

An Emerging Leader in Targeted Internal Radiation Therapy

Investor Presentation

March 2022



NYSE American: ISR

Safe Harbor Statement

Statements in this presentation about Isoray's future expectations, including: the anticipated continued growth in revenues in fiscal year 2022, the impact of COVID-19 on our financial results and the timing of recovery in our brachytherapy procedures, suppliers, scheduling of procedures and employees, the advantages of our products including Blu Build and the GammaTile™ Therapy delivery system, whether interest in and use of our Cesium-131, commercially known as Cesium Blu™, products will increase or continue, whether use of Cesium-131 in non-prostate applications such as head and neck and GYN cancers will continue or increase revenue, whether further manufacturing and production process improvements will be completed or will result in lower costs, whether our market presence and growth will continue, the positive industry data fueling renewed interest in brachytherapy, strong patient results, the perception by patients of quality of life outcomes compared to other treatment options, whether peer-reviewed publications of treatment results using our products will report favorable results, whether our intellectual property will adequately protect our proprietary technologies, and all other statements in this release, other than historical facts, are "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. It is important to note that actual results and ultimate corporate actions could differ materially from those in such forward-looking statements based on such factors as physician acceptance, training and use of our products, market acceptance and recognition of our products, our ability to successfully manufacture, market and sell our products, the success of the GammaTile™ Therapy delivery system, the length and severity of the COVID-19 pandemic, our ability to manufacture our products in sufficient quantities to meet demand within required delivery time periods while meeting our quality control standards, our ability to enforce our intellectual property rights, whether additional studies are released and support the conclusions of past studies, whether ongoing patient results with our products are favorable and in line with the conclusions of past studies and patient results, patient results achieved when our products are used for the treatment of cancers and malignant diseases beyond prostate cancers, successful completion of future research and development activities, whether we, our distributors and our customers will successfully obtain and maintain all required regulatory approvals and licenses to market, sell and use our products in its various forms, continued compliance with ISO standards, the success of our sales and marketing efforts, changes in reimbursement rates, changes in laws and regulations applicable to our products, the scheduling of physicians who either delay or do not schedule patients in periods anticipated, the use of competitors' products in lieu of our products, less favorable reimbursement rates than anticipated for our products, and other risks detailed from time to time in Isoray's reports filed with the Securities and Exchange Commission. Unless required to do so by law, we undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

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Investment highlights

Emerging leader in radiotherapeutics focused on commercializing proprietary Cesium-131 therapy for the treatment of cancer



Investment Highlights

- **Growing body of evidence suggests that Cesium-131 can be used as a superior therapy option compared to alternatives**
 - Shorter half-life and stronger energy levels lead to better patient outcomes
- **Robust clinical pipeline targeting additional market opportunity**
 - Initiated immunotherapy study in Q4 2020 with Cesium-131 in combination with Pembrolizumab (Keytruda®) for the treatment of recurrent head and neck cancer
 - Initiated immunotherapy study in Q2 2021 With Cesium-131 in combination with Nivolumab (Opdivo®) for treatment of metastatic melanoma
 - Evaluating Cesium-131 for treatment of surgical cancers, including head and neck, lung and others



Investment Highlights

- **Consistent revenue growth trends in core markets:**
 - TTM Revenue of \$10.7M, 4 year CAGR of 19%⁽¹⁾
 - TTM Gross Margin of 46.4%⁽¹⁾
- **Strong balance sheet to fund growth**
 - \$60.4M of cash or \$0.42 cash per share and no long-term debt⁽²⁾
- **Experienced management team with deep industry expertise**



Lori Woods
Chief Executive Officer
& Member of the Board of Directors

(1) 1/1/2021 – 12/31/2021

(2) As of F2Q22 quarter ending 12/31/2021

Brachytherapy Overview

Safe and established treatment option
for the treatment of cancer



Brachytherapy Overview

Brachytherapy is a cancer treatment utilizing radioactive seeds placed directly inside the tumor or at the surgical margin, allowing for highly targeted treatment



Benefits



Out-patient single visit treatment

- Use less PPE and staff
- Less potential exposure to COVID-19



Low-cost effective treatment



Highly targeted and personalized treatment dose








Uniform and predictable radiation dose


- Mitigates damage to healthy tissue vs. external beam

The Power of Cesium-131: *A Best-in-Class Therapeutic Isotope*

Isoray's Cesium-131 therapy is proven to be a highly effective cancer treatment.

| | Cesium-131 Introduced 2004 |
|---|--|
|  Half-life | 9.7 day half life The amount of time for the radiation to half. A shorter half life means quicker to PSA baseline. |
|  Energy level | 30.4 Kev The energy level of the isotope. Higher energy leads to greater coverage of the infected organ. |
|  Speed of delivery | 33 Days for 90% Dose Faster dose delivery rate. |
|  Detectable in the body | 97 Days |

