



Initiating Coverage Report

## **Advanced Medical Isotope Corp.**

Moving towards commercialization

**RadioGel™**

Chief Research Analyst

**Marcel Wijma MSc**

+1 (917) 460 6185 (US)

+31 (6) 8489 2954 (NL)

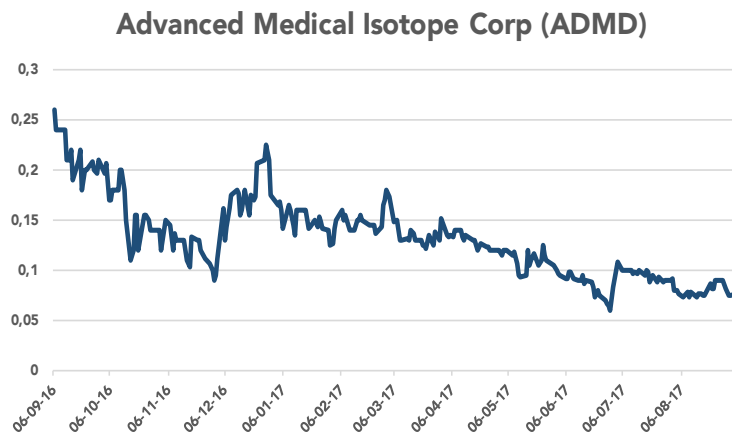
[m.wijma@leeuwenhoeck.com](mailto:m.wijma@leeuwenhoeck.com)

<http://www.leeuwenhoeck.com>



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<b>Name:</b>	<b>Advanced Medical Isotope Corp</b>
<b>Country:</b>	<b>United States</b>
<b>Price:</b>	<b>USD 0.076</b>
<b>ISIN Code:</b>	<b>US00765X2018</b>
<b>Reuters Code:</b>	<b>ADMD</b>
<b>Market Cap (USD m):</b>	<b>6.8</b>
<b>EV (USD m):</b>	<b>10.4</b>
<b>Cash &amp; cash eq. (USD m):</b>	<b>0.4</b>
<b>Shares outstanding (m):</b>	<b>88.9*)</b>
<b>Average Daily Volume:</b>	<b>174,066</b>
<b>Free float:</b>	<b>100%</b>
<b>52-week Range:</b>	<b>0.07-1.00</b>
<b>*) Both preferred and common stock</b>	





# Contents

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<i>Executive Summary</i>	<b>4</b>
<i>Company Profile</i>	<b>6</b>
<i>Overview Treatment Options in Radio Therapy</i>	<b>11</b>
<i>Animal Health Rapidly Growing Opportunity</i>	<b>14</b>
<i>SWOT Analysis</i>	<b>16</b>
<i>Financials</i>	<b>17</b>
<i>Management Capabilities</i>	<b>20</b>
<i>Competitive Landscape</i>	<b>23</b>
<i>Appendix: Filing Procedure Animal Health</i>	<b>29</b>



## Executive Summary

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- Advanced Medical Isotope Corp. (AMIC) is an US based Life Sciences company that provides an innovative technology for safer and more effective radiation therapies for difficult to treat cancers. Its lead product is Yttrium-90 RadioGel, which is a brachytherapy device comprising highly insoluble Y-90 particles delivered by needle injection using a water-polymer composite for high-dose treatment of non-resectable solid tumors that cannot be treated effectively by any other means. The company is engaging the FDA for permission to use RadioGel™ for the treatment of advanced basal and squamous skin cancers.
- Yttrium-90 is an ideal medical isotope with a short half-life (2.7 days) and is a pure beta-emitter. It is approved as a therapeutic agent as part of traditional delivery systems, specifically on monoclonal antibodies targeting cancer cells (Zevalin) and as the active ingredient in glass or resin microsphere in use for treating liver tumors (TheraSphere and SIR-Spheres).
- In the past few months, the company has strengthened its board and management with experienced people that have a background in the industry. Management is also working together with renowned FDA consultants to assist the company in its filing and approval process with the FDA.
- The financial position of the company was improved considerably with successful raise of additional interim capital to retire some maturing debt and exchanged the remaining maturing debt for debentures that mature in May 2018. This removes the near term uncertainty and now allows AMIC to fully focus on execution of their plan for an uplisting



later in the year. The Company is on track to ramp up product development and testing activities with their commercialization partner IsoTherapeutics Group.

- AMIC has launched its Veterinary Oncology division IsoPet in order to develop RadioGel for the treatment of various animal cancer. The IsoPet Solutions division is focused on demonstrating the safety and therapeutic effectiveness for different animal cancers in four different university veterinary hospitals. After this demonstration phase the plan is to sell RadioGel to the private animal clinics. According to the Center for Cancer Research and CanineCancer.com an estimated six million dogs are diagnosed with cancer each year in the USA. According to various market reports, the market for pet cancer therapeutics is estimated to be USD 300-500 million.
- The total market for inoperable cancers is estimated to be several billion dollars in size. The lack of effective treatments that offers significantly improved survival rates provides ample opportunity to be a game changer for the treatment of these cancers. We feel that Y-90 RadioGel therefore has the potential to be a blockbuster (sales > 1 billion) within a few years since the therapy would be useful in a range of soft tissue cancers.
- Based on our NPV valuation, we believe that AMIC is substantially undervalued at the current share price of USD 0.075. Considering Y-90 Radiogel's much higher potential commercial success compared to Sirtex' SIR-Spheres (with total annual sales of more than AUD 200 million) and the high unmet medical need in several types of cancer, induces us to increase our valuation to USD 35-55 million or USD 0.66-1.00 per share. This represents a substantial upside from the current share price.



