brachytherapy is combined with another treatment method (dual-therapy), fewer seeds are used (approximately 40 to 80) in the procedure. The isotope decays over time (half-life) and

eventually the seeds become inert (typically over 6 half-lives). The seeds may be used as a primary treatment (monotherapy) or as an adjunct therapy with other treatment modalities, or as treatment for residual disease after excision of primary tumors. The number of seeds for treatment sites other than prostate vary widely (as few as 8 seeds to more than 100 seeds) depending on the type of cancer, the tumor location, the prescribed activity level and any additional type of therapy being utilized.

IsoRay began the production and sales of Cs-131 brachytherapy seeds in October 2004 for the treatment of prostate cancer after receiving clearance of its premarket notification (510(k)) by the Food and Drug Administration. Prostate cancer treatment represents over 83% of the business for the three months ended March 31, 2018.

In late 2014, the first report of five-year clinical outcomes for patients treated with Cs-131 brachytherapy was published in a peer-reviewed medical journal (Benoit, et al., *Five Year Prostate-specific Antigen Outcomes after Caesium Prostate Brachytherapy*, Clin Oncol 25 (December 2014)). In this study of 485 prostate cancer patients treated with Cs-131 brachytherapy seeds, a “biochemical relapse free” success rate of 96% was reported for low-risk patients after five years.

Work is ongoing to employ Cs-131 brachytherapy seeds where trends are emerging in prostate cancer treatment, including the use of Cs-131 implants in combination with intensity modulated radiation therapy (IMRT – a form of external beam radiation) for high-risk localized prostate cancer (dual-therapy). For low-risk prostate cancer, studies are ongoing to evaluate the use of Cs-131 in “focal,” or sub-total brachytherapy of the prostate. It is hypothesized that low-risk patients using focal brachytherapy may achieve rates of prostate cancer control comparable to that of full gland treatment while significantly reducing side effects. (M.H. Mendez, et al., *Current trends and new frontiers in focal therapy for localized prostate cancer*, Current Urology Report 16, 35 (June 2015)).

Table of Contents

The Company's core product is its Cs-131 sealed source brachytherapy "seed." These seeds can be inserted individually into the prostate gland until the physician is satisfied with the radiation dose delivered. The Company also sells "pre-loaded" needles with Cs-131 brachytherapy seeds inserted in them. In addition to the five-year cancer control data mentioned above, a report from 2017 describes favorable long-term quality of life outcomes following Cs-131 brachytherapy in the treatment of prostate cancer (S.M. Glaser, et al., *Long-Term Quality of Life in Prostate Cancer Patients Treated With Cesium*, 131 Int J Radiat Oncol Biol Phys. 98(5):1053-1058 (2017)).

Individual seeds can also be placed via needle into the female reproductive tract for the treatment of various gynecologic cancers. This effort has been led by Dr. Jonathan Feddock of the University of Kentucky. In June 2016, the lead physician from the University of Kentucky conducted two presentations on gynecological cancer patients who underwent treatment with permanent implantation of Cs-131 brachytherapy seeds. In the first presentation, it was noted that 21 out of 26 recurrent cancer patients remained visually free of cancer at a median of 14 months after implantation which equates to 80.7% local control (J. Feddock, et al., *Permanent interstitial re-irradiation with cesium-131: a highly successful second chance for cure in recurrent pelvic malignancies*, Brachytherapy 15 (S1):S78-9 (2016)). In the second presentation, a series of 22 women with pelvic cancer underwent Cesium-131 brachytherapy seed implantation with other forms of radiation therapy treating patients who were recently diagnosed and had not yet undergone any treatment. All these cancers were successfully controlled at a median follow-up of 16 months. Side effects using the Cs-131 brachytherapy seeds were minor and all treatments were performed as outpatient procedures. (J. Feddock, et al., *Outpatient interstitial implants - integrating cesium-131 permanent interstitial brachytherapy into definitive treatment for gynecologic malignancies*, Brachytherapy 15 (S1):S93-4 (2016)). Dr. Feddock and his team are continuing ongoing research.

While the FDA clearance granted in August 2009 to permit loading Cesium-131 seeds into bio-absorbable braided sutures or "braided strands" gives the Company the ability to treat brain, lung, head and neck, colorectal, and chest wall cancers, and gynecological cancer, the Company is currently pursuing the brain and gynecological cancers applications in addition to its primary focus on prostate cancer. The Company has also received CE Mark clearance to commercially deliver Cs-131 brachytherapy seeds that are pre-loaded into braided strands in Europe. This clearance permits the product to be commercially distributed in Europe for treatment of prostate, brain, lung, and head and neck tumors, as well as tumors in other organs.

Starting in 2012, multiple institutions began utilizing Cs-131 brachytherapy seeds loaded in braided strands for treatment of brain and head cancers. The application of Cs-131 brachytherapy seeds loaded in braided strands to date has been primarily in salvage cases as a treatment of last resort for brain and head cancers where aggressive tumors had reoccurred multiple times following standard of care treatment. From 2014 to 2016, there have been numerous published abstracts and society presentations which have been presented and support the effectiveness of treating very difficult and aggressive cancers with Cs-131 in multiple body sites. Dr. Gabriella Wernicke's group, at Weill Cornell Medical College at the NY Presbyterian Hospital, published four papers on the efficacy, favorable side-effect profile and cost-effectiveness of Cs-131 brachytherapy seeds in the treatment of metastatic brain cancer. (A. Pham, et al., *Neurocognitive function and quality of life in patients with newly diagnosed brain metastasis after treatment with intra-operative cesium-131 brachytherapy: a prospective trial*, J Neurooncol 127(1):63-71 (2016); A.G. Wernicke, et al., *Surgical technique and clinically relevant resection cavity dynamics following implantation of cesium-131 brachytherapy in patients with brain metastases*, Operative Neurosurgery 12(1):49-60 (2016); A.G. Wernicke, et al.,

Cesium-131 brachytherapy for recurrent brain metastases: durable salvage treatment for previously irradiated metastatic disease, J Neurosurg DOI: 10.3171/2016.3.JNS152836 (Published online June 3, 2016); A.G. Wernicke, et al., *The cost-effectiveness of surgical resection and cesium-131 intraoperative brachytherapy versus surgical resection and stereotactic radiosurgery in the treatment of metastatic brain tumors*, J Neurooncol 127(1):145-53 (2016)). At the same institution, Dr. Bhupesh Parashar has published two journal articles on the effectiveness of Cs-131 brachytherapy seeds in the treatment of both head and neck and lung cancer. (B. Parashar, et al., *Analysis of stereotactic radiation vs. wedge resection vs. wedge resection plus Cesium-131 brachytherapy in early stage lung cancer*, Brachytherapy 14(5):648-54 (2015); A. Pham, et al., *Cesium-131 brachytherapy in high risk and recurrent head and neck cancers: first report of long-term outcomes*, J Contemp Brachytherapy 7(6):445-52 (2015)). In 2017, Dr. Wernicke's group published favorable results on a series of patients with large brain metastases treated with Cs-131 in braided strands. A. G. Wernicke, et al., *Clinical Outcomes of Large Brain Metastases Treated With Neurosurgical Resection and Intraoperative Cesium-131 Brachytherapy: Results of a Prospective Trial*, Int J Radiat Oncol Biol Phys. 98 (5):1059-1068 (2017)).

Table of Contents

During fiscal 2013, the Company began providing technical assistance and selling Cs-131 brachytherapy seeds for embedding in collagen tiles by physicians at Barrow Neurological Institute (Barrow) to treat malignant meningioma, primary brain cancers and metastases of cancers to the brain. These physicians from Barrow have formed a company, GT Medical Technologies, Inc. (“GT Tech”), and further refined this technology which integrates Cs-131 brachytherapy seeds and has resulted in the issuance of multiple patents to GT Tech for the treatment of brain cancers. In December 2014 and June 2016, physicians representing Barrow presented their findings at two society conferences for neuro-oncologists. Highlights of the presentation included a new treatment delivery system of Cs-131 brachytherapy seeds to the brain while embedded in collagen tiles by applying directly to brain tissue after tumor removal. The trial presented included 16 patients with 20 tumors. The patients in the study had multiple reoccurrences of tumors following previous surgeries in conjunction with treatments with external beam radiation and had an increased risk for additional reoccurrences. Following treatment with Cs-131, 95% of the treated tumors had no evidence of regrowth at the operative site (local control). The incidence of radiation side effects to the brain from Cs-131 brachytherapy seeds (a common side effect) occurred in only 2 of the 20 treatments. (D. Brachman, *Prospective trial of surgery and permanent intraoperative brachytherapy (S+BT) using a modular, biocompatible radiation implant for recurrent aggressive meningiomas*, Society of Neuro-Oncology Conference on Meningioma, Toronto, Canada (June 18, 2016)).

In November of 2016, Dr. Emad Youssef of the Barrow Neurological Institute presented a study conducted on 13 patients with recurrent high grade gliomas (primary brain cancer) at the annual meeting of the Society for Neuro-Oncology meeting. (E. Youssef, et al; *Rthp-23. Cs131 Implants For Salvage Therapy Of Recurrent High Grade Gliomas (Hgg)*, Neuro-Oncology Volume 18, Issue suppl_6, 1 November 2016, Pages vi179). These patients were reported to have achieved a 92% rate of local control of their cancers during the follow-up interval. Due to the fact that the GammaTile™ treatment has displayed promising results in difficult to control recurrent brain cancers, the Company has collaborated with GT Tech in filing applications to: the U.S. Food and Drug Administration (FDA) to clear GammaTile™ for clinical use; and a New Technology Add-on Payment (NTAP) to the Center for Medicare and Medicaid Services (CMS) seeking reimbursement for the GammaTile™ treatment in the in-patient setting.