**Higher Energy**

**Shorter half-life**

**Delivered faster than external radiation**

**Powerful, continuous, therapeutic energy**





We market Cesium-131 as

Cesium Blu™

17,000+ Patients treated over 10 years

The Power of Cesium-131: *A Best-in-Class Therapeutic Isotope*

Isoray's Cesium-131 therapy is proven to be a highly effective cancer treatment

| | Cesium-131 Introduced 2004 | Paladium-103 Introduced 1986 | Iodine-125 Introduced 1965 |
|--|--|---------------------------------|-------------------------------|
|  Half-life | 9.7 day half life The amount of time for the radiation to half. A shorter half life means quicker to PSA baseline. | 17 Day Half Life (18) | 60 Day Half Life (18) |
|  Energy level | 30.4 Kev The energy level of the isotope. Higher energy leads to greater coverage of the infected organ. | 20.8 Kev | 28.5 Kev |
|  Speed of delivery | 33 Days for 90% Dose Faster dose delivery rate. | 58 Days for 90% Dose | 204 Days for 90% Dose |
|  Detectable in the body | 97 Days | 170 Days | 600 Days |

Source: Armpilla C, Dale R, Coles I, et al. The determination of radiobiologically optimized half-lives for radionuclides used in permanent brachytherapy implants. Int J Rad Onc Biol Phys 2003; 55:378-385.

Large Market Opportunities

Expanding cancer treatment options across several oncology markets



Prostate

- Building market awareness with Cesium Blu brand & clinical
- Pandemic related procedure delays beginning to recover

\$983M

Est. 268k cases in 2022
61% cases treatable with Cesium-131



Surgical

- Opportunity for expansion in into HNC, lung and other cancers
- Addressing a large unmet need in post-resection treatment
- Immediate radiation delivery, no need for surgical healing
- Collaboration with MIM Software in recurrent HNC

\$208M

Est. 406k cases in 2022
8% cases treatable with Cesium-131



Brain

- Partnership with GT Medical Technologies
- Full scale commercialization efforts underway

\$217M

Est. 188k cases in 2022
33% cases treatable with Cesium-131

Note: Market data backup on slide 24

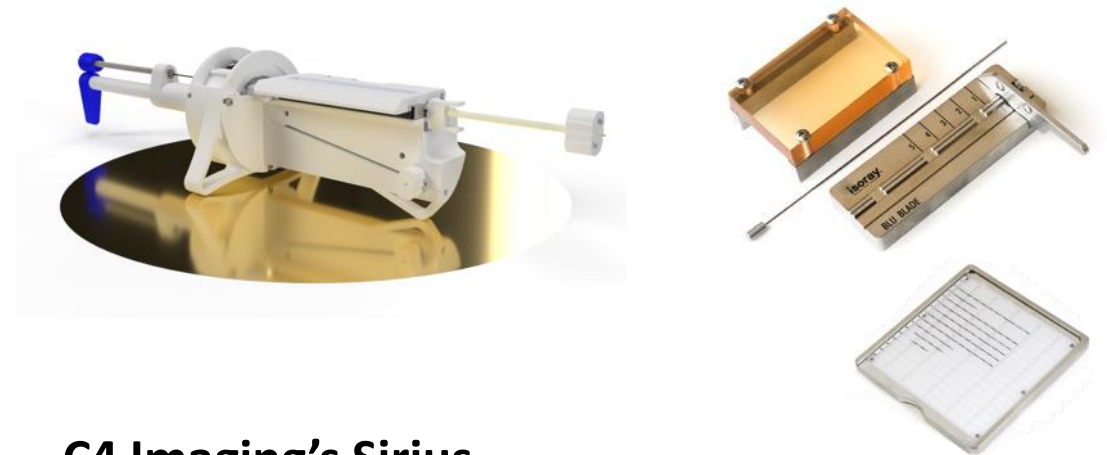
Prostate Cancer: Isoray's Growing Core Market

Renewed sales strategy driving growth in Prostate

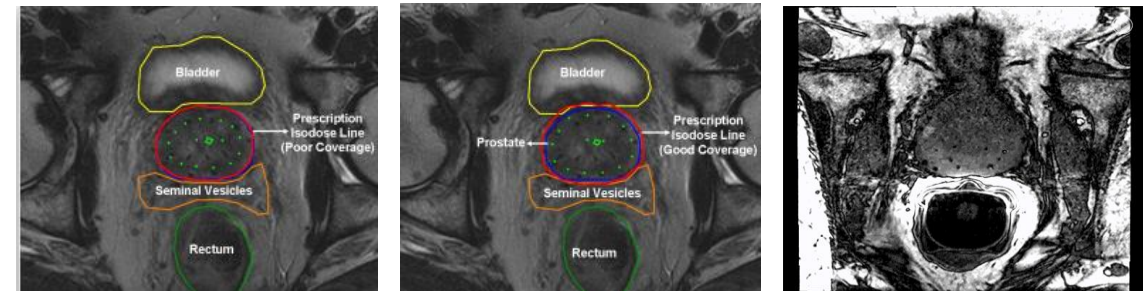
Growth Drivers

- Growing direct sales force to expand coverage in the U.S.
- Innovative training for physicians and residents
- Leveraging 10+ years of clinical evidence to build awareness among physicians
- Investing in additional clinical data and research
- Collaboration with C4 Imaging's Sirius® positive-signal MRI markers with Cesium-131 Seeds
- Partnering with patient advocacy groups