## Company Profile & Technology

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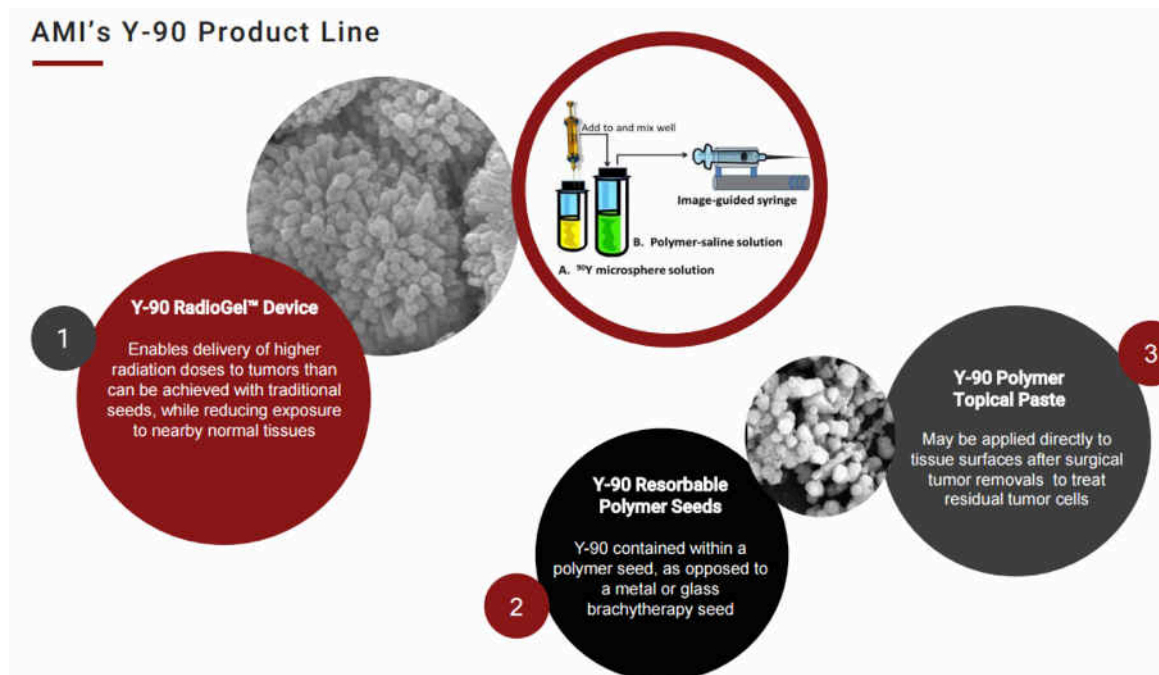
Advanced Medical Isotope Corporation (AMIC) is a late stage radiation oncology medical device company engaged in the development of its yttrium-90 based brachytherapy device, RadioGel™, for the treatment of non-resectable tumors. A prominent team of radiochemists, scientists and engineers, collaborating with strategic partners, including national laboratories, universities and private corporations, lead the Company's development efforts. The Company's overall vision is to globally empower physicians, medical researchers and patients by providing them with new isotope technologies that offer safe and effective treatments for cancer.

AMIC has exclusively licensed Yttrium-90 (Y-90) polymer composite technology from Battelle Memorial Institute, developed at Pacific Northwest National Laboratory, a leading research institute for government and commercial customers. Its primary product is Y-90 RadioGel™ device - combines Y-90 particles with a polymer carrier that injected directly into the tumor. Advanced Medical utilizes IsoTherapeutics Group, LLC for its manufacturing and testing engaged Hogan Lovells for FDA regulatory advice., has a grant from The Life Sciences Discovery Fund and is preparing for animal testing at the Colorado State University, Washington State University, University of Missouri and University of California Davis

According to Global Industry Analysts, by 2016 the U.S. brachytherapy market will reach USD 2 billion. It is estimated that the US market represents approximately half of the global market. AMIC has selected skin cancer therapy for its first indication for use with the Food and Drug Administration. In the US there are 5.4 million cases of skin cancer in 3.3 million people. Treating 10% of these patients could generate annual revenue at greater than USD 1 billion. AMIC believes



there are significant future opportunities in treating lymph nodes, prostate, breast, liver, pancreatic, head and neck cancers.



Source: AMIC

### *RadioGel for Humans and IsoPet for Use in Animals*

The Company's current focus is on the development of its RadioGel™ device. RadioGel™ is an injectable particle-gel for brachytherapy radiation treatment of cancerous tumors in people and animals. RadioGel™ is comprised of a hydrogel, or a substance that is liquid at room temperature and then gels when reaching body temperature after injection into a tumor. In the gel are small, one micron, yttrium-90 phosphate particles ("Y-90"). Once injected, these inert particles are locked in place inside the tumor by the gel, delivering a very high local radiation dose. The radiation is





beta, consisting of high-speed electrons. These electrons only travel a short distance so the device can deliver high radiation to the tumor with minimal dose to the surrounding tissue. Optimally, patients can go home immediately following treatment without the risk of radiation exposure to family members. Advanced Medical Isotope Corporation has obtained an exclusive license to eight patents related to the Y-90 RadioGel™ device technology for use in high-dose radiation therapy. The license was granted by \*Battelle pursuant to an option between Battelle and AMIC announced in February 2011. The Agreement grants AMI an exclusive license to make, have made, use and sell the Y-90 RadioGel™ device

Yttrium-90 is a well-established medical isotope with many applications in cancer treatment. The combination of insoluble Yttrium-90 particles and the polymer gel carrier offers physicians an opportunity to deliver a safe, effective treatment option at a low cost.

The RadioGel™ device places Y-90 particles in tumor tissue and Yttrium-90 containment within the tumor following injection. According to the company there are several benefits of the RadioGel device:

- **Maximizing Therapeutic Index:** The short-range beta particles emitted by Y-90 deliver radiation energy within a tight range. This enables radiation to be selectively delivered to target tissues while minimizing radiation dose to nearby normal tissues. High therapeutic indices imply that more radiation energy may be imparted to target tissues, with less radiation reaching adjacent normal tissues.
- **Half Life: Y-90 has a half-life of just 2.7 days.** Many traditional brachytherapy products use isotopes with longer half-lives such as 9.7 days for cesium-131, and sixty days for I-125.
- **Optimized Delivery Method:** Current brachytherapy devices place permanent metal seeds in the prostate by using up to 30 large needles. By contrast, AMIC's Y-90





RadioGel™ device is designed to be administered in a minimally invasive procedure with small-gauge needles.