On July 6, 2018, we received FDA clearance for GammaTile™ therapy. This therapy allows IsoRay, Inc. in collaboration with GT Medical Technology (“GT”) to use our proprietary Cesium-131 seeds within GT’s customizable collagen-based carriers for the treatment of recurrent brain tumors. Although the Centers for Medicare and Medical Services (CMS) has already clarified coding for GammaTile™ in the hospital setting, GT will need to file a new NTAP application, but will not be eligible (assuming NTAP approval is obtained) for Medicare coverage until fiscal 2020.

On July 9, 2018, we filed Supplement No. 1 to Prospectus Supplement to suspend and to terminate the continuous at-the-market offering pursuant to a Sales Agreement with Wainwright entered into on May 8, 2018. As of July 6, 2018, the Company had raised gross proceeds of \$487,353 through the sale of an aggregate of 980,918 shares of common stock.

Our Corporate Information

Edgar Filing: IsoRay, Inc. - Form 424B5

Our principal executive offices are located at 350 Hills Street, Suite 106, Richland, Washington 99354, and our telephone number is (509) 375-1202. We maintain an Internet website at www.isoray.com. Information on or accessible through our website does not constitute part of this prospectus supplement and should not be relied upon in connection with making any investment decision with respect to the securities offered by this prospectus supplement.

Although our predecessor operating company was organized in 1998, IsoRay, Inc. was incorporated in 1983 in Minnesota and operated under the name Century Park Pictures Corporation until the merger with IsoRay Medical, Inc. on July 28, 2005.

S-3

Table of Contents

THE OFFERING

The following is a brief summary of some of the terms of the offering and is qualified in its entirety by reference to the more detailed information appearing elsewhere in this prospectus supplement and the accompanying prospectus. For a more complete description of the terms of our common stock, see the “Description of the Securities We Are Offering” section in this prospectus supplement.

Securities We Are Offering 11,000,000 shares of common stock, par value \$0.001 per share.

Common Stock Outstanding Before This Offering 56,331,147 shares.

Common Stock To Be Outstanding After This Offering 67,331,147 shares assuming no other shares of common stock are issued.

Concurrent private placement of Warrants We are offering 11,000,000 shares of our common stock in this offering pursuant to this prospectus supplement and the accompanying base prospectus and securities purchase agreements at a price of \$0.75 per share. In a concurrent private placement, we are also selling to investors Warrants to purchase an additional 5,500,000 shares of our common stock which represent 50% of the number of shares of our common stock purchased in this offering. Each Warrant will be exercisable for one share of our common stock at an exercise price of \$0.75 per share. The Warrants and the Warrant Shares are not being registered under the Securities Act, pursuant to the registration statement of which this prospectus supplement and the accompanying base prospectus form a part nor are such Warrants and the Warrant Shares being offered pursuant to such prospectus supplement and base prospectus and are being offered pursuant to an exemption provided in Section 4(a)(2) of the Securities Act and Rule 506(b) promulgated thereunder. The Warrants are not and will not be listed for trading on any national securities exchange. Each purchaser will be an “accredited investor” as such term is defined in Rule 501(a) under the Securities Act.

Use of Proceeds We estimate that the net proceeds to us from this offering after placement agent fees and offering expenses payable by us will be approximately \$7.6 million. We intend to use the net proceeds from the sale of common stock offered by this prospectus supplement for general corporate purposes, including without limitation, working capital needs with particular focus on marketing the brain application and Build-Blu™ delivery system for real time brachytherapy. See “Use of Proceeds.”

Risk Factors Our business is subject to substantial risk. Please carefully consider the “Risk Factors” beginning on page S-4 of this prospectus supplement, page 3 of the accompanying prospectus and other

information included and incorporated by reference in this prospectus supplement and the accompanying prospectus including, but not limited to, the “Risk Factors” in our Annual Report on Form 10-K for the fiscal year ended June 30, 2017 (together with any material changes thereto contained in any subsequent filed Quarterly Reports on Form 10-Q), for a discussion of the factors you should consider carefully before deciding to purchase these securities. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. You should be able to bear a complete loss of your investment.

NYSE
American ISR
Symbol

(1) The number of shares of our common stock to be outstanding immediately after this offering is based on 56,331,147 shares of our common stock outstanding as of July 6, 2018, and excludes as of such date: 250,000 shares of common stock issuable upon the exercise of warrants with a weighted average exercise price of \$0.54; 59,065 shares of common stock issuable upon the conversion of preferred stock; 3,759,840 shares of common stock issuable upon the exercise of options with a weighted average exercise price of \$0.69; 1,221,875 shares of common stock reserved for future stock option grants under our equity compensation plans; 5,500,000 Warrant Shares issuable upon the exercise of the Warrants to be offered in the concurrent private placement, with an exercise price of \$0.75 per share; and 330,000 shares of our common stock issuable upon the exercise of the warrants to be issued as compensation to the placement agent of this offering, with an exercise price of \$0.9375 per share.

Except as otherwise indicated herein, all information in this prospectus supplement, including the number of shares that will be outstanding after this offering, does not assume or give effect to the exercise of options or warrants outstanding as of July 6, 2018 or to the exercise of the Warrants offered in the concurrent private placement or to the warrants to be issued to the placement agent in connection with this offering.

Table of Contents

Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks listed below and other information included and incorporated by reference in this prospectus supplement and accompanying prospectus. There may also be risks of which we are currently unaware, or that we currently regard as immaterial based on the information available to us that later prove to be material. If any of these risks occur, our business, operating results and financial condition could be seriously harmed, the trading price of our common stock could decline, and you could lose some or all of your investment.

Risks Related to this Offering

The Price Of Our Common Stock May Be Adversely Affected By The Future Issuance And Sale Of Shares Of Our Common Stock Or Other Equity Securities. We cannot predict the size of future issuances or sales of our common stock or other equity securities, future acquisitions or capital raising activities, or the effect, if any, that such issuances or sales may have on the market price of our common stock. The issuance and sale of substantial amounts of common stock or other equity securities or announcement that such issuances and sales may occur, could adversely affect the market price of our common stock.

Future Sales By Shareholders, Or The Perception That Such Sales May Occur, May Depress The Price Of Our Common Stock. The sale or availability for sale of substantial amounts of our shares in the public market or exercise of common stock warrants and options, or the perception that such sales could occur, could adversely affect the market price of our common stock and also could impair our ability to raise capital through future offerings of our shares. As of July 6, 2018, we had 56,331,147 outstanding shares of common stock, and the following additional shares were reserved for issuance: 3,759,840 shares upon exercise of outstanding options, 250,000 shares upon exercise of outstanding warrants, and 59,065 shares upon conversion of Series B preferred stock. Any decline in the price of our common stock may encourage short sales, which could place further downward pressure on the price of our common stock and may impair our ability to raise additional capital through the sale of equity securities.

The Issuance Of Shares Upon Exercise Of Derivative Securities May Cause Immediate And Substantial Dilution To Our Existing Shareholders. The issuance of shares upon conversion of the Series B preferred stock and the exercise of common stock warrants and options may result in substantial dilution to the interests of other shareholders since these selling shareholders may ultimately convert or exercise and sell all or a portion of the full amount issuable upon exercise. If all derivative securities outstanding as of July 6, 2018 were converted or exercised into shares of common stock, there would be approximately an additional 4,068,905 shares of common stock outstanding as a result. The issuance of these shares will have the effect of further diluting the proportionate equity interest and voting power of holders of our common stock.

Since We Have Broad Discretion In How We Use The Proceeds From This Offering, We May Use The Proceeds In Ways In Which You Disagree. Our management will have significant flexibility in applying the net proceeds of this offering. You will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the net proceeds will be invested in a way that does not yield a favorable, or any, return for our company. The failure of our management to use such funds effectively could have a material adverse effect on our business, financial condition, operating results and cash flow.

Purchasers Of The Shares Will Incur Immediate Dilution. Purchasers of shares of common stock in this offering will experience immediate and substantial dilution because the purchase price of the common stock will be higher than the net tangible book value per share of the outstanding common stock immediately after this offering. In addition, purchasers will experience dilution, which may be substantial, when we issue additional shares of common stock that we are permitted or required to issue under options, warrants, our stock option plans or other employee or director compensation plans. In this offering, after deducting the placement agent fees and estimated offering expenses payable by us, you will experience immediate dilution of \$0.53 per share, representing the difference between our as adjusted net tangible book value per share as of our most recent Form 10-Q for the period ending March 31, 2018 and utilizing the shares outstanding after giving effect to this offering. See “Dilution” for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

Table of Contents

Use of Proceeds

Assuming we sell 11,000,000 shares of our common stock in this offering, we estimate that the net proceeds from the sale will be approximately \$7.6 million, based on the offering price of \$0.75 per share, after deducting the placement agent fees and the estimated offering expenses payable by us.