Comprehensive Solution for Prostate Cancer



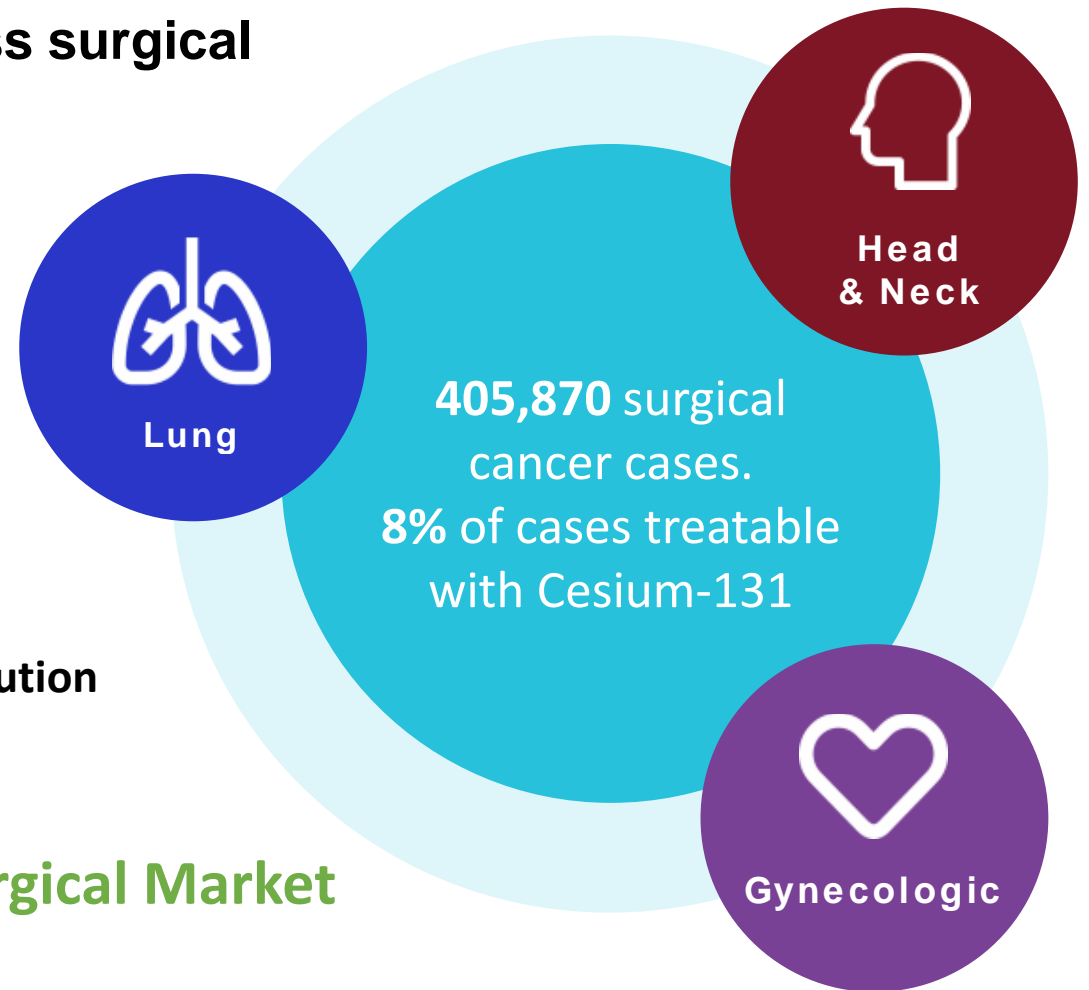
C4 Imaging's Sirius



Use of Cesium-131 in Surgery

Isoray is actively expanding its efforts to address surgical oncology indications with Cesium-131

- **Targeting cancers with large unmet medical needs**
 - Cesium-131 placed at the site of tumor recurrence
 - Immediate radiation delivery, no need for surgical healing
- **New data emerging in Head and Neck, Lung, GYN and other surgical sites**
- **Collaboration with MIM Software to deliver treatment solution for recurrent Head and Neck cancer**