- **No Permanent Seeds Remaining:** Current brachytherapy devices place permanent metal seeds in the tumor. AMIC's Y-90 RadioGel™ device utilizes a biodegradable, non-toxic polymer that is ultimately absorbed by the body. This eliminates the possibility of a long-term seed migration or other problems that may sometimes arise when seeds remain in the body.
- **Good Safety Profile:** Many traditional brachytherapy devices utilize isotopes that emit x-rays (akin to gamma radiation). X-rays or gamma radiation travels within and outside of the body and have long half-lives. AMIC's brachytherapy products use the Yttrium-90 isotope, which is a beta-emitter. The Yttrium-90 beta-emissions travel only a short distance and has a short half life of 2.7 days.
- **Potential Lower Cost:** Yttrium-90 supplies are readily accessible and are relatively inexpensive. The elimination of the metal or glass enclosures used in traditional brachytherapy seeds greatly reduces manufacturing costs.

The initial target for Y-90 RadioGel should be inoperable cancer, as first line treatment in conjunction with standard chemotherapy. Treatment currently is multiple weekly courses of intravenous chemotherapy for inoperable disease, which only creates on average a few months survival advantage compared to having no treatment administered. Therefore, there is a major unmet need for additional therapies that can reduce the tumor burden and increase quality of life in late stage cancer patients.

The FDA has classified RadioGel as a device. This increase chances of a timely approval considerably. The critical path on the overall schedule to approval is firstly to complete laboratory



testing concurrent with veterinary animal studies and then continue into human clinical trials. AMIC intends to align the animal treatments in its veterinarian business division to support the animal testing required for the FDA to synergize the two divisions, and potentially create time and cost savings. In this parallel strategy, the company looks to move to first-in-man trials as soon as possible, while aggressively pursuing near-term revenues through the veterinary division, IsoPet, and through licensing.

In 2017Q1 the company selected four veterinary centres, each to focus on a different cancer type:

- Washington State University - feline sarcom (Dr. Janean Fidel and Dr. Megan Duffy)
- University of Missouri -canine prostate cancer, equine sarcoid (Dr. Jimmy Lattime, Dr. Jeffrey Bryan, and Dr. Charles Maitz)
- UC Davis - University of California -sarcomas, liver cancer (Dr. William Culp)
- Colorado State University – soft tissue sarcomas, oral squamous cancer (Dr. Jac Nickloff and Dr. Susan LaRue)

These tumors in animals serve as models for a variety of related human cancers. Clear demonstration of therapeutic benefits in animals would directly enhance our pending FDA application for human use.

In July, the company announced that it has finalized an improved manufacturing process for our yttrium phosphate particles. The company conducted more than thirty process development runs to achieve the most cost-effective process to reproducibly give it the small particles that are desired. Small particles perfuse further into the tumor and reduce the number of injections required for dose coverage in large tumors. In parallel, AMIC concentrated on reducing the time and cost required for manufacturing and increasing the batch yield. As an example, one production step was reduced from 20 hours to just an hour. Product yield increased from 80% to 99.99%.



## Overview Treatment Options in Radio Therapy

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As there are only two chemotherapy drugs on the market that have shown to extend survival marginally, radiation therapy is used in combination of chemotherapy. Radiation therapy is a cancer treatment that uses high-energy radiation, in the form of waves (such as x-rays) or particles (such as protons), to kill cancer cells or prevent them from growing and dividing. Radiation therapy can prevent pancreatic tumors from growing and sometimes shrinks them. There are two main types of radiation therapy, external beam radiation therapy and internal radiation therapy (or brachytherapy).

### *External beam radiation therapy*

This radiation therapy delivers radiation by using a machine outside the body, which directs a beam or multiple beams of radiation through the skin to the tumor or tumor bed. External beam radiation therapy is commonly used in treating pancreatic cancer patients.

### *Internal radiation therapy (brachytherapy)*

Brachytherapy delivers radiation through radioactive material implanted in or near the cancer. This type of radiation therapy is still rarely used in pancreatic cancer patients. OncoSil may well change this dramatically. In addition to standard external beam radiation therapy, the following two methods of planning and delivering external beam radiation are currently used in pancreatic cancer treatment. These specialized methods are able to minimize the amount of radiation delivered to normal tissues and are used when a higher dose of radiation is recommended:

- *Intensity-modulated radiation therapy (IMRT)*



**IMRT** is a type of external beam radiation therapy that delivers focused radiation to the tumor by modulating (varying) the intensity of the radiation beam under precise computer control. By using three-dimensional computer imaging to determine the size, shape and location of the tumor, and by varying the intensity of the radiation dose, IMRT allows a higher dose of radiation to be administered to the tumor while minimizing the amount of radiation delivered to healthy tissue near the pancreas, such as the duodenum (the first portion of the small intestine). This may lead to fewer side effects and allow higher doses of radiation to be delivered safely, compared to standard radiation therapy.

- *Stereotactic body radiation therapy (SBRT)*

SBRT is a type of external beam radiation therapy designed to deliver high doses of radiation precisely to small tumors, usually in five or fewer treatments. SBRT uses multiple narrow radiation beams to target small, well-defined areas. In order for SBRT to be delivered safely in pancreatic cancer patients, the tumor must remain motionless or the machine delivering the radiation must be able to adjust for any movement of the tumor, such as during breathing. Patients may be fitted with a customized device to keep the body perfectly still or the treatment machine may have the ability to limit, monitor and adjust for any movement during the treatment. Also, small metallic seeds may be implanted near the tumor before treatment begins to better track the location of the tumor during treatment. CyberKnife® is one type of SBRT. Some studies have suggested that the delivery of high doses of radiation in a few treatments is difficult to accomplish without damaging the intestinal tract.