We intend to use our net proceeds from this offering for general corporate purposes, including without limitation working capital needs with particular focus on marketing the brain application and Build-Blu™ delivery system for real time brachytherapy.

Although we have identified some of the potential uses of the proceeds from this offering, we have and reserve broad discretion in the application of these proceeds. Accordingly, we reserve the right to use these proceeds for different purposes or uses which we have not listed above, particularly if there is a change in demand for certain applications of our Cesium-131 and other products which may require increased investment in protocols and research studies and the hiring of additional sales staff. See “Risk Factors – *Since We Have Broad Discretion In How We Use The Proceeds From This Offering, We May Use The Proceeds In Ways In Which You Disagree.*”

Based on our current plans, we believe that our net proceeds from this offering, together with our existing cash, cash equivalents and restricted cash will be sufficient to fund our anticipated operating expenses and capital expenditures for at least the next several fiscal years.

Pending any ultimate use of any portion of the proceeds from this offering, we intend to invest the proceeds in short- and medium-term interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

In addition, while we have not entered into any agreements, commitments or understandings relating to any significant transaction as of the date of this prospectus supplement, we may use a portion of the proceeds to pursue acquisitions, joint ventures and other strategic transactions.

DETERMINATION OF OFFERING PRICE

We will sell our common stock in this offering at a negotiated price of \$0.75 per share of common stock. The principal factors considered in determining the terms and conditions of the sale of our shares hereunder include:

the market price and volatility of our common stock;
the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
other factors deemed relevant by the placement agent and us.

S-6

Table of Contents**Dilution**

If you invest in our common stock, your interest in the common stock may be diluted to the extent of the difference between the price you pay for each share of common stock and the net tangible book value per share of our common stock immediately after this offering.

Our net tangible book value on March 31, 2018 was approximately \$6,424,000 or approximately \$0.11 per share. “Net tangible book value” is total assets minus the sum of liabilities and intangible assets. “Net tangible book value per share” is net tangible book value divided by the total number of shares of common stock outstanding at March 31, 2018.

Net tangible book value dilution per share to new investors represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after completion of this offering. Assuming we sell shares of our common stock in this offering at the offering price of \$0.75 per share and after deducting the placement agent fees and estimated offering expenses, our as-adjusted net tangible book value as of March 31, 2018 would have been \$0.22 per share. This amount represents an immediate increase in net tangible book value of \$0.11 per share to existing shareholders and an immediate dilution of \$0.53 per share to purchasers of common stock in this offering at the offering price, as illustrated in the following table:

Offering price per share	\$0.75
Net tangible book value per share as of March 31, 2018	\$0.11
Increase in net tangible book value per share attributable to this offering and ATM offering	\$0.11
Pro forma net tangible book value per share as of March 31, 2018 after giving effect to this offering and ATM offering	\$0.22
Dilution per share to new investors in this offering	\$0.53

The table above excludes, as of July 6, 2018, the following securities:

250,000 shares of common stock issuable upon the exercise of warrants with a weighted average exercise price of \$0.54;

59,065 shares of common stock issuable upon the conversion of preferred stock;

3,759,840 shares of common stock issuable upon the exercise of options with a weighted average exercise price of \$0.69;

1,221,875 shares of common stock reserved for future stock option grants under our equity compensation plans;

5,500,000 Warrant Shares issuable upon the exercise of the Warrants to be offered in the concurrent private placement, with an exercise price of \$0.75 per share; and

330,000 shares of our common stock issuable upon the exercise of the warrants to be issued as compensation to the placement agent of this offering, with an exercise price of \$0.9375 per share.

To the extent that any outstanding options, warrants and convertible securities are exercised or converted, there may be further dilution to new investors.

DESCRIPTION OF THE SECURITIES WE ARE OFFERING

Description of the Common Stock

A description of the common stock we are offering pursuant to this prospectus supplement is set forth under the heading "Description of Capital Stock," starting on page 5 of the accompanying prospectus. As of July 6, 2018, we had 56,331,147 shares of common stock outstanding.

Table of Contents

PLAN OF DISTRIBUTION

We are offering the shares of our common stock through our placement agent, H.C. Wainwright & Co., LLC. Subject to the terms and conditions contained in the letter agreement, dated July 9, 2018, H.C. Wainwright & Co., LLC has agreed to act as the placement agent for the offering on a reasonable best efforts basis. The placement agent is not purchasing or selling any shares by this prospectus supplement or the accompanying prospectus. The letter agreement does not give rise to any commitment by the placement agent to purchase any of our shares of common stock and the placement agent will have no authority to bind us by virtue of the letter agreement.

We will sell the offered common stock to institutional and accredited investors under one or more securities purchase agreements entered into between us and each of the investors at the offering price stated on the cover of this prospectus supplement. We currently anticipate that the closing of the sale of the common stock offered hereby will take place on or about July 11, 2018. In accordance with the terms of the letter agreement, we will pay the placement agent an aggregate placement agent cash fee equal to 6% of the gross proceeds of the sale of the common stock in the offering. We will also pay the placement agent a management fee equal to 1% of the gross proceeds of the sale of the common stock in the offering, \$25,000 for non-accountable expenses and an expense allowance of \$30,000 for legal fees and other out-of-pocket expenses. In addition, we have agreed to issue to the placement agent warrants to purchase up to 3.0% of the aggregate number of shares of common stock sold in this offering (330,000 shares). The placement agent warrants will have substantially the same terms as the Warrants issued to the investors in the concurrent private placement, except that the placement agent warrants will have an exercise price equal to \$0.9375, or 125% of the offering price per share in this offering and such placement agent warrants will have a term of five years from the effective date of this offering. Pursuant to FINRA Rule 5110(g), the placement agent warrants and any shares issued upon exercise of the placement agent warrants shall not be sold, transferred, assigned, pledged, or hypothecated, or be the subject of any hedging, short sale, derivative, put or call transaction that would result in the effective economic disposition of the securities by any person for a period of 180 days immediately following the date of effectiveness or commencement of sales of this offering, except the transfer of any security: (i) by operation of law or by reason of our reorganization; (ii) to any FINRA member firm participating in this offering and the officers or partners thereof, if all securities so transferred remain subject to the lock-up restriction set forth above for the remainder of the time period; (iii) if the aggregate amount of our securities held by the placement agent or related persons do not exceed 1% of the securities being offered; (iv) that is beneficially owned on a pro-rata basis by all equity owners of an investment fund, provided that no participating member manages or otherwise directs investments by the fund and the participating members in the aggregate do not own more than 10% of the equity in the fund; or (v) the exercise or conversion of any security, if all securities remain subject to the lock-up restriction set forth above for the remainder of the time period.

The estimated offering expenses payable by us, in addition to the placement agent fee of \$495,000, are \$182,500, which includes the company legal, accounting and printing costs and management fee and various other fees associated with registering and listing the common stock.

We have agreed to indemnify the placement agent against certain liabilities, including liabilities under the Securities Act of 1933, as amended, and liabilities arising from breaches of representations and warranties contained in the letter agreement. We have also agreed to contribute to payments the placement agent may be required to make in respect of such liabilities.

The transfer agent for our common shares to be issued in this offering is Computershare Trust Company. Our common shares are traded on the NYSE American equities exchange under the symbol "ISR".

S-8

Table of Contents

The placement agent may be deemed to be an underwriter within the meaning of Section 2(a)(11) of the Securities Act, and any commissions received by it and any profit realized on the resale of the securities sold by it while acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. As an underwriter, the placement agent would be required to comply with the requirements of the Securities Act and the Exchange Act, including, without limitation, Rule 415(a)(4) under the Securities Act and Rule 10b-5 and Regulation M under the Exchange Act. These rules and regulations may limit the timing of purchases and sales of shares of common stock and warrants by the placement agent acting as principal. Under these rules and regulations, the placement agent:

may not engage in any stabilization activity in connection with our securities; and

may not bid for or purchase any of our securities or attempt to induce any person to purchase any of our securities, other than as permitted under the

Exchange Act, until it has completed its participation in the distribution.

Wainwright and its affiliates may in the future provide various investment banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. We have entered into a sales agreement with Wainwright relating to a continuous sale of our shares of common stock pursuant to an at-the-market offering, for which Wainwright receives compensation. We have suspended any sales under such offering as of the date of this prospectus supplement.

We are filing a copy of the form of securities purchase agreement with the SEC on a Current Report on Form 8-K concurrently with the filing of this prospectus supplement.

PRIVATE PLACEMENT OF WARRANTS

In a concurrent private placement, we are selling to each of the investors in this offering Warrants to purchase an additional 50% of the number of shares purchased in this offering. The aggregate number of Warrant Shares exercisable pursuant to the Warrants is 5,500,000 Shares. The Warrants will be exercisable commencing six months following the date of issuance, have a term of exercise equal to five and one-half years, and have an exercise price of \$0.75, subject to adjustment. The exercise price and number of Warrant Shares issuable upon the exercise of the Warrants will be subject to adjustment in the event of any stock dividend and split, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Warrants.