Multiple Opportunities in the Surgical Market

Note: Market data backup on slide 24

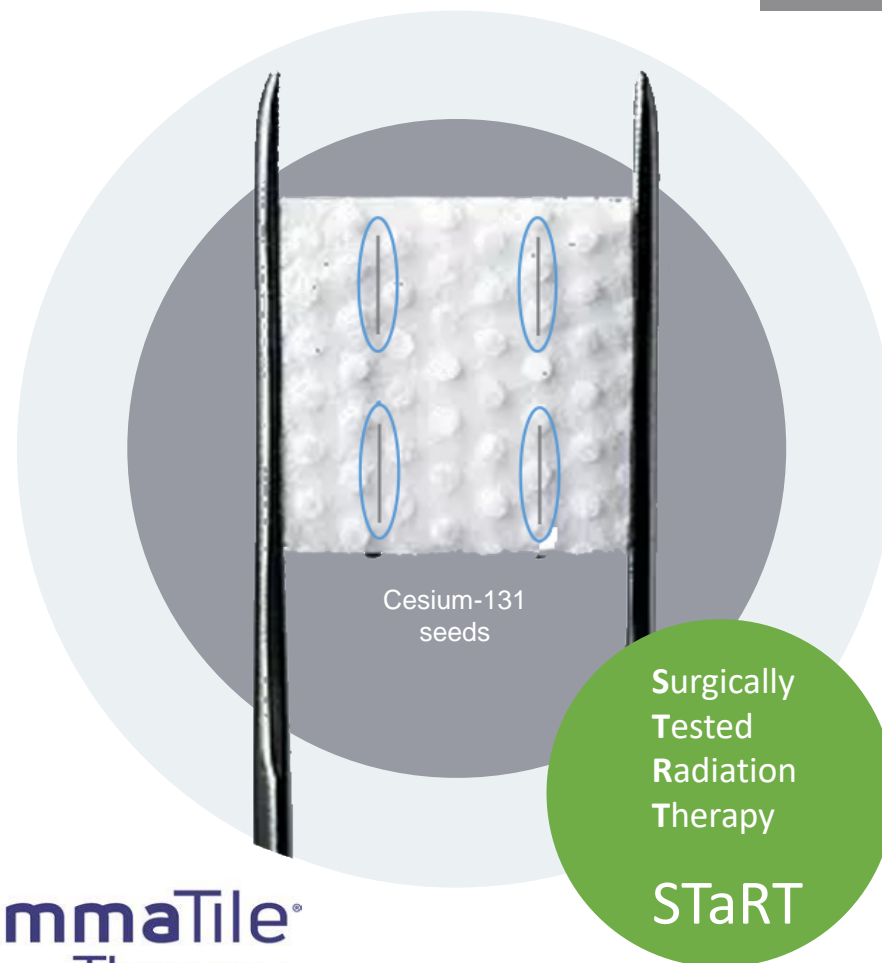


Brain

Brain Cancer: Opportunity for Significant Growth

Commercialization efforts underway to treat brain cancer with Cesium-131

- **Exclusive agreement with GT Medical Technologies to supply Cesium-131 seeds for use in GammaTile® Therapy**
 - FDA clearance for recurrent brain tumors in 2018 and expanded clearance for newly diagnosed tumors in 2020
 - Accelerating sales efforts
 - ICD-10-PCS codes tied to the highest DRG reimbursement
- **Cesium-131 in brain cancer supported by a growing number of clinical studies at major U.S. institutions**