There are ongoing studies to determine the appropriate radiation dose and frequency of radiation doses given using SBRT to avoid damaging the duodenum. Therefore, SBRT is still being studied in clinical trials for pancreatic cancer and its usage is only recommended as part of a clinical trial.

### *Proton beam radiation therapy*



This is a type of external beam radiation therapy that uses proton beams rather than x-rays. Protons are charged particles that deposit most of their energy at a very narrow area within the body. Because of this characteristic, proton beam therapy allows a higher, more conformed dose of radiation to be delivered to the tumor, while sparing surrounding healthy tissue. Therefore, it generally causes fewer side effects. Proton therapy is only available at very few centers throughout the US and is being studied in clinical trials for pancreatic cancer.

### *Comparison Brachytherapy*

	CS-131	I-125	Pd-103	Y-90	Y-90 advantage
<b>Primary Emissions</b>	Auger x-rays	Auger x-rays	Auger x-rays	Beta rays	High energy, finite path
<b>Average Path length</b>	Infinite	Infinite	Infinite	4mm	Safer for Healthy tissue and medical staff
<b>Half Life</b>	9.7 days	60 days	17 days	2.7 days	Short Half Life Shorter treatment
<b>Delivery Form</b>	Metal seeds	Metal seeds	Metal seeds	Biodegradable polymer	No casing remains
<b>Costs</b>	Utilize expensive isotopes	Utilize expensive isotopes	Utilize expensive isotopes	Readily accessible less expensive	Cost Savings



## Animal Health Rapidly Growing Opportunity

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The overall market for veterinary medical products is more than USD 22 billion – and as more and more households acquire a pets, the market has continued to grow. In the USA, the number of dogs has increased from 68 million to 83.3 million between 2000 and 2014. The total market for veterinary services in the USA is estimated to be just over USD 15.7 billion in 2015. An estimated 60 million dogs are kept as pets in the EU10 and around 15 million dogs in Japan. Households are also becoming increasingly inclined to spend money on their pets. For example a 2011 study found that a majority of American dog owners considered their dog to be a member of the family. Over the past ten years households' average increase in animal-related expenditure has been 3-4% per year. In particular, dogs receive veterinary medical treatment to a greater and greater extent. According to American Pet Products, almost 80 percent of all dog owners have their dogs treated with drugs, compared to about 50 percent in 1998.

### *Cancer in Animals*

According to the Center for Cancer Research and CanineCancer.com an estimated six million dogs are diagnosed with cancer each year in the USA. Approximately one third of these have skin cancer. Cancer in animals is similar to cancer in humans and the risk increases with age. Some cancers are more common in certain species, for example lymphoma is the most prevalent cancer in dogs. Most existing cytostatics for intravenous use have been designed for humans and have not been optimized or clinically tested for animals. This means that it is difficult to make an accurate assessment of the overall market and to predict its growth. Among veterinarians, there is a strong interest in pursuing new methods of treatment specifically adapted to animals. When more drugs are approved for use in animals, this is expected to contribute positively to the development of the



market. Improved knowledge about diagnosing cancer and about the treatment of cancer is leading to more dogs receiving treatment. In addition, access to oncology specialists is improving, and veterinarians tend to be more and more willing to refer to specialists.

According to a recent report of Global Market Insights Inc, the pet cancer therapeutics market share is projected to surpass USD 300 million by 2024. Swedish-based pharmaceutical company Oasmia Pharmaceutical, which makes one of the three FDA-approved cancer treatments for dogs, estimates the size of the market at USD 500 million.

Chemotherapy has been the mainstream medication for pet cancers till recent times. However, other therapies like brachytherapy entered the market and are gaining significant market share. With number of chemotherapy drugs in pipeline, the industry should witness considerable growth over the coming years. For owners of dogs and cats stricken with cancer, one of the leading causes of death among companion animals over the age of 6, costly treatments only add to the emotional difficulties. According to Dr. David Vail, a veterinary oncologist who's also a professor at the University of Wisconsin, an initial cancer diagnosis can cost between USD 1,000 and USD 2,000. A standard course of chemotherapy costs between USD 3,000 and USD 5,000, and radiation treatments used for brain and nasal tumors run between USD 6,000 and USD 10,000. Costs vary by region and the type of cancer, among other factors.

Just as with humans, veterinarians are able to cure some types of cancers such as soft tissue sarcoma in dogs, at a cost of about USD 9,000 for the surgery and follow-up radiation treatments, according to Vail.





# SWOT Analysis

Strengths	Weaknesses
Initial focus on animal health dramatically shortens time to market (IsoPet)	Operating losses cumulating year-on-year
Trials for CE-Mark and FDA IDE demands much less costly clinical trials	RadioGel commercialization requires efforts to educate medical professionals
Direct product cost savings and work place cost efficiencies	Competition with established players
Opportunities	Threats
Additional products to leverage off current platform technology, additional markets	Delay in trials and filing with RadioGel
High unmet medical need in treatment of various cancers	Delay in roll out in major markets
Large growing markets	Failure to sign partnerships in key markets



## Financials

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For the six months ended 30 June 2017, total income was negligible. Consulting revenue is currently the only source of revenue. Consulting revenues consist of providing a company with assistance in strategic targetry services, and research into production of radiopharmaceuticals and the operations of radioisotope production facilities. Management does not anticipate that the Company will generate revenue sufficient to sustain operations until such time as the Company secures revenue-generating arrangements with respect to RadioGel™ and/or any of our other brachytherapy technologies.