A holder of Warrants will have the right to exercise the Warrants on a “cashless” basis in certain circumstances as described in the Warrants, including, among others, while there is no effective registration statement registering the Warrant Shares issuable upon exercise of the Warrants. Subject to limited exceptions, a holder of Warrants will not have the right to exercise any portion of its Warrants if the holder, together with its affiliates, would beneficially own in excess of 4.99% of the number of shares of our common stock outstanding immediately after giving effect to such exercise, provided that the holder may increase or decrease the beneficial ownership limitation up to 9.99%, provided, further, that any increase in the beneficial ownership limitation shall not be effective until 61 days following notice of such change to the Company.

The Warrants and the Warrant Shares are not being registered under the Securities Act pursuant to the registration statement of which this prospectus supplement and the accompanying base prospectus form a part and are not being offered pursuant to this prospectus supplement and the accompanying base prospectus. The Warrants and the Warrant Shares are being offered pursuant to the exemption provided in Section 4(a)(2) of the Securities Act and Rule 506(b) promulgated thereunder. All purchasers are required to be “accredited investors” as such term is defined in Rule 501(a) under the Securities Act.

LEGAL MATTERS

The validity of the issuance of the securities offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Gallagher & Kennedy, P.A., Phoenix, Arizona. Certain shareholders of Gallagher & Kennedy, P.A. hold common stock of the Company, which in the aggregate equal less than one-tenth of a percent (0.10%) of the total issued and outstanding shares of our common stock.

EXPERTS

The financial statements incorporated by reference in this prospectus supplement have been so incorporated by reference in reliance upon the report of DeCoria, Maichel & Teague, P.S., independent registered public accountants, upon the authority of said firm as experts in accounting and auditing in giving said reports.

Table of Contents

Where You Can Find More Information

This prospectus supplement and accompanying prospectus constitute a part of a registration statement on Form S-3 that we filed with the SEC under the Securities Act. We refer you to this registration statement for further information about us and our common stock offered hereby.

We file annual, quarterly and special reports and other information with the SEC (Commission File Number 001-33407). These filings contain important information that does not appear in this prospectus supplement or the accompanying prospectus. For further information about us, you may read and copy any reports, statements and other information filed by us at the SEC's Public Reference Room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549-0102. You may obtain further information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Our SEC filings are also available on the SEC Internet site at www.sec.gov, which contains periodic reports and other information regarding issuers that file electronically.

Incorporation of Certain Documents by Reference

The SEC allows us to “incorporate by reference” into this prospectus the information we file with it. This means that we can disclose important information to you by referring you to those documents. The information we incorporate by reference is considered to be a part of this prospectus supplement, and later information we file with the SEC will automatically update and supersede this information. The following documents filed with the SEC (in each case, under our Commission File No. 001-33407) are incorporated by reference in this prospectus supplement:

Annual Report on Form 10-K for the fiscal year ended June 30, 2017, filed on September 28, 2017;

Quarterly Reports on Form 10-Q for the fiscal quarters ended September 30, 2017, December 31, 2017 and March 31, 2018, filed on November 14, 2017, February 9, 2018, and May 4, 2018, respectively;

Current Reports on Form 8-K filed on July 7, 2017, August 31, 2017, September 28, 2017, October 10, 2017, October 27, 2017, November 14, 2017, December 19, 2017, January 4, 2018, January 8, 2018, January 24, 2018, February 8, 2018, April 20, 2018, May 3, 2018, May 8, 2018, May 11, 2018, May 21, 2018, June 5, 2018, June 19, 2018, and June 29, 2018;

Proxy Statement on Schedule 14A filed on November 3, 2017 in definitive form;

the description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on April 12, 2007 (File No. 001-33407), including any amendments or reports filed for the purpose of updating such description;

the description of our rights contained in our Registration Statement on Form 8-A filed on February 7, 2007 (File No. 000-14247), including any amendments or reports filed for the purpose of updating such description; and

all documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act, (i) after the date on which this registration statement that includes this prospectus supplement was initially filed with the SEC and prior to the effectiveness of such registration statement, and (ii) after the date of this prospectus supplement and prior to the termination of this offering, unless otherwise stated therein.

Notwithstanding the foregoing, information furnished under Items 2.02 and 7.01 of any Current Report on Form 8-K, including the related exhibits, is not incorporated by reference in this prospectus supplement.

Any statement contained herein or made in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained herein, or in any other subsequently filed document which also is incorporated or deemed to be incorporated by reference herein, modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

We will provide without charge to each person to whom this prospectus supplement is delivered, upon oral or written request, a copy of any or all of the foregoing documents incorporated herein by reference (other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the information that this prospectus supplement incorporates). Written or telephone requests should be directed to: IsoRay, Inc., 350 Hills Street, Suite 106, Richland, Washington 99354, telephone number (509) 375-1202, Attn: Corporate Secretary.

You should rely only on the information contained or incorporated by reference in this prospectus supplement. We have not authorized anyone else to provide you with different or additional information. We will not make an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date of this document.

Table of Contents

ISORAY, INC.

\$20,000,000

Common Stock

Preferred Stock

Warrants

Units

We may offer to the public from time to time in one or more series or issuances at prices and on terms that we will determine at the time of each offering, shares of our common stock, shares of preferred stock, warrants to purchase shares of our common stock and/or preferred stock, units consisting of a combination of the foregoing securities, or any combination of these securities. The aggregate initial offering price of all securities sold by us pursuant to this prospectus will not exceed \$20,000,000.

This prospectus describes the general manner in which our securities may be offered using this prospectus. Each time we offer and sell securities, we will provide you with a prospectus supplement that will contain specific information about the terms of that offering. Any prospectus supplement may also add, update, or change information contained in this prospectus. You should carefully read this prospectus and the applicable prospectus supplement as well as the documents incorporated or deemed to be incorporated by reference in this prospectus before you purchase any of the securities offered hereby. This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement.

We may offer the securities directly or through agents or to or through underwriters or dealers. If any agents or underwriters are involved in the sale of the securities their names, and any applicable purchase price, fee, commission

or discount arrangement between or among them, will be set forth, or will be calculable from the information set forth, in an accompanying prospectus supplement. The securities may be offered and sold through public or private transactions at market prices prevailing at the time of sale, at a fixed price or fixed prices, at negotiated prices, at various prices determined at the time of sale or at prices related to prevailing market prices. We can sell the securities through agents, underwriters or dealers only with delivery of a prospectus supplement describing the method and terms of the offering of such securities. In addition, shares of our common stock may be offered from time to time through ordinary brokerage transactions on the NYSE MKT. See “Plan of Distribution.”

Our principal executive offices are located at 350 Hills Street, Suite 106, Richland, Washington 99354, and our telephone number is (509) 375-1202.

Our common stock is listed on the NYSE MKT under the symbol “ISR” and as of October 6, 2015, the closing price of our common stock was \$1.39.

Investing in the securities we may offer involves various risks. See the sections entitled “Risk Factors” on page 3 and “Note Regarding Forward-Looking Statements” on page 3. Additional risks associated with an investment in us as well as with the particular types of securities will be described in the related prospectus supplement and certain of our filings with the Securities and Exchange Commission. You should read the entire prospectus carefully before you make your investment decision.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Table of Contents

The date of this prospectus is November 23, 2015.

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	1
<u>ABOUT ISORAY</u>	1
<u>RISK FACTORS</u>	3
<u>NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	3
<u>USE OF PROCEEDS</u>	4
<u>GENERAL DESCRIPTION OF SECURITIES</u>	4
<u>DESCRIPTION OF CAPITAL STOCK</u>	5
<u>DESCRIPTION OF PREFERRED STOCK</u>	8
<u>DESCRIPTION OF WARRANTS</u>	10
<u>DESCRIPTION OF UNITS</u>	11
<u>PLAN OF DISTRIBUTION</u>	11
<u>LEGAL MATTERS</u>	13
<u>EXPERTS</u>	13
<u>INTERESTS OF NAMED EXPERTS AND COUNSEL</u>	13
<u>MATERIAL CHANGES</u>	14
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	14
<u>INCORPORATION BY REFERENCE</u>	14
<u>COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES</u>	15

The registration statement, including the exhibits and the documents incorporated herein by reference, can be read on the Securities and Exchange Commission website or at the Securities and Exchange Commission offices mentioned under the heading “Where You Can Find More Information.”



Table of Contents

ABOUT THIS PROSPECTUS

You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale 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 front cover of this prospectus. You should not assume that the information incorporated by reference in this prospectus is accurate as of any date other than the date the respective information was filed with the Securities and Exchange Commission. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a “shelf” registration process. Under this shelf registration process, we may sell any of the securities, or any combination of the securities, described in this prospectus, in each case in one of more offerings up to a total dollar amount of proceeds of \$20,000,000. This prospectus describes the general manner in which our securities may be offered by this prospectus. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of those securities and terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus or in documents incorporated by reference in this prospectus. To the extent that any statement that we make in a prospectus supplement is inconsistent with statements made in this prospectus or in documents incorporated by reference in this prospectus, you should rely on the information in the prospectus supplement. You should carefully read both this prospectus and any prospectus supplement together with the additional information described under “Where You Can Find More Information” before buying any securities in this offering.

ABOUT ISORAY

In this prospectus, the terms “IsoRay,” the “Company,” “we,” “us,” “our” and similar terms refer to IsoRay, Inc. and its subsidiaries IsoRay, Medical, Inc. (Medical) and IsoRay International LLC.