 **GammaTile®**
Therapy
Powered by Cesium Blu

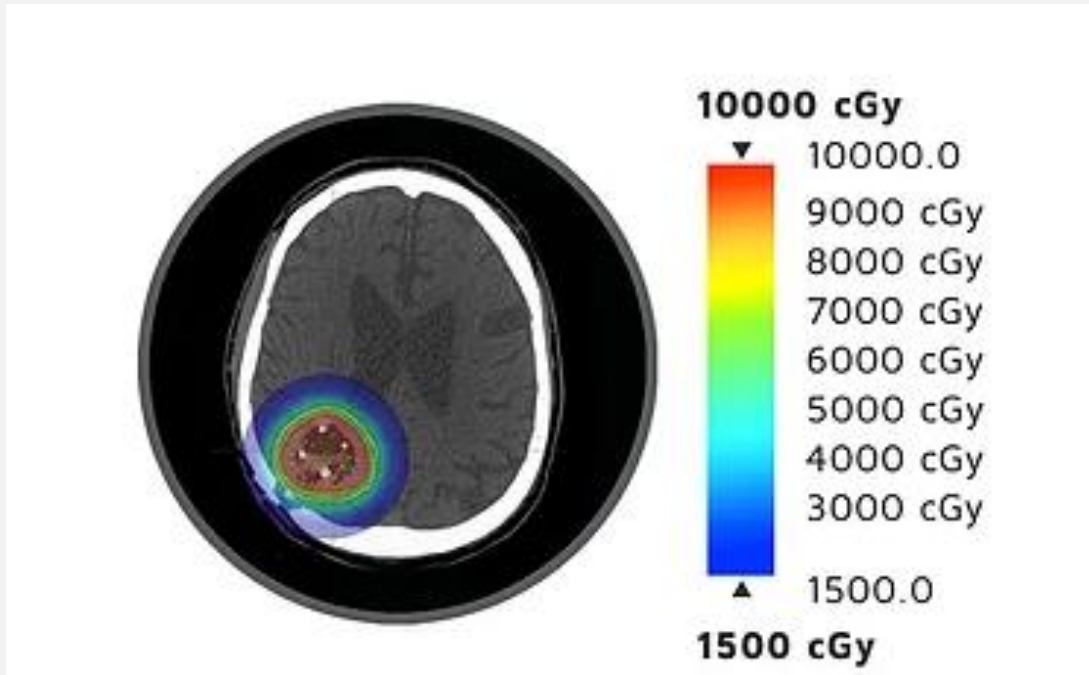
Source: GT Medical Technologies

Brain Cancer: The GammaTile Difference

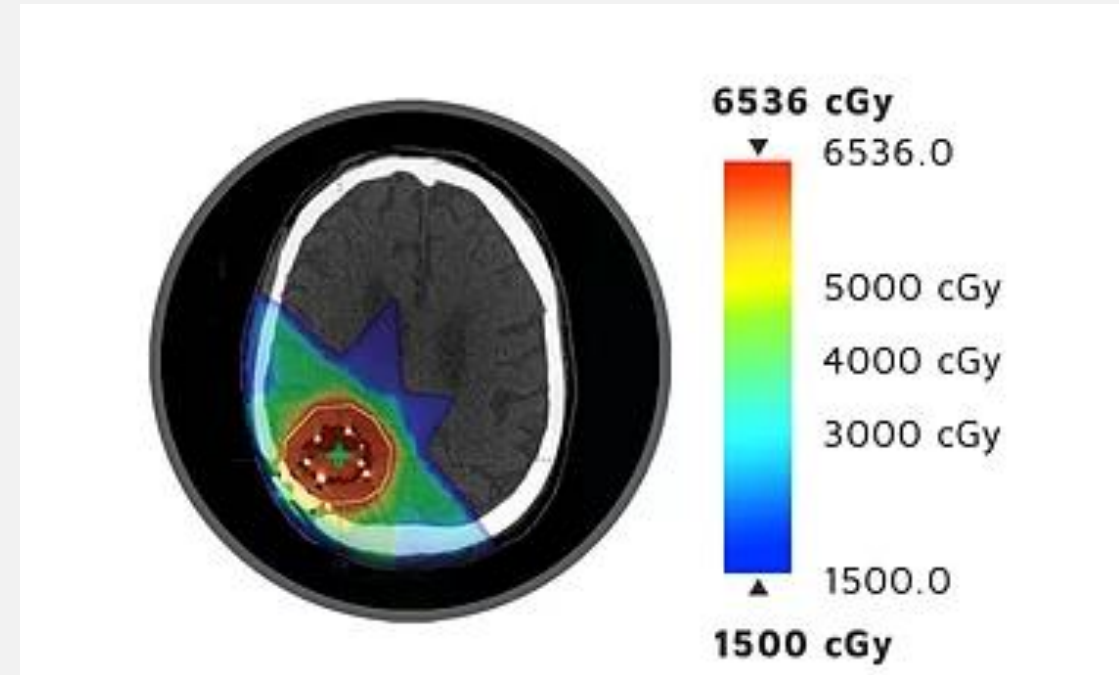


GammaTile with Cesium-131 provides a targeted and effective alternative to IMRT

GammaTile Therapy⁽¹⁾



Intensity-Moderated Radiation Therapy (IMRT)⁽¹⁾



Source: GT Medical

(1) Nakaji P, Youssef E, Dardis C, Smith K, Pinnaduwege D, Brachman D. Surgically targeted radiation therapy: a prospective trial in 79 recurrent, previously irradiated intracranial neoplasms. Poster presented at: 2019 AANS Annual Scientific Meeting; April 2019; San Diego, CA.