In 2017H1 operating expenses decreased to USD 987,940 from USD 3,901,381. The decrease in operating expenses from 2016 to 2017 can be attributed to the decrease in professional fees expense (USD 1,631,616 for the three months ended June 30, 2016 versus USD 295,544 for the three months ended June 30, 2017); a decrease in sales and marketing expense from 2016 to 2017 (USD 135,708 for the three months ended June 30, 2016 versus USD 15,251 for the three months ended June 30, 2017); a decrease in stock options granted from 2016 to 2017 (USD 584,916 for the three months ended June 30, 2016 versus USD 27,059 for the three months ended June 30, 2017); and the decrease in general and administrative expense (USD 703,350 for the three months ended June 30, 2016 versus USD 99,090 for the three months ended June 30, 2017). The main contributors to the decrease in general and administrative expense was a decrease in loan fees (nihil for the three months ended June 30, 2017 versus USD 294,703 for the three months ended June 30, 2016); repairs and maintenance (nihil for the three months ended June 30, 2017 versus USD 222,281 for the three months ended June 30, 2016); and a decrease in research expense (USD 80,523 for the three months ended June 30, 2017 versus USD 111,304 for the three months ended June 30, 2016).



During the six months ending June 30, 2017, the Company received proceeds from the issuance of 7.5% Original Issue Discount Senior Secured Convertible Debentures ("Debentures") of USD 1,080,334 and obtained advances from shareholders of USD 137,000 that were reclassified into Debentures. The Company also assigned or exchanged USD 1,358,750 worth of Outstanding Notes into Debentures, while also reclassifying USD 120,403 worth of accrued interest to note principal. Each Debenture is convertible at the option of the holder into that number of shares of common stock equal to the outstanding principal balance, plus all accrued by unpaid interest, divided by USD 0.20. The Debentures accrue interest at a rate of 7.5% per annum and will become due and payable on or about May 9, 2018.

As of June 30, 2017, the Company has USD 369,449 cash on hand. The Company anticipates a requirement of USD 1.5 million in funds over the next twelve months to maintain current operating activities. The Company may also require up to approximately USD 4.6 million to retire outstanding debt and past due payables. As of June 30, 2017 the Company had convertible promissory notes in the aggregate principal amount of USD 3,254,130 outstanding, of which approximately USD 45,000 are currently past due and payable. Assuming the Company is successful in its sales/development effort, the Company is confident that it will be able to raise additional funds through strategic agreements or the sale of the Company's securities to either current stockholders or new investors.



## *Profit & Loss Statement*

USD mln	2016H1	2017H1
Revenues	8,108	4,054
Operating expenses	3,901,381	987,940
Operating loss	(3,901,381)	(983,886)
Interest expense	(449,733)	(1,309,090)
Net gain/(loss)	(5,637,671)	357,416
Income (Loss) before taxes	(9,988,785)	(1,953,560)
Income Taxes	0	0
Net Profit/(Loss)	(9,988,785)	(1,935,560)

## *Consolidated statement of cash flows*

USD mln	June 30th 2016H1A (6 months)	June 30th 2017H1A (6 months)
Cashflow from operating activities	(1,485,624)	(776,944)
Cash flow from investing activities	-	2,800
Cash flow from financing activities	1,306,775	1,115,703
Cash and cash equivalents at beginning of the period	179,032	27,889
Net change in cash and cash equivalents	(178,849)	341,560



## Management Capabilities

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Seasoned innovators in healthcare are building further on AMIC. The company is led by an experienced and partly renewed Board and management team, which has been responsible for AMIC moving forward and for the recent improvement of its financial structure and the launch of the Veterinary Oncology Division with RadioGel. They have a successful track record of developing, protecting and commercializing innovative scientific products and processes. AMIC has been investing in developing a team of experts that have a focus on patient outcomes and can deliver results. Its board and senior management team are highly experienced in the development and commercialization of therapies in oncology

### Management Team

#### Dr. Mike Korenko Chief Executive Officer

Dr. Korenko formerly served as Vice-President of Westinghouse, where he was tasked with overseeing 300 and 400 areas, including the Fast Flux Testing Facility (FFTF) and all engineering, safety analysis, and projects for the Hanford site. He also served as Executive Vice President of Closure for Safe Sites of Colorado at Rocky Flats. His most previous assignment was as Chief Operating Officer for Curtiss-Wright, producer of the nuclear components for all the United States submarine and aircraft carriers, as well as components for commercial nuclear power companies. Dr. Korenko has a Doctor of Science from MIT, was a NATO Postdoctoral Fellow at Oxford University, and was selected as a White House Fellow for the Department of Defense, reporting to Secretary Cap Weinberger. Dr. Korenko currently is the author of 28 patents and has received many awards, including the National Energy Resources Organization Research and Development Award, the U.S. Steelworkers Award for Excellence in Promoting Safety, and the Westinghouse Total Quality Award for Performance Manager of the Year.



### **Leonard Bruce Jolliff Chief Financial Officer**

Leonard Bruce Jolliff, joined Advanced Medical Isotope Corporation as Chief Financial Officer in 2006. For nine years prior to joining the Company, Mr. Jolliff was a sole practitioner in the role of CFO for Hire and as a Forensic Accountant, working with companies ranging from Fortune 500 to small family operations. Mr. Jolliff is a CPA and a member of the Washington Society of CPAs. He is also a Certified Fraud Examiner and a member of the Association of Certified Fraud Examiners. Mr. Jolliff has held CFO and Controller positions in an array of industries and has worked as a CPA in public practice. Currently all of Mr. Jolliff's energy is focused on supporting AMI's isotope production and securing new investments which will enable the growing company to meet its goals.

### **Dr David J. Swanberg, Chief Technology Officer**

Mr. Swanberg has over 30 years' experience in Radiochemical Processing, Medical Isotope Production, Nuclear Waste Management, Materials Science, Regulatory Affairs, and Project Management. He has worked in diverse organizations ranging from small start-up businesses to corporations with multi-billion dollar annual revenues. He previously served as Executive Vice President of Operations for IsoRay Medical Inc. managing day-to-day operations, R&D, and New Product Development. Mr. Swanberg was a co-founder of IsoRay and led the initial Cs-131 brachytherapy seed product development, FDA 510(k) submission/clearance, and NRC Sealed Source review and registration. He led the radiation dosimetry evaluations to meet American Association of Physicists in Medicine guidelines and is a current member of the AAPM. Mr. Swanberg served on the IsoRay Board of Directors and participated in several capital financing rounds totalling over USD 30M. He holds a BA in Chemistry from Bethel University (MN) and an MS in Chemical Engineering from Montana State University. He has numerous technical publications and holds several patents.