In 2003, IsoRay obtained clearance from the FDA for treatment for all solid tumor applications using Cesium-131. As of the date of this prospectus, such applications include prostate cancer; ocular melanoma; head, neck and lung tumors; breast cancer; liver cancer; brain cancer; colorectal cancer; gynecological cancer; esophageal cancer; and pancreatic cancer. The brachytherapy seed form of Cesium-131 may be used in surface, interstitial and intracavity applications for tumors with known radio sensitivity. Management believes its Cs-131 technology will allow it to become a leader in the brachytherapy market. Management believes that the IsoRay Proxcelan® Cesium-131 brachytherapy seed represents the first major advancement in brachytherapy technology in approximately 30 years with attributes that could make it the long-term “seed of choice” for internal radiation therapy procedures.

Brachytherapy seeds are small devices used in an interstitial radiation procedure. The procedure has become one of the primary treatments for prostate cancer. The brachytherapy procedure places radioactive seeds as close as possible to (in or near) the cancerous tumor (the word “brachytherapy” means close therapy). The seeds deliver therapeutic radiation thereby killing the cancerous tumor cells while minimizing exposure to adjacent healthy tissue. This procedure allows doctors to administer a higher dose of radiation directly to the tumor. Each seed contains a radioisotope sealed within a titanium capsule. When brachytherapy is the only treatment (monotherapy) used in the prostate, approximately 70 to 120 seeds are permanently implanted in the prostate in an outpatient procedure. The number of seeds used varies based on the size of the prostate and the activity level specified by the physician. When brachytherapy is combined with external beam radiation or intensity modulated radiation therapy (dual therapy), then approximately 40 to 80 seeds are used in the procedure. The isotope decays over time and eventually the seeds become inert. The seeds may be used as a primary treatment or as an adjunct therapy with other treatment modalities, such as chemotherapy, or as treatment for residual disease after excision of primary tumors. The number of seeds for other treatment sites commonly vary from as few as 8 seeds to more than 100 seeds depending on the type of cancer, the location of the tumor being treated and the type of therapy being utilized.

Table of Contents

IsoRay began production and sales of Proxcelan[®] Cesium-131 brachytherapy seeds in October 2004 for the treatment of prostate cancer after clearance of its premarket notification (510(k)) by the Food and Drug Administration (FDA). In December 2007, IsoRay began selling its Proxcelan[®] Cs-131 seeds for the treatment of ocular melanoma, however, the market for the treatment has been limited generating a minimal amount of revenue for the Company. The Company continues to make the treatment available to interested physicians and medical facilities. In June 2009, the Company began selling its Proxcelan[®] Cs-131 seeds for treatment of head and neck tumors, commencing with treatment of a tumor that could not be accessed by other treatment modalities. The Company obtained clearance in August 2009 from the FDA to permit loading Cesium-131 into bioabsorbable braided sutures which are commonly referred to in the industry as braided strands, facilitating treatment of brain, lung, and head and neck tumors as well as tumors in other organs with Proxcelan[®] Cs-131. During the fiscal year ended June 30, 2010, the Company expanded the number of areas of the body in which the Proxcelan[®] Cs-131 seeds were being utilized for treatment by adding lung cancer in August 2009, colorectal cancer in October 2009, and chest wall cancer in December 2009. During the fiscal year ended June 30, 2011, the Company continued the expansion in the number of areas of the body in which the Proxcelan[®] Cs-131 seeds were being utilized through the addition of the treatment of brain cancer in September 2010 and the treatment of gynecological cancer in December 2010.

In March 2011, the Company received clearance to commercially deliver Proxcelan[®] Cesium-131 brachytherapy seeds that are preloaded into bioabsorbable braided sutures into Europe. This clearance permits the product to be commercially distributed for treatment of brain, lung, and head and neck tumors as well as tumors in other organs in Europe.

In August 2011, Medical received clearance from the FDA for its premarket notification (510(k)) for the GliaSite[®] Radiation Therapy System (GliaSite[®] RTS). The GliaSite[®] RTS is the only FDA-cleared balloon catheter device used in the treatment of brain cancer.

In May 2012, Medical received a CE mark for the GliaSite[®] RTS which states that the Company conforms with the product requirements of the European Council Directive 93/42/EEC. The CE mark allows the GliaSite[®] RTS to be sold in 31 European countries and to be marketed in the European Free Trade Associate member states and the European Union. In June 2012, the first Cesium-131 brachytherapy seed sutured mesh was implanted on a patient suffering from a recurring meningioma tumor.

Management focused in fiscal 2012 and 2013 on obtaining its regulatory clearances and final research and development of its GliaSite[®] RTS, entering into international distribution agreements to sell the product in Europe and Australia, and marketing its brain and lung products. The GliaSite[®] RTS is the world's only system that enables doctors to use liquid radiation in areas where the cancer is most likely to remain after brain surgery and tumor removal. In fiscal 2013, the Company began supporting the use of a system developed at the Barrow Neurological Institute to deliver doses of Cesium-131 to treat malignant meningioma, brain metastases, and primary cancers of the brain. A multi-institutional study was conducted to explore the use of braided sutures containing Proxcelan[®] Cs-131 seeds placed directly into the cavity following surgical resection of brain metastases.

In August 2013, Medical received an approval for an extension to the scope of the CE mark for the GliaSite® RTS. This approval allows Medical to implement certain product improvements that management believes will enhance GliaSite® RTS's acceptance by customers in the European market.

In December 2013, the Company received clearance for Cesitrex™ from the US Food and Drug Administration. Cesitrex™ is the liquid form of Cesium-131 and can be used in place of Iotrex®, the liquid form of Iodine-125, in the Company's GliaSite® RTS. In May 2014, the Company received clearance for Cesitrex™ from the Washington Department of Health. In June 2014, the Company delivered its first order of Cesitrex™ for use in treating a patient.

Table of Contents

In October 2014, IsoRay announced early success for a young Peruvian girl utilizing Cesium-131 in the first stereotactic implant for inoperable brain cancer. This 7 year old girl is back in school as of August 2015 with no restrictions and normal activities. In December 2014, Barrow Neurological Institute released its findings that IsoRay's Cesium-131 therapy stops brain cancers from recurring in treated locations where previous conventional treatments failed.

Also, in December 2014, Cesium-131 was used in the world's first veterinary implant in a horse with cancer.

In January 2015, the first Cesium-131 prostate cancer treatment was performed in Russia at the Neftyanik Hospital, a center providing cutting edge cancer treatments. In May 2015, the five-year 96% success in local control and 100% survival rates for lung cancer treatment using Cesium-131 were released in a peer-reviewed study.

In June 2015, Cesium-131 was selected by Chicago Prostate Cancer Center for use in the launch of a study of focal treatment of prostate cancer.

While management has not identified additional opportunities to expand treatment to other sites in the body, we continue to investigate potential new opportunities with interested physicians and medical facilities. Management is now focusing primarily on the brain, lung and gynecological markets while the Company continues to research delivery systems other than those historically used by the Company.

Our principal executive offices are located at 350 Hills Street, Suite 106, Richland, Washington 99354, and our telephone number is (509) 375-1202. We maintain an Internet website at www.isoray.com. Information on or accessible through our website does not constitute part of this prospectus and should not be relied upon in connection with making any investment decision with respect to the securities offered by this prospectus.

Although our predecessor operating company was organized in 1998, IsoRay, Inc. was incorporated in 1983 in Minnesota and operated under the name Century Park Pictures Corporation until the merger with IsoRay Medical, Inc. on July 28, 2005.

RISK FACTORS

An investment in our securities involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described under “Risk Factors” in the applicable prospectus supplement and in our most recent Annual Report on Form 10-K, or any updates in our Quarterly Reports on Form 10-Q, together with all of the other information appearing in this prospectus or incorporated by reference into this prospectus and any applicable prospectus supplement, in light of your particular investment objectives and financial circumstances. The risks so described are not the only risks facing our company. Additional risks not presently known to us or that we currently deem immaterial may also impair our business operations. Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our securities could decline due to any of these risks, and you may lose all or part of your investment.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

In addition to historical information, this prospectus, any prospectus supplement and the documents incorporated by reference herein contain certain “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 (PSLRA). This statement is included for the express purpose of availing IsoRay, Inc. of the protections of the safe harbor provisions of the PSLRA.

All statements contained in this prospectus, any prospectus supplement and the documents incorporated by reference herein, other than statements of historical facts, that address future activities, events or developments are forward-looking statements, including, but not limited to, statements containing the words “believe,” “expect,” “anticipate,” “intends,” “estimate,” “forecast,” “project,” and similar expressions. All statements other than statements of historical fact are statements that could be deemed forward-looking statements, including any statements of the plans, strategies and objectives of management for future operations; any statements concerning proposed new products, services, developments or industry rankings; any statements regarding future revenue, economic conditions or performance; any statements of belief; and any statements of assumptions underlying any of the foregoing. These statements are based on certain assumptions and analyses made by us in light of our experience and our assessment of historical trends, current conditions and expected future developments as well as other factors we believe are appropriate under the circumstances. However, whether actual results will conform to the expectations and predictions of management is subject to a number of risks and uncertainties that may cause actual results to differ materially.

