

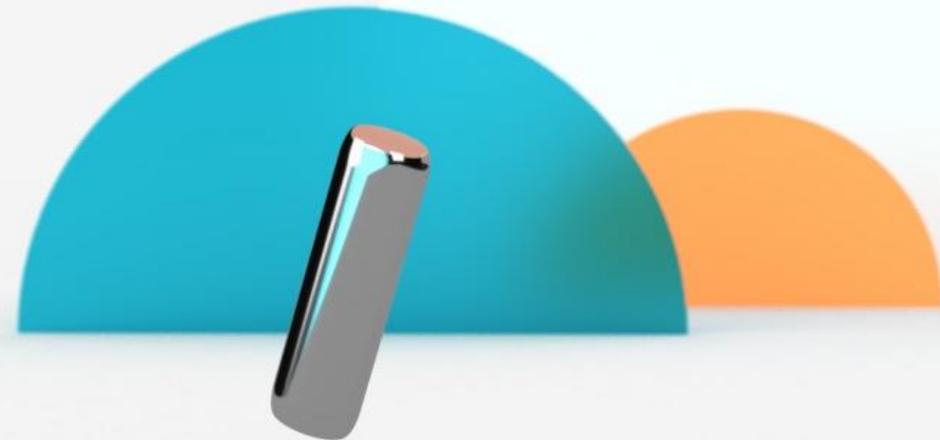


# An Emerging Leader in Targeted Internal Radiation Therapy

March 2021

## Investor Presentation

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 2021, the impact of COVID-19 on our financial results and the timing of recovery in our brachytherapy procedures, suppliers, scheduling of procedures, and employees, 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 will continue to 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, and all other statements in this presentation, 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 Blu Build products and the success of the GammaTile Therapy, 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 that support the conclusions of past studies, whether ongoing patient results with our products are favorable and in line with the conclusions of clinical studies and initial patient results, patient results achieved when our products are used for the treatment of cancers and malignant diseases, 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, the procedures and regulatory requirements mandated by the FDA for 510(k) approval and reimbursement codes, 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 each of our products, and other risks detailed from time to time in Isoray's reports filed with the SEC. 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.

This presentation is not a prospectus and is not an offer to sell, nor a solicitation of an offer to buy, securities. Isoray has filed a registration statement on Form S-3 (including a prospectus) with the Securities and Exchange Commission (the "SEC") and has filed or will file with the SEC a prospectus supplement to the prospectus for the offering to which this communication relates. Before you invest, you should read the prospectus supplement and the accompanying prospectus in that registration statement and the documents incorporated by reference or filed as exhibits to the registration statement for more complete information about Isoray and this offering. You can obtain these documents for free by visiting EDGAR on the SEC website at [www.sec.gov](http://www.sec.gov).

For more information regarding risks and uncertainties that could affect Isoray's results of operations or financial condition, review Isoray's filings with the SEC (in particular, its most recently filed Form 10-K and Form 10-Qs). This presentation shall not constitute an offer to sell or the solicitation of an offer to sell or the solicitation of an offer to buy any securities of Isoray nor shall there be any sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction.

# Investment Highlights

- **Emerging leader in radiotherapeutics focused on commercializing proprietary Cesium-131 therapy for the treatment of cancer**
- **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
- **Consistent revenue growth and improving gross margin trends in core markets:**
  - TTM Revenue of \$9.9M, increased 18%<sup>(1)</sup>
  - TTM Gross Profit Growth of 26%<sup>(1)</sup>
  - TTM Gross Margin of 52.4%<sup>(1)</sup>
- **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
  - Evaluating Cesium-131 for treatment of surgical cancers, including GYN, lung and others
- **Experienced management team with deep industry expertise**

(1) 1/1/2020 – 12/31/2020

# Brachytherapy Overview

Safe and established treatment option for the treatment of cancer

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 proprietary solution



- **Isoray's Cesium-131 therapy is proven to be a highly effective cancer treatment**
  - Marketed under the Cesium Blu® brand name
  - Higher energy and a shorter half-life than competitors
  - Treatment delivered faster than external radiation (90% in 33 days)
  - Powerful, continuous, therapeutic energy
- **15,000+ patients treated over 10 years**