Expansion into Biopharma

Ongoing initiatives using Cesium-131 in immuno-oncology serve as future value drivers

- **Studying Cesium-131 in combination with Keytruda to treat recurrent head and neck cancer**
 - 50 patient Phase 1/2 study with the University of Cincinnati with enrollment ongoing
 - Using immunotherapy (immune checkpoint inhibition) in tandem with resection and Cesium-131 may assist the patient in the clearing of disease sites outside the surgical and radiation fields
 - First brachytherapy +PD-1 inhibitor combination study in recurrent head and neck cancer
- **A prospective study concluded that Cesium-131 implants after surgical resection in recurrent head and neck cancer is feasible and safe as there were no unexpected severe toxicities and most failures were out-of-field or distant⁽¹⁾**
- **Developing collaborations with additional institutions to expand immuno-oncology treatment options**



(1) Kharouta, Zender, Phd, Rezaee, Lavertu, Fowler, Thuener, Li, Clancy, Xu and Yao. "Permanent interstitial Cesium-131 brachytherapy in treating high-risk recurrent head and neck cancer: A prospective pilot study." Jan 25, 2021

Robust Body of Evidence for Cesium-131

Cesium-131 enjoys a strong record of safety and efficacy across multiple clinical studies

Meta-Analysis Data from 1,240 patients in published reports



- 10-year PSA control between 90-95% for low and intermediate risk patients
- Prostate brachytherapy with **Cesium-131** achieves excellent long-term biological control



- In brain cancer **Cesium-131** allows for a more reliable dose delivery than Iodine-125



- Positive safety profile observed with **Resection + Cesium-131** Brachytherapy, with AEs at similar or lower rate than expected



BRACHYTHERAPY

Brachytherapy 19 (2020) 298–304

Prostate

Cesium-131 prostate brachytherapy: A single institutional long-term experience

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²Department of Radiation Oncology, Allegheny Health Network Cancer Institute, Pittsburgh, PA

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BRACHYTHERAPY

Brachytherapy 18 (2019) 800–805

Prostate

Long-term biochemical outcomes using cesium-131 in prostate brachytherapy

Brian J. Moran¹, Stephanie R. Rice², Arpit M. Chh...
Manuj Agarw...

¹Prostate Cancer Foundation of M...

²Department of Radiation Oncology, University of M...

³Department of Radiation Oncology, University of M...

Cureus

DOI: 10.7759/cureus.2079

Published 01/16/2018

Resection Cavity Contraction Effects in the Use of Radioactive Sources (1-25 versus Cs-131) for Intra-Operative Brain Implants

stein¹, David Raleigh¹, Patricia K. Sneed¹, Michael

University of California, San Francisco². Department of
ornia, San Francisco

JNS

J Neurosurg May 15, 2020

A matched-pair analysis of clinical outcomes after intracavitary cesium-131 brachytherapy versus stereotactic radiosurgery for resected brain metastases

*Diana A. Julie, MD, MPH,¹ Stefanie P. Lazow, MD,² Daniel B. Vanderbilt, MD, PhD,¹ Shoshana Taube, MD,¹ Menachem Z. Yondorf, MD,¹ Albert Sabbas, PhD,¹ Susan Pannullo, MD,¹ Theodore H. Schwartz, MD,³ and A. Gabriella Wernicke, MD, MSc^{1,3}

¹Stich Radiation Oncology, Weill Cornell Medical College/NewYork-Presbyterian Hospital, New York, New York; ²Department of Surgery, Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, Massachusetts; and ³Department of Neurosurgery, Brain and Spine Center, Weill Cornell Medical College/NewYork-Presbyterian Hospital, New York, New York

Intellectual Property

Multiple layers of technology and product protection

- Process, product and associated patents owned by Isoray
- Patents cover methods and compositions of chemical separation of Cesium-131 from Barium Carbonate
 - Four U.S. patents in force until 2027
 - Three international patents families including in the EU, Russia, India, Hong Kong and UK
- Product patents in process for Isoray developed devices
 - **Blu Build Loader**: hand-held device to customize treatment in the OR at time of implant in force until 2037
 - **Device Designed to Achieve Directional Dosing**: U.S. Provisional Patent Application filed May 2020



Reimbursement Overview

Isoray is well-positioned in a changing reimbursement landscape

- Isoray's Brachytherapy solution has the advantage of being low-cost, highly effective and supported by 10+ years of outcome data
- Isoray has reimbursement for both inpatient & outpatient treatment
- CMS proposed RO-APM effective January 1, 2023 – a pilot program to evaluate changing the payment methodology to a flat rate per disease site
 - 5 year program is expected to affect reimbursement for 30% of radiation oncology clinics