Table of Contents

You should not place undue reliance on our forward-looking statements because the matters they describe are subject to known and unknown risks, uncertainties and other unpredictable factors, many of which are beyond our control. Our forward-looking statements are based on the information currently available to us and speak only as of the date on the cover of this prospectus, the date of any prospectus supplement, or, in the case of forward-looking statements incorporated by reference, as of the date of the filing that includes the statement. New risks and uncertainties arise from time to time, and it is impossible for us to predict these matters or how they may affect us. Over time, our actual results, performance or achievements will likely differ from the anticipated results, performance or achievements that are expressed or implied by our forward-looking statements, and such difference might be significant and materially adverse to our security holders. We do not undertake and specifically decline any obligation to update any forward-looking statements or to publicly announce the results of any revisions to any statements to reflect new information or future events or developments.

We have identified some of the important factors that could cause future events to differ from our current expectations and they are described in this prospectus and supplements to this prospectus under the caption “Risk Factors” as well as in our most recent Annual Report on Form 10-K, including without limitation under the captions “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and in other documents that we may file with the SEC, all of which you should review carefully. Please consider our forward-looking statements in light of those risks as you read this prospectus and any prospectus supplement.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of our securities offered by us hereby. Except as described in any prospectus supplement, we currently intend to use the net proceeds from the sale of securities offered by us pursuant to this prospectus for working capital, capital expenditures, research and development, and other general corporate purposes. We may also use such proceeds to fund acquisitions of businesses, technologies or product lines that complement our current business. However, we currently have no commitments or agreements for any specific acquisitions. Pending application of the net proceeds, we intend to invest the net proceeds of the offering of securities by us in investment-grade, interest-bearing securities.

The intended application of proceeds from the sale of any particular offering of securities using this prospectus will be described in the accompanying prospectus supplement relating to such offering. The precise amount and timing of the application of these proceeds will depend on our funding requirements and the availability and costs of other funds.

GENERAL DESCRIPTION OF SECURITIES

•We may offer and sell, at any time and from time to time:

• shares of our common stock;

• shares of our preferred stock;

• warrants to purchase shares of our common stock and/or preferred stock;

• units consisting of a combination of the foregoing; or

• any combination of these securities.

The terms of any securities we offer will be determined at the time of sale. When particular securities are offered, a supplement to this prospectus will be filed with the SEC, which will describe the terms of the offering and sale of the offered securities.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

The following is a summary description of the rights of our common stock and related provisions of our amended Articles of Incorporation and our Bylaws. The following description of our capital stock is intended as a summary only and is qualified in its entirety by reference to our amended Articles of Incorporation and our Bylaws, which are filed as exhibits to the registration statement of which this prospectus forms a part, and to the applicable provisions of Minnesota law.

Common Stock

Our common shares are listed on the NYSE MKT under the symbol “ISR”. As of August 20, 2015, 55,013,553 shares of common stock were issued and outstanding, and there were approximately 237 holders of record.

The Company’s Articles of Incorporation provide that the Company has the authority to issue 200 million shares of capital stock, which are currently divided into two classes as follows: 192,998,329 shares of common stock, par value of \$0.001 per share; and 7,001,671 shares of preferred stock, also with a par value of \$0.001 per share.

The holders of our common stock have no preemptive or other subscription rights, and there are no conversion rights or redemption or sinking fund provisions with respect to such shares. All of the outstanding shares of our common stock are, and the shares of our common stock when issued will be, fully paid and nonassessable.

Voting. Holders of the common stock are entitled to one vote per share on all matters to be voted on by the Company’s shareholders. The Company’s Bylaws provide that a majority of the outstanding shares of the corporation entitled to vote constitute a quorum at a meeting of the shareholders.

Dividends. The Company’s Board of Directors, in its sole discretion, may declare and pay dividends on the common stock, payable in cash or other consideration, out of funds legally available, if all dividends due on the preferred stock have been declared and paid. The Company has not paid any cash dividends on its common stock and does not plan to pay any cash dividends on its common stock for the foreseeable future.

Liquidation, Subdivision, or Combination. In the event of any liquidation, dissolution or winding up of the Company or upon the distribution of its assets, all assets and funds remaining after payment in full of the Company’s debts and

liabilities, and after the payment to holders of any then outstanding preferred stock of the full preferential amounts to which they were entitled, would be divided and distributed among holders of the common stock.

Anti-Takeover Effects Of Provisions Of The Articles Of Incorporation. The authorized but unissued shares of our common and preferred stock are available for future issuance without our shareholders' approval. These additional shares may be utilized for a variety of corporate purposes including but not limited to future public or direct offerings to raise additional capital, corporate acquisitions and employee incentive plans. The issuance of such shares may also be used to deter a potential takeover of IsoRay that may otherwise be beneficial to shareholders by diluting the shares held by a potential suitor or issuing shares to a shareholder that will vote in accordance with IsoRay's Board of Directors' desires. A takeover may be beneficial to shareholders because, among other reasons, a potential suitor may offer shareholders a premium for their shares of stock compared to the then-existing market price.

On February 1, 2007, the Board of Directors of IsoRay, Inc. declared a dividend of one preferred share purchase right (a "Right") for each outstanding Common Share of the par value of \$.001 per share (the "Common Shares") of the Company. The dividend is payable on February 16, 2007 (the "Record Date") to shareholders of record on that date.

Each Right entitles the registered holder to purchase from the Company one one-hundredth of a Series C Junior Participating Preferred Share of the par value of \$.001 per share (the "Preferred Shares") of the Company at a price of \$25 per one one-hundredth of a Preferred Share (the "Purchase Price"), subject to adjustment. The description and terms of the Rights are set forth in a Rights Agreement (the "Rights Agreement"), dated as of February 1, 2007, between the Company and Computershare Trust Company N.A., as Rights Agent (the "Rights Agent").

Table of Contents

Initially, the Rights will attach to all certificates representing Common Shares then outstanding and no separate Right Certificates will be distributed. The Rights will separate from the Common Shares and a Distribution Date for the Rights will occur upon the earlier of:

- (i) the close of business on the fifteenth day following a public announcement that a person or group of affiliated or associated persons has become an “Acquiring Person” (i.e., has become, subject to certain exceptions, the beneficial owner of 15% or more of the voting power of the outstanding shares of voting capital stock of the Company in the election of directors), or

- (ii) the close of business on the fifteenth day following the first public announcement relating to a tender offer or exchange offer the consummation of which would result in a person or group of affiliated or associated persons becoming, subject to certain exceptions, the beneficial owner of 15% or more of the voting power of the outstanding shares of voting capital stock of the Company in the election of directors (or such later date as may be determined by the Board of Directors of the Company prior to a person or group of affiliated or associated persons becoming an Acquiring Person).

Until the Distribution Date,

- (i) the Rights will be evidenced by the Common Share certificates and will be transferred with and only with the Common Shares,

- (ii) new Common Share certificates issued after the Record Date upon transfer or new issuance of the Common Shares will contain a notation incorporating the Rights Agreement by reference, and

- (iii) the surrender for transfer of any Common Share certificate, even without such notation or a copy of this Summary of Rights attached thereto, will also constitute the transfer of the Rights associated with the Common Shares represented by such certificate.

As promptly as practicable following the Distribution Date, separate certificates evidencing the Rights (“Right Certificates”) will be mailed to holders of record of the Common Shares as of the close of business on the Distribution Date and such separate Right Certificates alone will evidence the Rights.

The Rights are not exercisable until the Distribution Date. The Rights will expire on February 16, 2017, unless extended or earlier redeemed or exchanged by the Company as described below.

The Purchase Price payable, and the number of Preferred Shares or other securities or property issuable, upon exercise of the Rights are subject to adjustment from time to time to prevent dilution:

- (i) in the event of a stock dividend on, or a subdivision, combination or reclassification of, the Preferred Shares,

- (ii) upon the grant to holders of the Preferred Shares of certain rights, options or warrants to subscribe for or purchase Preferred Shares or convertible securities at less than the then current market price of the Preferred Shares, or

- (iii) upon the distribution to holders of the Preferred Shares of evidences of indebtedness or assets (excluding regular periodic cash dividends or dividends payable in Preferred Shares) or of subscription rights or warrants (other than those described in clause (ii) hereof).

The number of Preferred Shares issuable upon the exercise of a Right is also subject to adjustment in the event of a dividend on Common Shares payable in Common Shares, or a subdivision, combination or consolidation of the Common Shares.

With certain exceptions, no adjustment in the Purchase Price will be required until cumulative adjustments require an adjustment of at least 1% in the Purchase Price. No fractional Preferred Shares will be issued (other than fractional shares which are integral multiples of one one-hundredth (subject to adjustment) of a Preferred Share, which may, at the election of the Company, be evidenced by depositary receipts) if in lieu thereof a payment in cash is made based on the closing price (pro-rated for the fraction) of the Preferred Shares on the last trading date prior to the date of exercise.

Table of Contents

In the event that any person or group of affiliated or associated persons becomes an Acquiring Person, proper provision shall be made so that each holder of a Right, other than Rights that are or were beneficially owned by the Acquiring Person (which will thereafter be void), will thereafter have the right to receive upon exercise thereof at the then current exercise price of the Right that number of Common Shares having a market value of two times the exercise price of the Right, subject to certain possible adjustments.