Cesium-131 Introduced in 2004	Palladium-103 Introduced in 1986	Iodine-125 Introduced in 1965
<b>9.7 Day Half Life</b> The amount of time for the radiation to half. A shorter half life means quicker to PSA baseline. (8, 12, 13)	17 Day Half Life	60 Day Half Life
<b>30.4 Kev</b> The energy level of the isotope. Higher energy leads to greater coverage of the infected organ.	20.8 Kev	28.5 Kev
<b>33 Days for 90% Dose</b> Faster dose delivery rate.	58 Days for 90% Dose	204 Days for 90% Dose
<b>Detectable in the body for only 97 Days</b>	Detectable in the body for 107 Days	Detectable in the body for 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 outcomes data
- Three straight years of 20%+ revenue growth

**\$585M**

Est. 192k cases in 2020  
61% cases treatable with Cesium-131



## Surgical

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

**\$208M**

Est. 389k cases in 2020  
8% cases treatable with Cesium-131



## Brain

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

**\$217M**

Est. 188k cases in 2020  
33% cases treatable with Cesium-131

Note: Market data backup on slide 21

# Prostate Cancer: Isoray's Growing Core Market

## Renewed sales strategy driving growth in Prostate

### Growth Drivers

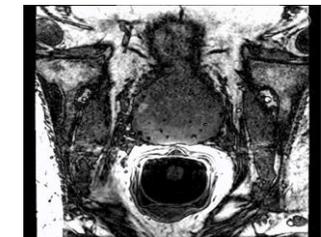
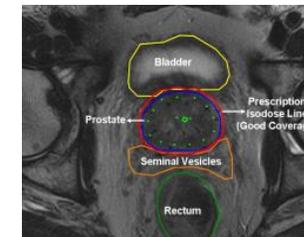
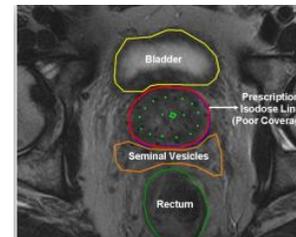
- **Recent FDA 510(k) clearance of C4 Imaging's Sirius® positive-signal MRI markers with Cesium-131 Seeds**
- **Highly trained direct sales force to expand coverage in the U.S.**
- **Leveraging 10+ years of clinical evidence to build awareness among physicians**
- **Aligning product portfolio under the Blu brand**
- **Investing in additional clinical data and research**
- **Innovative training for physicians and residents**
- **Digital and social media awareness programs**