### **Dr. Donald A. Ludwig, Director of Special Projects**

Donald A. Ludwig, PhD., is Director of Special Projects for AMI. As an expert in particle accelerator applications in radiation therapy, nuclear medicine and radioisotope production Dr. Ludwig also serves as an advisor to numerous entities in the field, both domestic and foreign. Among these are the Atomic Energy of Canada, the U. S. Department of Energy Labs at Los Alamos, Berkeley, Fermi, Hanford and Oak Ridge, the Israel Atomic Energy Agency, the Australian Nuclear Science and Technology Organization, the Budker Institute of Nuclear Physics in Novosibirsk, Siberia, the Malaysian Institute of Nuclear Technology and the Bhabha Atomic Research Center in Mumbai, India. He holds advanced degrees in nuclear physics, medical physics and marketing from top tier Universities. Dr. Ludwig's endeavors for AMIC are focused on facilitating the return of clinical radioisotope production to the US, and aiding AMIC in becoming the largest provider of radioisotopes in North America.

### **Dr. Nigel R. Stevenson, Chief Science Officer**

Dr. Stevenson is AMIC's Chief Science Officer. He brings with him an impressive background in isotope production. He began his career as a research scientist at TRIUMF, the Canadian Accelerator Facility, before heading up the Isotope Production and Applied Technology group at TRIUMF responsible for the production of a wide variety of radioactive medical isotopes for Nordion in addition to specialized isotope production technology. In 1999 he became the V.P. of Isotope Production and Research for Theragenics Corporation in Atlanta, GA. In this role he was responsible for installing and operating the world's largest cyclotron facility (14 machines) used to produce radiochemicals for pharmaceuticals and medical devices. He also had technical oversight of a large scale stable isotope separation facility in Oak Ridge, TN. He was appointed the Chief Operating Officer of Trace Life Sciences, before assuming his current role as Chief Operating Officer of Clear Vascular. Additionally, he is the CEO of TcNet, LLC, a company that is investigating the use of PET cyclotron systems to produce a number of additional radiochemicals.





## Competitive Landscape

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During examination of comparable companies, we looked at medical device companies that have radiology therapy products in cancer. Companies like Sirtex, Oncosil Medical, Oncura, Isoray, Elekta and BTG. As AMIC aims to sell its product first on the veterinary market for cancer therapy for cats and dogs, we also took into account various animal health companies that have cancer products in development or already on the market. As mentioned before, the market potential for animal cancer therapy is considerable and growing fast.

### *Accuray (ARAY)*

Accuray is a radiation oncology company. The Company develops, manufactures, sells and supports treatment solutions. Its suite of products includes the CyberKnife Systems and the TomoTherapy Systems. Its technologies, the CyberKnife and TomoTherapy Systems, are designed to deliver treatments, including radiosurgery, stereotactic body radiation therapy, intensity modulated radiation therapy (IMRT), image guided radiation therapy (IGRT) and adaptive radiation therapy. Its principal radiosurgery products, the CyberKnife Systems are robotic full-body radiosurgery system designed to treat tumors anywhere in the body non-invasively, which include the CyberKnife M6 Series with configuration options of fixed collimators plus iris variable aperture collimator (FI), fixed collimators plus the InCise MLC (FM) and fixed collimators plus iris variable aperture collimator and the InCise MLC (FIM). The TomoTherapy Systems include the TomoTherapy H Series with configuration options of TomoH, TomoHD and TomoHDA. The Company has operations in Americas, Europe, Middle East, India, Africa and Japan. The CyberKnife Systems are robotic systems that deliver stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) and are used to treat multiple types of cancer and tumors throughout the body. The CyberKnife Systems track, detect and correct tumor and patient movement in real-time during the procedure. Treatment with the CyberKnife Systems requires no anesthesia, and can be performed



in one to five staged treatment sessions on an outpatient basis. The CyberKnife Systems deliver treatments for intra- and extra-cranial disease sites throughout the body, including prostate, lung, brain, spine, liver, pancreas and kidney. The CyberKnife M6 Series System is available with the InCise multi-leaf collimator (InCise MLC), which is available on a robotic platform. Its configurations of CyberKnife Systems include the CyberKnife M6 Series with configurations of FI, FM and FIM and CyberKnife VSI System. The CyberKnife M6 Series system includes disease-specific tracking and treatment delivery solutions for brain, spine, lung and prostate tumors, treatment speed improvements and options to configure the treatment room. The CyberKnife VSI System comes with fixed collimators or an optional Iris collimator.

### *BTG plc (BTG.L)*

BTG plc is a specialist healthcare company. The Company operates in three business segments: Interventional Medicine (IM) (oncology, vascular and pulmonology products), Specialty Pharmaceuticals (antidote products) and Licensing (royalties from licensed assets). The Company's Interventional Medicine segment offers a portfolio of interventional medicine products that are designed to advance the treatment of liver tumors, advanced emphysema, severe blood clots and varicose veins. The Company's Specialty Pharmaceuticals segment offers a portfolio of antidote products that alleviate toxicity and treat rare conditions. The Company's Licensing segment receives royalties relating to the sales of products that are subject to intellectual property and license agreements between the Company and various partners. The Company's subsidiaries include BTG International (Holdings) Ltd, Provensis Ltd, BTG International Ltd and BTG Employee Share Schemes Ltd, among others.