In the event that, after the Distribution Date or within 15 days prior thereto, the Company is acquired in certain mergers or other business combination transactions or 50% or more of the assets or earning power of the Company and its subsidiaries (taken as a whole) are sold after the Distribution Date or within 15 days prior thereto, each holder of a Right (other than Rights which have become void under the terms of the Rights Agreement) will thereafter have the right to receive, upon exercise thereof at the then current exercise price of the Right, that number of common shares of the acquiring company (or, in certain cases, one of its affiliates) having a market value of two times the exercise price of the Right.

In certain events specified in the Rights Agreement, the Company is permitted to temporarily suspend the exercisability of the Rights.

At any time after a person or group of affiliated or associated persons becomes an Acquiring Person (subject to certain exceptions) and prior to the acquisition by a person or group of affiliated or associated persons of 50% or more of the voting power of the outstanding shares of voting capital stock of the Company in the election of directors, the Board of Directors of the Company may exchange all or part of the Rights (other than Rights which have become void under the terms of the Rights Agreement) for Common Shares or equivalent securities at an exchange ratio per Right equal to the result obtained by dividing the exercise price of a Right by the current per share market price of the Common Shares, subject to adjustment.

At any time prior to such time as a person or group of affiliated or associated persons becomes an Acquiring Person, the Board of Directors of the Company may redeem the Rights in whole, but not in part, at a price of \$.001 per Right, subject to adjustment (the "Redemption Price"), payable in cash. The period of time during which the Rights may be redeemed may be extended by the Board of Directors of the Company if no person has become an Acquiring Person. The redemption of the Rights may be made effective at such time, on such basis and with such conditions as the Board of Directors in its sole discretion may establish. The Board of Directors and the Company shall not have any liability to any person as a result of the redemption or exchange of the Rights pursuant to the provisions of the Rights Agreement.

The terms of the Rights may be amended by the Board of Directors of the Company, subject to certain limitations after such time as a person or group of affiliated or associated persons becomes an Acquiring Person, without the consent of the holders of the Rights, including an amendment prior to the date a person or group of affiliated or associated persons becomes an Acquiring Person to lower the 15% threshold for exercisability of the Rights to not less

than the greater of (i) the sum of .001% and the largest percentage of the outstanding shares of voting capital stock of the Company with voting power in the election of directors then known by the Company to be beneficially owned by any person or group of affiliated or associated persons (subject to certain exceptions) or (ii) 10%.

Until a Right is exercised, the holder thereof, as such, will have no rights as a shareholder of the Company, including, without limitation, the right to vote or to receive dividends.

The foregoing description of the Rights Agreement is qualified in its entirety by reference to the full text of the Rights Agreement.

Transfer Agent and Registrar. The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent's address is 8774 Lucent Blvd., Ste 225, Highlands Ranch, CO 80129, and its telephone number is (303) 262-0600.

Table of Contents

Listing

Our shares of common stock are traded on the NYSE MKT under the ticker symbol “ISR.”

DESCRIPTION OF PREFERRED STOCK

We may issue our preferred stock, par value \$0.001 per share, from time to time in one or more series. Of the 7,001,671 shares of presently authorized preferred stock, 1,000,000 are designated as Series A Preferred Stock, 5,000,000 are designated as Series B Preferred Stock, 1,000,000 are designated as Series C Junior Participating Preferred Stock, and 1,671 are designated as Series D. Convertible Preferred Stock. The Series C preferred shares are related to the Rights Agreement described above. As of August 20, 2015, no shares of our Series A, Series C or Series D preferred stock were outstanding and 59,065 shares of our Series B preferred stock were outstanding.

Series A

Series A preferred shares are entitled to a 10% dividend annually on the stated par value per share. These shares are convertible into shares of common stock at the rate of one share of common stock for each share of Series A preferred stock, and are subject to automatic conversion into common stock upon the closing of an underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933 covering the offer and sale of common stock in which the gross proceeds to the Company are at least \$4 million. Series A preferred shareholders have voting rights equal to the voting rights of common stock, except that the vote or written consent of a majority of the outstanding preferred shares is required for any changes to the Company’s Articles of Incorporation, Bylaws or Certificate of Designation, or for any bankruptcy, insolvency, dissolution or liquidation of the Company. Upon liquidation of the Company, the Company’s assets are first distributed ratably to the Series A preferred shareholders.

Series B

Series B preferred shares are entitled to a cumulative 15% dividend annually on the stated par value per share. These shares are convertible into shares of common stock at the rate of one share of common stock for each share of Series B preferred stock, and are subject to automatic conversion into common stock upon the closing of an underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933 covering the offer and sale of common stock in which the gross proceeds to the Company are at least \$4 million. Series B preferred shareholders have voting rights equal to the voting rights of common stock, except that the vote or written consent of a majority of the outstanding preferred shares is required for any changes to the Company’s Articles of Incorporation,

Bylaws or Certificate of Designation, or for any bankruptcy, insolvency, dissolution or liquidation of the Company. Upon liquidation of the Company, the Company's assets are first distributed ratably to the Series A preferred shareholders, then to the Series B preferred shareholders.

Series D

Established in August 2013, Series D preferred shares are entitled to dividends in the same form as dividends actually paid on shares of common stock. Additionally, the Company shall not pay any dividends on shares of common stock (other than dividends in the form of common stock) unless the holders of Series D Convertible Preferred Stock shall first receive dividends on shares of Series D Convertible Preferred Stock held by them (on an as-if-converted-to-common-stock-basis) in an amount equal to and in the same form as any such dividends (other than dividends in the form of common stock) to be paid on shares of common stock. Except as required by law, shares of Series D Convertible Preferred Stock shall not have the right to vote on any matter other than those set forth in the Certificate of Designation with the potential to specifically adversely affect the Series D Convertible Preferred Stock. Series D Convertible Preferred shares are convertible into shares of common stock at the rate of 1,869.15 shares of common stock for each share of Series D Convertible Preferred Stock at any time at the option of the holder, provided that the holder will be prohibited from converting shares of Series D Convertible Preferred Stock into shares of our common stock if, as a result of the conversion, the holder, together with its affiliates, would beneficially own more than 9.99% of the total number of shares of our common stock then issued and outstanding, which is referred to herein as the "Beneficial Ownership Limitation".

Table of Contents

Undesignated Preferred Stock

Our Articles of Incorporation authorize our Board of Directors to issue preferred stock from time to time with such designations, preferences, conversion or other rights, voting powers, restrictions, dividends or limitations as to dividends or other distributions, qualifications or terms or conditions of redemption as shall be determined by the Board of Directors for each class or series of stock subject to the provisions of our Articles of Incorporation. Preferred stock is available for possible future financings or acquisitions and for general corporate purposes without further authorization of stockholders unless such authorization is required by applicable law, the rules of the NYSE MKT or other securities exchange or market on which our stock is then listed or admitted to trading.

The Board of Directors, without approval of holders of common stock, can issue preferred stock with voting, conversion or other rights that could adversely affect the voting power and other rights of the holders of common stock. Preferred stock could thus be issued quickly with terms calculated to delay or prevent a change in control of or make removal of management more difficult and/or impair the liquidation rights of our common stock. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of the common stock.

If we offer a specific series of new preferred stock under this prospectus, we will describe the terms of the preferred stock in the prospectus supplement for such offering and will file a copy of the certificate establishing the terms of the preferred stock with the SEC. To the extent required, this description will include:

• the title and stated or par value of the preferred stock;

• the number of shares of the preferred stock offered, the liquidation preference per share and the offering price of the preferred stock;

• the dividend rate(s), period(s) and/or payment date(s) or method(s) of calculation thereof applicable to the preferred stock;

• whether dividends shall be cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock shall accumulate;

• the procedures for any auction and remarketing, if any;

• the provisions for a sinking fund, if any, for the preferred stock;

any voting rights of the preferred stock;

the provisions for redemption, if applicable, of the preferred stock;

any listing of the preferred stock on any securities exchange or market;

the terms and conditions, if applicable, upon which the preferred stock will be convertible into our common stock, including the conversion price or the manner of calculating the conversion price and conversion period, and any other terms of conversion (including any anti-dilution provisions, if any);

the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the affairs of the Company;

any material limitations on issuance of any series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the Company;

Table of Contents

- any other affirmative, negative or other covenants or contractual rights which might be attendant with the specific series of preferred stock;
- if appropriate, a discussion of Federal income tax consequences applicable to the preferred stock; and
- any other specific terms, preferences, rights, limitations or restrictions of the preferred stock.

The preferred stock offered by this prospectus, when issued, will not have, or be subject to, any preemptive or similar rights, and will, when issued, be fully paid and non-assessable.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock and/or preferred stock in one or more series together with other securities or separately, as described in each applicable prospectus supplement. Warrants may be issued independently or together with any preferred stock or common stock, and may be attached to or separate from any offered securities.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

• the specific designation and aggregate number of, and the price at which we will issue, the warrants;

• the currency or currency units in which the offering price, if any, and the exercise price are payable;

• the designation, amount and terms of the securities purchasable upon exercise of the warrants;

• if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;

•

if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise of the warrants, and a description of that series of our preferred stock;

the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if the warrants may not be continuously exercised throughout that period, the specific date or dates on which the warrants may be exercised;

whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;

any applicable material U.S. federal income tax consequences;

the identity of any warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;

the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange or market;

if applicable, the date from and after which the warrants and the common stock and/or preferred stock will be separately transferable;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

Table of Contents

- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of the warrants, if any;
- any redemption or call provisions;
- whether the warrants are to be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

DESCRIPTION OF UNITS

We may issue units composed of one or more of the other securities described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We may evidence units by unit certificates that we issue under a separate agreement. We may issue the units under a unit agreement between us and one or more unit agents. If we elect to enter into a unit agreement with a unit agent, the unit agent will act solely as our agent in connection with the units and will not assume any obligation or relationship of agency or trust for or with any registered holders of units or beneficial owners of units. We will indicate the name and address and other information regarding the unit agent in the applicable prospectus supplement relating to a particular series of units if we elect to use a unit agent.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described herein; and

any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The other provisions regarding our common stock, preferred stock and/or warrants as described in this section will apply to each unit to the extent such unit consists of shares of our common stock, preferred stock and/or warrants.