### Proven Comprehensive Solution for Prostate Cancer

#### Proprietary Blu Build® Delivery Platform



C4 Imaging's Sirius

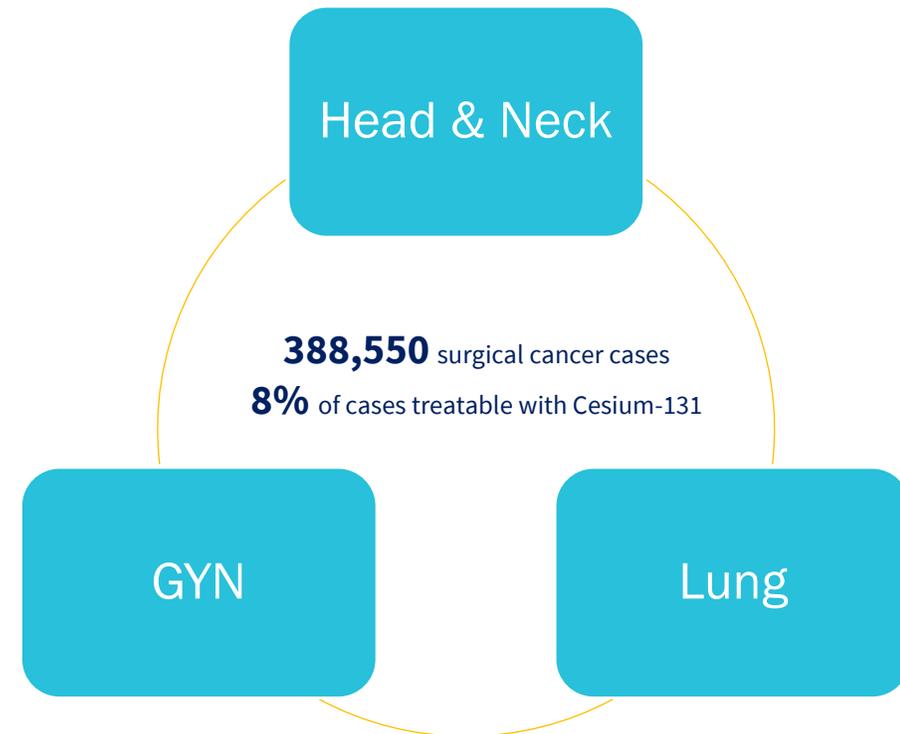


# Use of Cesium-131 in Surgery

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 21

# Brain Cancer: Opportunity for Significant Growth

Commercialization efforts underway to treat brain cancer with Cesium-131



Powered by Cesium Blu

- **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
  - In early stage commercialization; 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**