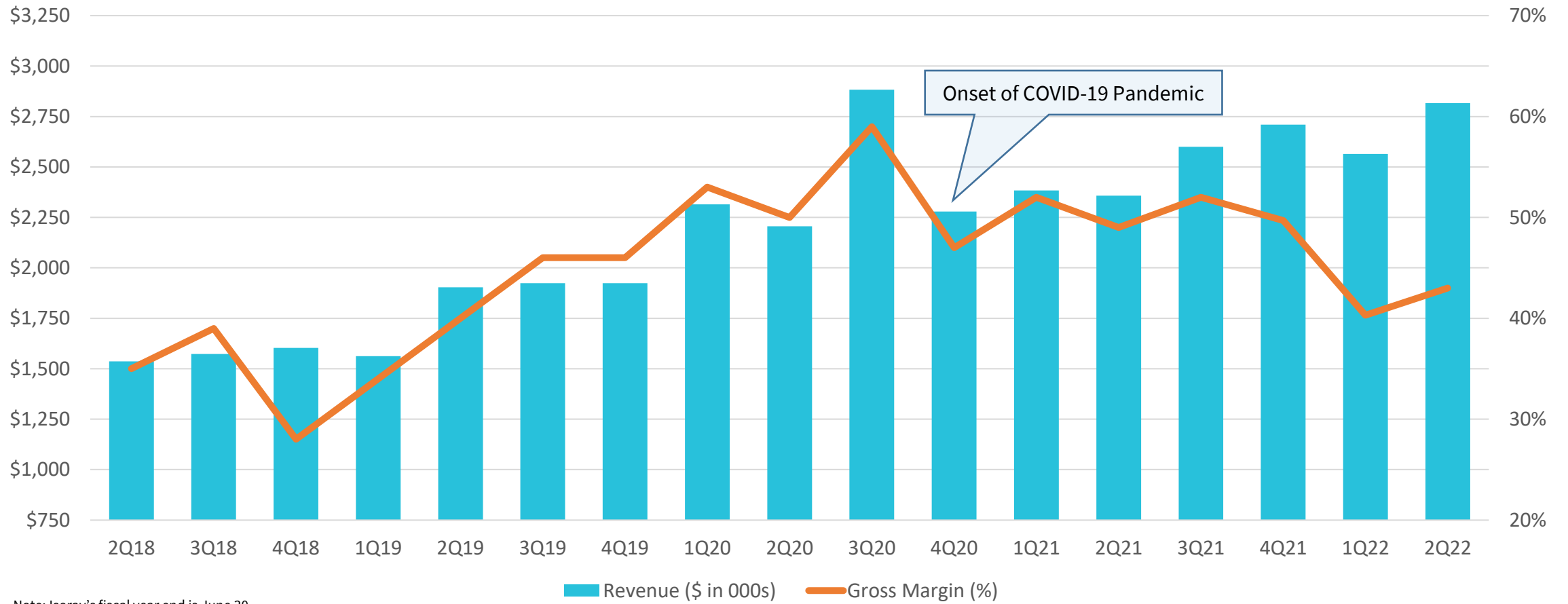
Inpatient

- For hospital stays in excess of two days
- Some surgical procedures and brain procedures
- Isoray has 64 ICD-10-PCS codes for reimbursement in all areas of the body

Outpatient

- Same day treatment and release
- Primarily prostate brachytherapy and some other treatments allowing quick release
- Isoray's seeds are reimbursed separately through 2 separate C-codes for (i) individual seeds and (ii) seeds in sleeves

Revenue and Gross Margin Trends



Note: Isoray's fiscal year end is June 30

Financial Snapshot

| NYSE American | ISR |
|---|-----------------|
| Market Data | |
| Share Price ⁽¹⁾ | \$0.33 |
| Market Cap ⁽²⁾ | \$46.9M |
| Common Shares Outstanding ⁽²⁾ | ~142.0M |
| Fully Diluted Shares Outstanding ⁽³⁾ | ~149.1M |
| Financial Data | |
| Current Cash ⁽⁴⁾ | ~\$60.4M |
| TTM/ 2FQ 2022 Revenue ⁽⁴⁾ | \$10.7M/ \$2.8M |

(1) Closing price on 03/16/2022

(2) Based on common shares outstanding on 12/31/2021

(3) Includes 2.7M warrants and 4.9M options

(4) As of 12/31/2021; quarter ending 12/31/2021



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(1) 1/1/2021 – 12/31/2021

(2) As of F2Q22 quarter ending 12/31/2021



Experienced Management Team with deep industry expertise

| | |
|---|--|
| <p>Lori A. Woods Chief Executive Officer</p> | <ul style="list-style-type: none"> • 30+years of experience in the healthcare industry and is particularly well-known and respected in the brachytherapy community • Previously served as VP and COO of Isoray from 2006 to 2010 • Extensive leadership experience in operations, supply chain management, reimbursement and marketing • Since assuming the role of CEO two years ago, Ms. Woods has brought respected expertise, strategic vision and insight that has built Isoray's reputation as an innovator and industry leader in the field of brachytherapy |
| <p>William A. Cavanagh Chief R&D Officer</p> | <ul style="list-style-type: none"> • 30+years of experience in research and development in cancer treatment technologies • Joined Isoray in 2010 and has served in a variety of executive leadership roles with research and development and operations • Guides research and development on technology, products, and clinical strategy • Mr. Cavanaugh has designed several cancer treatment-related studies, is listed as an author on 34 peer-reviewed publications and is the listed inventor on a U.S. patent application detailing a novel treatment for cancer |
| <p>Jonathan Hunt Chief Financial Officer</p> | <ul style="list-style-type: none"> • 25+ years of finance and accounting expertise including managerial roles within a range of growth companies • Returned to Isoray in 2018 after previously serving as CFO from 2006 to 2009 • Successful track record in turnarounds, startups, mergers, divestitures, growth strategies, performance and operations management and analysis at multiple organizations, including Fortune 500 companies |
| <p>Jennifer Streeter Chief Operating Officer & Vice President of Human Resources</p> | <ul style="list-style-type: none"> • 20+years of experience of progressive growth in leading teams across multiple industries in many different capacities • Joined Isoray in 2016 and assumed COO duties in 2019 to focus on manufacturing scale and future growth • Extensive managerial experience in building and implementing staffing models, performance management and providing overall training and organizational development activities |