### *Isoray (ISR)*

Isoray develops, manufactures and sells isotope-based medical products and devices for the treatment of cancer and other malignant diseases. The Company is engaged in treatment for all solid tumors using Cesium-131. Cesium-131 is a radioactive isotope that can be produced by the



neutron bombardment of Barium-130 (Ba-130). The brachytherapy seed form of Cesium-131 may be used in surface, interstitial and intracavity applications for tumors with known radio sensitivity. The Company's product candidate is Proxcelan Cesium-131. The Company markets the Proxcelan Cesium-131 brachytherapy seed for the treatment of prostate cancer; brain cancer; lung cancer; head and neck cancers; gynecological cancer: pelvic/abdominal cancer; colorectal cancer, and ocular melanoma. To produce the Proxcelan seed, the purified Cesium-131 isotope is adsorbed onto a ceramic core containing a gold X-ray marker. The Company also markets the GliaSite RTS for the treatment of brain cancer, such as primary and recurrent gliomas and metastatic brain tumors. GliaSite RTS is a cleared balloon catheter device. The main components included in the GliaSite RTS are the GliaSite Catheter Tray, GliaSite Access Tray, Iotrex Solidifier and either Iotrex or Cesitrex as the radiotherapy solution. The catheter tray includes a GliaSite RTS catheter, two non-coring needles, and two right anchoring clips. 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.

### *Oncosil Medical*

Oncosil Medical (ASX:OSL) is an Australia based Life Sciences company that is developing a novel therapy device that implanted locally emits cancer killing radiation into a tumor, called OncoSil™. The therapy showed favorable results in four Phase II clinical trials in pancreatic and primary liver cancer and the company has recently filed for CE Mark approval that is expected to be announced in early 2017. The CE Mark is required to market and sell OncoSil™ in the EU. The OncoSil™ therapy is an example of brachytherapy. The device consists of a mixture of very small particles of silicon and phosphorus. When the particles are placed in a nuclear reactor for ten days, the phosphorus becomes radioactive. That radioactivity is emitted as beta particles, which only travel about one centimeter through tissues



### *Sirtex (SRX.AX)*

Sirtex Medical Limited is an Australia-based healthcare and medical device company, which manufactures and distributes liver cancer treatments utilizing small particle technology. The Company's segments are based on the regional markets it operates, which include Asia Pacific, The Americas, and Europe, the Middle East and Africa (EMEA). The Company's lead product is a focused radiation therapy known as SIR-Spheres Y-90 resin microspheres, which is a radioactive treatment for liver cancer. The treatment is called Selective Internal Radiation Therapy (SIRT) and consists of a minimally invasive surgical procedure performed by an interventional radiologist. The SIR-Spheres microspheres lodge in the small blood vessels of the tumor where they destroy it from the inside over a short period while sparing the surrounding healthy tissue. It is available in more than 40 countries and over 900 hospitals. The Company has manufacturing and operations in the United States, Germany and Singapore.

### *AB Science (AB.PA)*

AB Science is a pharmaceutical company specializing in the research, development and commercialization of protein kinase inhibitors (PKIs), a class of targeted proteins whose action are key in signaling pathways within cells. Its programs target only diseases with high unmet medical needs, often lethal with short term survival or rare or refractory to previous line of treatment in cancers, inflammatory diseases, and central nervous system diseases, both in humans and animal health. Its lead program Masitinib has been registered in the treatment of canine mast cell tumors, the most common cutaneous tumors in dogs, accounting for between 7 and 21% of all canine tumors. In a randomized placebo-controlled Phase 3 clinical trial, 202 dogs of different breeds were treated with either masitinib (12.5mg/kg) or placebo. This study demonstrated that masitinib is safe and effective in the treatment of dogs with grade II or grade III cutaneous mast cell tumors. In dogs with non-resectable mast cell tumors, masitinib was superior to placebo in terms of time to tumor progression (median of 173 days versus 75 days for placebo,  $p=0.001$ ), and overall survival time



(median of 617 days versus 322 days for placebo,  $p=0.078$ ).

### *Aratana Therapeutics (PETX)*

Aratana Therapeutics is a pet therapeutics company focused on licensing, developing and commercializing innovative therapeutics for dogs and cats. Aratana believes that it can leverage the investment in the human biopharmaceutical industry to bring therapeutics to dogs and cats in a capital and time efficient manner. The Company's pipeline includes therapeutic candidates for the potential treatment of pain, inappetence, viral diseases, allergy, cancer and other serious medical conditions.

### *Kindred Biosciences (KIN)*

Kindred Biosciences is a pre-commercialization biopharmaceutical company focused on saving and improving the lives of pets. Its mission is to bring to pets the same kinds of safe and effective medicines that human family members enjoy. The Company's strategy is to identify compounds and targets that have already demonstrated safety and efficacy in humans and to develop therapeutics based on these validated compounds and targets for dogs, cats and horses. The Company has a deep pipeline of drugs and biologics in development for animal-use indications across many therapeutic classes.

### *Oasmia Pharmaceutical AB (OASM.ST)*

Oasmia Pharmaceutical AB is a Sweden-based pharmaceutical company engaged in the field of human and veterinary oncology. The Company's activities are divided into two segments: Human Health and Animal Health. The Human Health segment specializes in ovarian and breast cancer. The Animal Health area focuses on developing cancer treatments for dogs. Its drugs portfolio comprises six candidates: Paclical, Doxophos, Docecal and OAS-19, which are implemented in human treatment, as well as Paccal Vet-CA1 and Doxophos Vet, introduced in cancer in dogs. The



Company's medicines are based on the patented XR-17 excipient, which forms micelles with water-soluble substances. Furthermore, It cooperates with Abbott Laboratories, Pharmasintez, Nippon Zenyaku Kogyo and Medison Pharma. The Company is a parent of Oasmia Global Supplies AB and Oasmia Animal Health AB.



## Appendix: Filing Procedure Animal Health

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The development, approval and sale of animal health products are governed by the laws and regulations of each country in which the company intends to sell its products.

### *United States*

Three federal regulatory agencies regulate the health aspects of animal health products in the United States: the FDA; the United States Department of Agriculture, or the USDA; and the Environmental Protection Agency, or the EPA. The CVM at the FDA regulates animal pharmaceuticals under the Food, Drug and Cosmetics Act. The USDA Center for Veterinary Biologics regulates veterinary vaccines and some biologics pursuant to the Virus, Serum, Toxin Act. The EPA regulates veterinary pesticides under the Federal Insecticide, Fungicide and Rodenticide Act. Many topical products used for treatment of flea and tick infestations are regulated by the EPA.