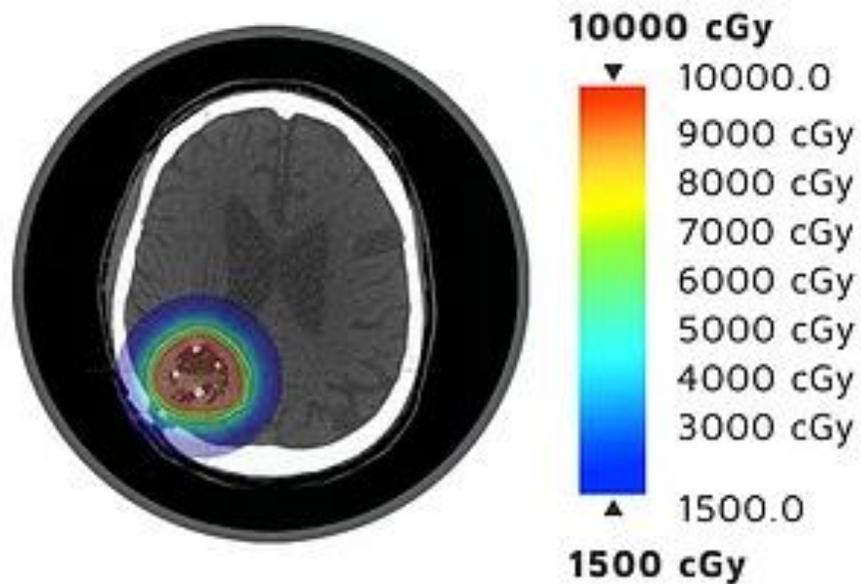


Source: GT Medical Technologies

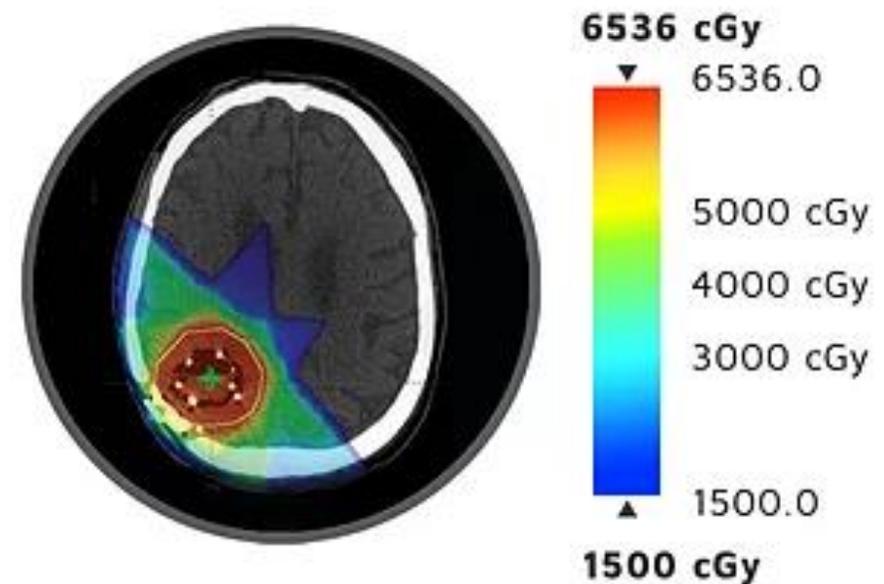
# The GammaTile Difference

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

## GammaTile Therapy<sup>(1)</sup>



## Intensity-Modulated Radiation Therapy (IMRT)<sup>(1)</sup>

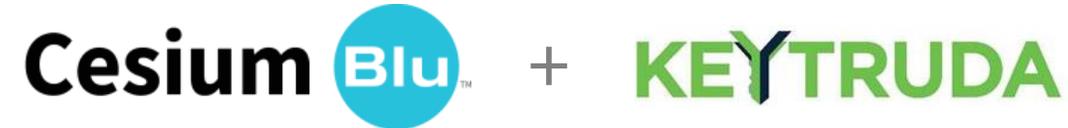


Source: GT Medical

(1) Nakaji P, Youssef E, Dardis C, Smith K, Pinnaduwa 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**
  - Planned 50 patient Phase 1/2 study with the University of Cincinnati
  - 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<sup>(1)</sup>**
- **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

ELSEVIER

Brachytherapy 19 (2020) 298–304

Prostate

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

BRACHYTHERAPY

ELSEVIER

Brachytherapy 18 (2019) 800–805

Prostate

Long-term biochemical outcomes using cesium-131 in prostate

BRACHYTHERAPY

JNS

J Neurosurg May 15, 2020

A matched-pair analysis of intracavitary cesium-131 stereotactic radiosurgery

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

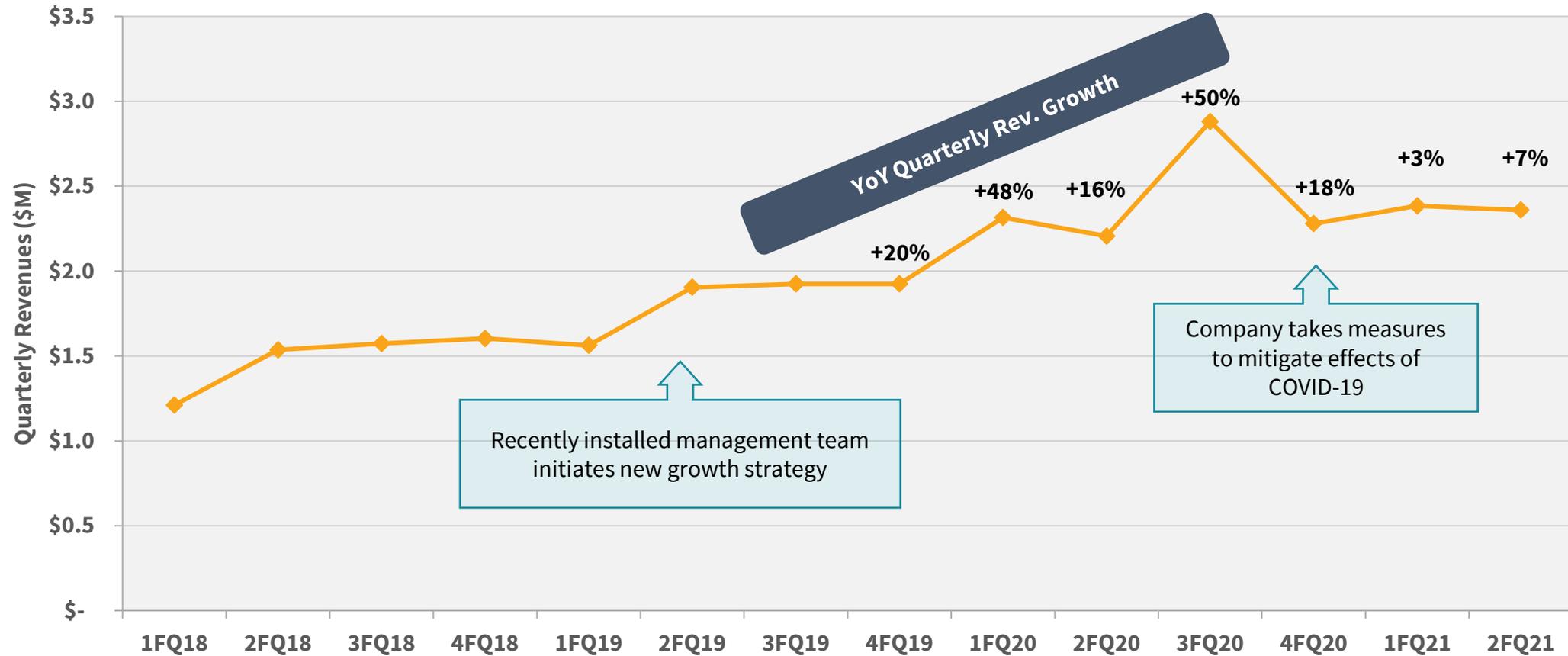
Dae Y. Han<sup>1</sup>, Lijun Ma<sup>1</sup>, Steve Braunstein<sup>1</sup>, David Raleigh<sup>1</sup>, Patricia K. Sneed<sup>1</sup>, Michael McDermott<sup>2</sup>