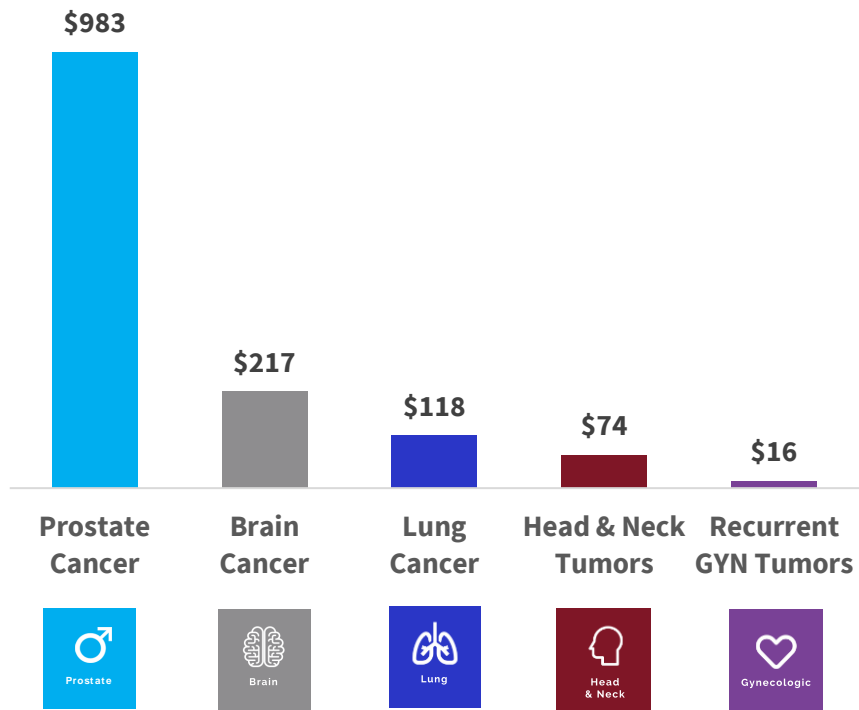
Appendix



NYSE American: ISR

Addressable Market with Cesium-131

Cesium-131 Targeting \$1B+ Opportunity



| Disease State | 2022 Estimated Annual Diagnosis ^{1, 3} | Potential LDR Patients ^{*, 2} | Potential Revenue [*] |
|--|--|--|--|
| Prostate Cancer | 268,490 | 163,779 (61% Treatable with Cs-131) | \$983M @ \$6,000 per Treatment w/Cs-131 |
| Brain Cancer • Primary CNS • Cancer • New Metastases • Recurrent Cancer | 187,820 25,050 100,000 62,770 | 61,980 (33% Treatable with Cs-131) | \$217M @ \$3,500 per Treatment w/Cs-131 |
| Lung Cancers | 236,740 | 11,837 (5% Treatable with Cs-131) | \$118M @ \$10,000 per Treatment w/Cs-131 |
| Head & Neck Tumors • Mouth • Pharynx • Tongue • Other oral cavity | 54,000 14,490 19,270 17,860 2,380 | 13,500 (25% Treatable with Cs-131) | \$74M @ \$5,500 per Treatment w/Cs-131 |
| Gynecological Cancers • Uterus • Ovary • Cervix • Vagina & Other • Vulva | 115,130 65,950 19,880 14,100 8,870 6,330 | 5,757 (20% Recurrence Rate) (25% Treatable with Cs-131) | \$16M @ \$2,700 per Treatment w/Cs-131 |
| Total Opportunity | 862,410 | 256,853 Patients | ~\$1.4B |

(1) <https://www.cancer.org/research/cancer-facts-statistics.html>

(2) <https://www.mskcc.org/cancer-care/types/brain-tumors-metastatic>

(3) https://academic.oup.com/neuro-oncology/article/20/suppl_4/iv1/5090960

* Estimates of cases based on internal assessments from ACS data, market reports.