PLAN OF DISTRIBUTION

We may sell the securities offered through this prospectus (i) to or through underwriters or dealers, (ii) directly to a single purchaser or multiple purchasers, including our affiliates, (iii) through agents, or (iv) through a combination of any these methods. The securities may be distributed at a fixed price or prices, which may be changed, market prices prevailing at the time of sale, prices related to the prevailing market prices, or negotiated prices. The prospectus supplement will include the following information:

• the terms of the offering;

• the names of any underwriters or agents;

• the name or names of any managing underwriter or underwriters;

Table of Contents

- the purchase price of the securities;
- any over-allotment options under which underwriters may purchase additional securities from us;
- the net proceeds from the sale of the securities;
- any delayed delivery arrangements;
- any underwriting discounts, commissions and other items constituting underwriters' compensation;
- any initial public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers;
- any commissions paid to agents; and
- any securities exchange or market on which the securities may be listed.

Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

Sale Through Underwriters or Dealers

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, the underwriters will acquire the securities for their own account, including through underwriting, purchase, security lending or repurchase agreements with us. The underwriters may resell the securities from time to time in one or more transactions, including negotiated transactions. Underwriters may sell the securities in order to facilitate transactions in any of our other securities (described in this prospectus or otherwise), including other public or private transactions and short sales. Underwriters may offer securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless otherwise indicated in the prospectus supplement, the obligations of the underwriters to

purchase the securities will be subject to certain conditions, and the underwriters will be obligated to purchase all the offered securities if they purchase any of them. The underwriters may change from time to time any initial public offering price and any discounts or concessions allowed or reallocated or paid to dealers.

If dealers are used in the sale of securities offered through this prospectus, we will sell the securities to them as principals. They may then resell those securities to the public at varying prices determined by the dealers at the time of resale. The prospectus supplement will include the names of the dealers and the terms of the transaction.

In compliance with the guidelines of the Financial Services Regulatory Authority, Inc., or FINRA, the maximum compensation to be received by a FINRA member or independent broker-dealer may not exceed 8% of the offering proceeds.

Direct Sales and Sales Through Agents

We may sell the securities offered through this prospectus directly. In this case, no underwriters or agents would be involved. Such securities may also be sold through agents designated from time to time. The prospectus supplement will name any agent involved in the offer or sale of the offered securities and will describe any commissions payable to the agent. Unless otherwise indicated in the prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of its appointment.

Table of Contents

We may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any sale of those securities. The terms of any such sales will be described in the prospectus supplement.

Delayed Delivery Contracts

If the prospectus supplement indicates, we may authorize agents, underwriters or dealers to solicit offers from certain types of institutions to purchase securities at the public offering price under delayed delivery contracts. These contracts would provide for payment and delivery on a specified date in the future. The contracts would be subject only to those conditions described in the prospectus supplement. The applicable prospectus supplement will describe the commission payable for solicitation of those contracts.

Market Making, Stabilization and Other Transactions

We may elect to list offered securities on an exchange or in the over-the-counter market. Any underwriters that we use in the sale of offered securities may make a market in such securities, but may discontinue such market making at any time without notice. Therefore, we cannot assure you that the securities will have a liquid trading market.

Certain persons participating in an offering may engage in over-allotment, stabilizing transactions, syndicate covering transactions and penalty bids in accordance with rules and regulations under the Exchange Act. Over-allotment involves the sale in excess of the offering size, which create a short position. Stabilizing transactions involve bids to purchase the underlying security in the open market for the purpose of pegging, fixing or maintaining the price of the securities. Syndicate covering transactions involve purchases of the securities in the open market after the distribution has been completed in order to cover syndicate short positions.

Penalty bids permit the underwriters to reclaim a selling concession from a syndicate member when the securities originally sold by the syndicate member are purchased in a syndicate covering transaction to cover syndicate short positions. Stabilizing transactions, syndicate covering transactions and penalty bids may cause the price of the securities to be higher than it would be in the absence of the transactions. The underwriters may, if they commence these transactions, discontinue them at any time.

General Information

Agents, underwriters, and dealers may be entitled, under agreements entered into with us, to indemnification by us against certain liabilities, including liabilities under the Securities Act. Our agents, underwriters, and dealers, or their affiliates, may be customers of, engage in transactions with or perform services for us, in the ordinary course of business.

LEGAL MATTERS

Certain legal matters with respect to the securities being offered hereby will be passed on by Gallagher & Kennedy, P.A., Phoenix, Arizona.

EXPERTS

The consolidated financial statements of IsoRay and Subsidiaries as of June 30, 2015 and 2014 and for each of the three years in the period ended June 30, 2015 and management's assessment of the effectiveness of internal control over financial reporting as of June 30, 2015 have been incorporated by reference herein in reliance on the report of DeCoria, Maichel & Teague, P.S., an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

INTERESTS OF NAMED EXPERTS AND COUNSEL

None.

Table of Contents

MATERIAL CHANGES

None.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC relating to the securities offered by this prospectus. This prospectus does not contain all of the information set forth in the registration statement and the exhibits and schedules thereto. We have omitted parts of the registration statement, as permitted by the rules and regulations of the SEC. Statements contained in this prospectus as to the contents of any contract or other document referred to are not necessarily complete and in each instance reference is made to the copy of such contract or other document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference. For further information with respect to us and the securities offered hereby, reference is made to such registration statement, exhibits and schedules.

We are subject to the information and periodic reporting requirements of the Exchange Act, and in accordance therewith file periodic reports, current reports, proxy statements and other information with the SEC. Such periodic reports, current reports, proxy statements, other information and a copy of this registration statement on Form S-3 may be inspected by anyone without charge and copies of these materials may be obtained upon the payment of the fees prescribed by the SEC, at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. This registration statement on Form S-3 and the periodic reports, current reports, proxy statements and other information filed by us are also available through the Internet web site maintained by the SEC at the following address: <http://www.sec.gov>.

INCORPORATION BY REFERENCE

This prospectus is part of a registration statement filed with the SEC. The SEC allows us to “incorporate by reference” into this prospectus the information that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. The following documents were filed with the SEC pursuant to the Exchange Act and are incorporated by reference and made a part of this prospectus:

• Annual Report on Form 10-K for the fiscal year ended June 30, 2015, filed on September 14, 2015;

• Current Reports on Form 8-K filed on September 2, 2015 and September 15, 2015;

the description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on April 12, 2007 (File No. 001-333407), including any amendments or reports filed for the purpose of updating such description;

the description of our rights contained in our Registration Statement on Form 8-A filed on February 7, 2007 (File No. 001-14247), including any amendments or reports filed for the purpose of updating such description; and

all documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), (i) after the date on which this registration statement that includes this prospectus was initially filed with the SEC and prior to the effectiveness of such registration statement, and (ii) after the date of this prospectus and prior to the termination of this offering, unless otherwise stated therein.

Notwithstanding the foregoing, information furnished under Items 2.02 and 7.01 of any Current Report on Form 8-K, including the related exhibits, is not incorporated by reference in this prospectus.

Table of Contents

Any statement contained herein or made in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained herein, or in any other subsequently filed document which also is incorporated or deemed to be incorporated by reference herein, modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus

We will provide without charge to each person to whom this prospectus is delivered, upon oral or written request, a copy of any or all of the foregoing documents incorporated herein by reference (other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the information that this prospectus incorporates). Written or telephone requests should be directed to: IsoRay, Inc., 350 Hills Street, Suite 106, Richland, Washington 99354, telephone number (509) 375-1202, Attn: Corporate Secretary.

You should rely only on the information contained or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone else to provide you with different or additional information. We will not make an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or any supplement is accurate as of any date other than the date of those documents.

COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

The Company's Articles of Incorporation provide to directors and officers indemnification to the full extent provided by law, and provide that, to the extent permitted by Minnesota law, a director will not be personally liable for monetary damages to the Company or its shareholders for breach of his or her fiduciary duty as a director, except for liability for certain actions that may not be limited under Minnesota law. On July 1, 2006, the Company entered into Indemnification Agreements with each of its directors and executive officers, and has entered into Indemnification Agreements with each officer and director who took office subsequent to July 1, 2006, and the Company intends to enter into substantially identical agreements with any officers and directors who take office in the future. The purpose of the Indemnification Agreements is to provide all officers and directors with indemnification to the fullest extent permitted under the Minnesota Business Corporations Act.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable.

Table of Contents

11,000,000

Common Stock

PROSPECTUS SUPPLEMENT

H.C. Wainwright & Co.

July 9, 2018