<sup>1</sup>Stich Radiation Oncology, Weill Cornell Medical College of Surgery, Beth Israel Deaconess Medical Center/Harvard Neurosurgery, Brain and Spine Center, Weill Cornell Me

1. Department of Radiation Oncology, University of California, San Francisco 2. Department of Neurological Surgery, University of California, San Francisco

# Accelerating Revenue Growth

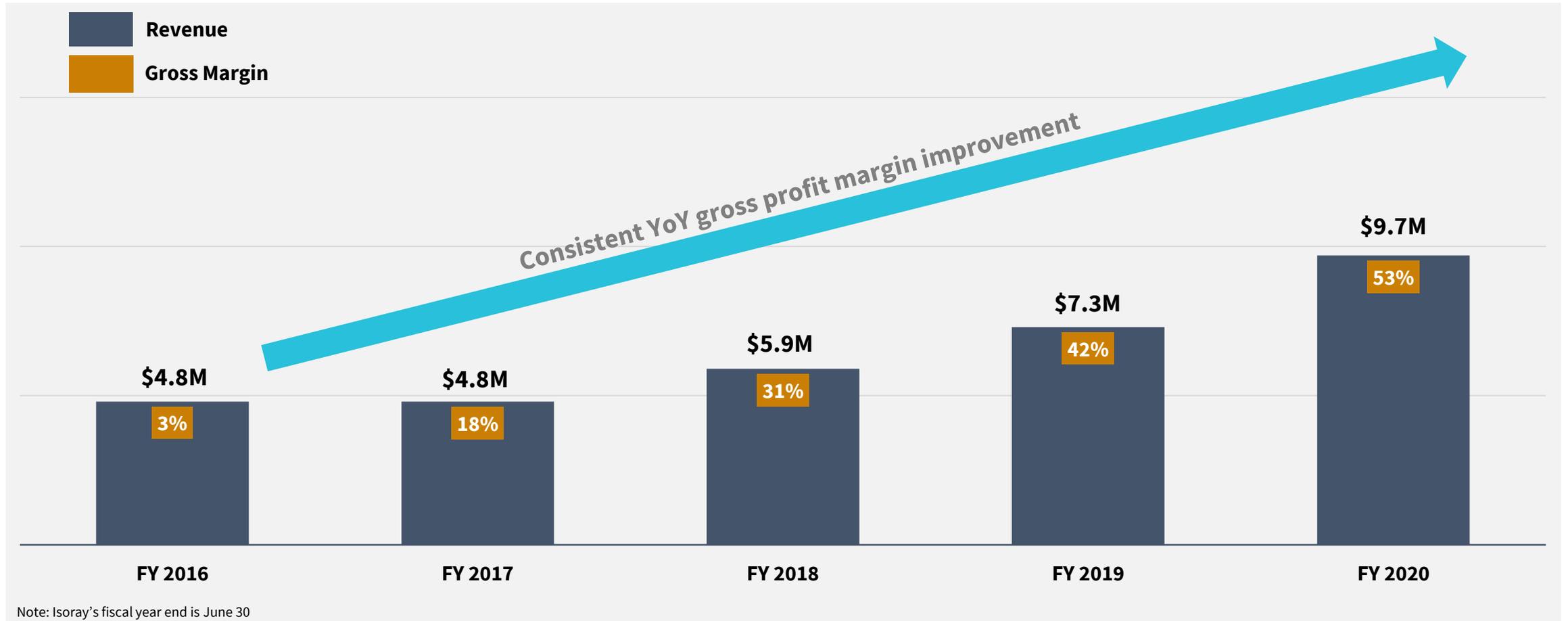
Despite COVID-19 related challenges, Isoray continues to exhibit strong YoY quarterly growth