All of the future product candidates that are animal pharmaceuticals, will be regulated by the CVM. Manufacturers of animal health pharmaceuticals must show their products to be safe, effective and produced by a consistent method of manufacture. The CVM's basis for approving a drug application is documented in a Freedom of Information Summary. The company will be required to conduct post-approval monitoring of products and to submit reports of product quality defects, adverse events or unexpected results to the CVM's Surveillance and Compliance group.

### *European Union*

The European Medicines Agency, or the EMA, regulates the scientific evaluation of medicines developed by pharmaceutical companies for use in the European Union, or the EU. Its veterinary review section is distinct from the review section for human drugs. The Committee for Medicinal Products for Veterinary Use, or CVMP, is responsible for scientific review of the submissions for animal pharmaceuticals and vaccines but the EMA makes the final decision on the approval of products. Once a centralized marketing authorization is granted by the EMA, it is valid in all EU and European Economic Area European Free Trade Association states. In general, the requirements for regulatory approval of an animal health product in the EU are similar to those in the United States, requiring demonstrated evidence of purity, safety, efficacy and consistency of manufacturing processes.





### *Requirements for Approval of Veterinary Pharmaceuticals for Pets*

As a condition to regulatory approval for sale of animal products, regulatory agencies worldwide require that a product to be used for pets be demonstrated to:

- be safe for the intended use in the intended species;
- have substantial evidence of effectiveness for the intended use;
- have a defined manufacturing process that ensures that the product can be made with high quality consistency; and
- be safe for humans handling the product and for the environment.

### **Safety**

To determine that a new veterinary drug is safe for use, regulatory bodies will require us to provide data from a safety study generated in laboratory cats and dogs tested at doses higher than the intended label dose, over a period of time determined by the intended length of dosing of the product. In the case of the CVM, the design and review of the safety study and the study protocol are completed prior to initiation of the study to help assure that the data generated will meet FDA requirements. These studies are conducted under rigorous quality control, including GLP, to assure integrity of the data. They are designed to clearly define a safety margin, identify any potential safety concerns, and establish a safe dose for the product. This dose and effectiveness is then evaluated in the pivotal field effectiveness study where the product is studied in the animal patient population in which the product is intended to be used. Field safety data, obtained in a variety of breeds and animals kept under various conditions, are evaluated to assure that the product will be safe in the target population. Safety studies are governed by regulations and regulatory pronouncements that provide the parameters of required safety studies and are utilized by regulatory bodies in the United States, the European Union and Japan.

### **Effectiveness**

Early pilot studies may be done in laboratory cats or dogs to establish effectiveness and the dose range for each product. Data on how well the drug is absorbed when dosed by different routes and the relationship of the dose to the effectiveness are studied. When an effective dose is established, a study protocol to test the product in real world conditions is developed prior to beginning the study. In the case of the CVM, the pivotal effectiveness field study protocol is submitted for review and concurrence prior to study initiation, to help assure that the data



generated will meet requirements. The pivotal field effectiveness study must be conducted with the formulation of the product that is intended to be commercialized, and is a multi-site, randomized, controlled study, generally with a placebo control. To reduce bias in the study, individuals doing the assessment are not told whether the subject is in the group receiving the treatment being tested or the placebo group. In both the United States and the European Union, the number of patients enrolled in the pivotal field effectiveness studies is required to be approximately 100 to 150 animal subjects treated with the test product and a comparable number of subjects in the control group that receive the placebo. In many cases, a pivotal field study may be designed with clinical sites in both the European Union and the United States, and this single study may satisfy regulatory requirements in both the European Union and the United States.

### **Chemistry, Manufacturing and Controls, or CMC**

To assure that the product can be manufactured consistently, regulatory agencies will require us to provide documentation of the process by which the API is made and the controls applicable to that process that assure the API and the formulation of the final commercial product meet certain criteria, including purity and stability. After a product is approved, we will be required to communicate with the regulatory bodies any changes in the procedures or manufacturing site. Both API and commercial formulations are required to be manufactured at facilities that practice cGMP.

### **Environmental and Human Safety**

AMIC will not be required under United States law to provide an environment impact statement for products currently in development if the products are given at the home of the pet's owner or in a veterinary hospital. If products might result in some type of environmental exposure or release, the environmental impact must be assessed. For approval in the EU, a risk assessment for potential human exposure will be required.

### *Regulatory Process at the FDA*

To begin the development process for its animal products in the United States, the company needs to establish an Investigational New Animal Drug, or INAD, file with the CVM. It will then hold a pre-development meeting with the CVM to reach a general agreement on the plans for providing the data necessary to fulfill requirements for an NADA. During development, we will submit pivotal protocols to the CVM for review and concurrence prior to conducting the required studies. The company will gather and submit data on manufacturing, safety and effectiveness to the CVM for review, and this review will be conducted according to timelines specified in the Animal Drug User Fee Act. Once all data have been submitted and reviewed for each technical section – safety,



effectiveness and CMC – the CVM will issue us a technical section complete letter as each section review is completed, and when the three letters have been issued, the company will compile a draft of the Freedom of Information Summary, the proposed labeling, and all other relevant information, and submit these as an administrative NADA for CVM review. Generally, if there are no deficiencies in the submission, the NADA will be issued within four to six months after submission of the administrative NADA. After approval, the company will be required to collect reports of adverse events and submit them on a regular basis to the CVM.



*Analyst: Marcel Wijma MSc*

*Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoek Research (VLR) to SNS Securities in 2006, he established an award winning analyst team in biotech/life sciences at SNS Securities. In 2009, Marcel was awarded by Financial Times/Starmine as being one of the Top-3 biotech analysts in Europe. Later that year, Marcel purchased VLR from SNS Securities after which the company was reconstituted. At VLR, he leads the professional VLR research organisation, which is augmented by selected external financial researchers with a specialisation in Life Sciences. Mr. Wijma has a Masters degree in Financial Economics from Erasmus University in Rotterdam.*

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