Note: Isoray's fiscal year end is June 30

# Continued Gross Margin Improvements

Scale and manufacturing efficiencies continue to drive margin expansion



# Financial Snapshot

NYSE American	ISR
<b>Market Data</b>	
Share Price <sup>(1)</sup>	\$1.26
Market Cap <sup>(2)</sup>	\$177.9M
Common Shares Outstanding <sup>(3)</sup>	~141.2M
Fully Diluted Shares Outstanding <sup>(4)</sup>	~149.4M
<b>Financial Data</b>	
Current Cash <sup>(5)</sup>	~\$64.8M
TTM/ 2FQ 2021 Revenue <sup>(6)</sup>	\$9.9M/ \$2.4M

(1) Closing price on 03/12/2021

(2) Based on common shares outstanding on 03/12/2021

(3) Includes exercise of 12.3M warrants exercised and 41.4M common shares sold since the last reporting period

(4) Includes 2.7M warrants and 5.5M options

(5) Estimated cash inclusive of warrants exercised and common shares sold since 12/31/2020

(6) As of 12/31/2020; quarter ending 12/31/2020

# Reimbursement Overview

## Isoray is well-positioned in a changing reimbursement landscape

- **CMS proposed RO-APM effective January 1, 2022 – a pilot program to evaluate changing the payment methodology to a flat rate per disease site**
  - The 5-year program is expected to affect reimbursement for 30% of radiation oncology clinics
- **Isoray’s Brachytherapy solution has the advantage of being low-cost, highly effective and supported by 10+ years of outcomes data**
- **Isoray has reimbursement for both inpatient & outpatient treatment**

Inpatient	Outpatient
<ul style="list-style-type: none"> <li>• For hospital stays in excess of two days</li> <li>• Some surgical procedures and brain procedures</li> <li>• Isoray has 64 ICD-10-PCS codes for reimbursement in all areas of the body</li> </ul>	<ul style="list-style-type: none"> <li>• Same day treatment and release</li> <li>• Primarily prostate brachytherapy and some other treatments allowing quick release</li> <li>• Isoray’s seeds are reimbursed separately through 2 separate C-codes for (i) individual seeds and (ii) seeds in sleeves</li> </ul>

# 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
- **Products 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

# Experienced Management Team

---

**Lori A. Woods**

Chief Executive Officer

- 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

---

**William A. Cavanagh**

Chief R&D Officer

- 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

---

**Jonathan Hunt**

Chief Financial Officer

- 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

---

**Jennifer Streeter**

Chief Operating Officer  
& Vice President of Human Resources

- 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

# Investment Highlights

- **Emerging leader in radiotherapeutics focused on commercializing proprietary Cesium-131 therapy for the treatment of cancer**
- **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
- **Consistent revenue growth and improving gross margin trends in core markets:**
  - TTM Revenue of \$9.9M, increased 18%<sup>(1)</sup>
  - TTM Gross Profit Growth of 26%<sup>(1)</sup>
  - TTM Gross Margin of 52.4%<sup>(1)</sup>
- **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
  - Evaluating Cesium-131 for treatment of surgical cancers, including GYN, lung and others
- **Experienced management team with deep industry expertise**

(1) 1/1/2020 – 12/31/2020



## Appendix

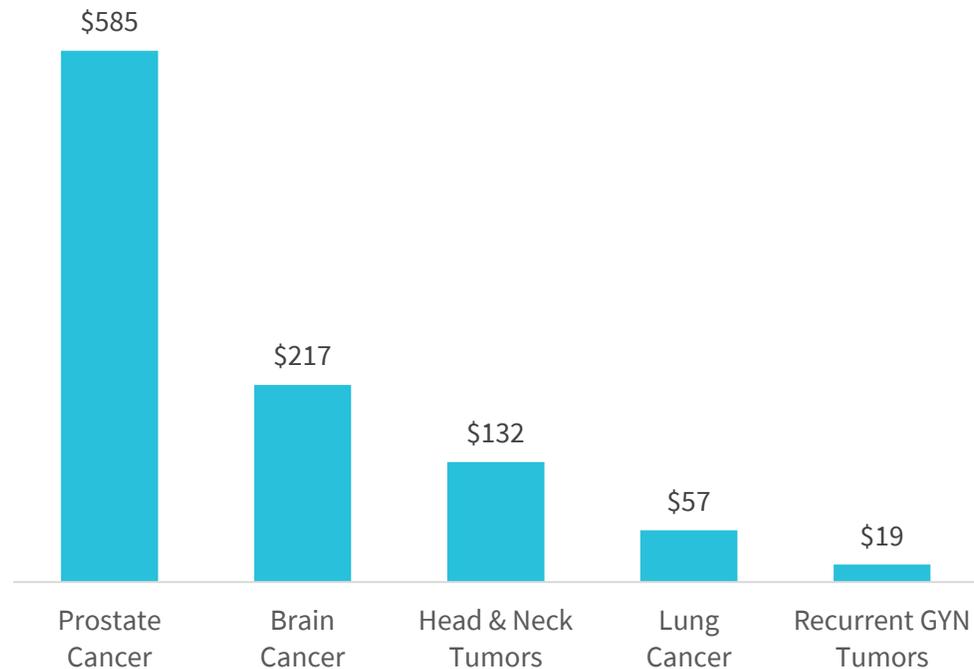


NYSE American: ISR

# Addressable Market with Cesium-131

## Cesium-131 Targeting \$1B+ Opportunity

In Millions



Disease State	2020 Estimated Annual Diagnosis <sup>1,3</sup>	Potential LDR Patients <sup>*,2</sup>	Potential Revenue*
<b>Prostate Cancer</b>	<b>191,930</b>	<b>117,077</b> (61% Treatable with Cs-131)	<b>\$585M</b> @ \$5,000 per Treatment w/ Cs-131
<b>Brain Cancer</b>	<b>187,820</b>	<b>62,000</b> (33% Treatable with Cs-131)	<b>\$217M</b> @ \$3,500 per Treatment w/ Cs-131
- Primary CNS Cancer	23,820		
- New Metastases	100,000 <sup>4</sup>		
- Recurrent Cancer	64,000 <sup>4</sup>		
<b>Gynecological Cancers</b>	<b>107,400</b>	<b>5,370</b> (20% Recurrence Rate) (25% Treatable with Cs-131)	<b>\$19M</b> @ \$3,500 per Treatment w/ Cs-131
- Uterus	61,880		
- Ovary	22,530		
- Cervix	13,170		
- Vagina & Other Genital	5,350		
- Vulva	6,070		
<b>Head &amp; Neck Tumors</b>	<b>53,000</b>	<b>13,250</b> (25% Treatable with Cs-131)	<b>\$132M</b> @ \$10,000 per Treatment w/ Cs-131
- Mouth	14,310		
- Pharynx	17,870		
- Tongue	17,060		
- Other oral cavity	3,760		
<b>Lung Cancers</b>	<b>228,820</b>	<b>11,441</b> (5% Treatable with Cs-131)	<b>\$57M</b> @ \$5,000 per Treatment w/ Cs-131
<b>Total Opportunity</b>	<b>768,970</b>	<b>209,138 Patients</b>	<b>~\$1B</b>

1. <https://cancerstatisticscenter.cancer.org/#/>

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

3. [https://academic.oup.com/neuro-oncology/article/20/suppl\\_4/iv1/5090960](https://academic.oup.com/neuro-oncology/article/20/suppl_4/iv1/5090960)

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