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Now to highlight the hard work of the Value Initiative Domains, with the rapid growth of Radiopharmaceuticals, our work in R&D is particularly exciting. From the R&D initiative, under Dr. Richard Wahl’s SNMMI Presidential leadership, we launched the Mars Shot Research Fund Continued on page 8. See Innovating Our Way to Mars

Dosimetry in Radiopharmaceutical Therapy, Joe O'Donoghue, Pat Zanonico, John Humm, Adam Kesner. https://jnm.snmjournals.org/content/63/10/1467


Innovating Our Way to Mars

SATOSHI MINOSHIMA, MD, PHD; VALUE INITIATIVE BOARD CHAIR

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Pursuing innovative cancer treatment

Shorter range, higher energy transfer: The unique properties of actinium-225 (Ac-225) make it the focus of many cancer clinical trials today. But a critical shortage of the isotope limits the number of trials possible. TerraPower Isotopes® and Cardinal Health™ Nuclear & Precision Health Solutions are dedicated to changing that — collaborating to help advance the next generation of cancer treatment by increasing the Ac-225 supply for further research.

The barrier to expanding research

The original source of Ac-225 was the U.S. Department of Energy (DOE), which provided a sufficient amount for the initial, basic research being conducted at the time. Ac-225 was obtained from thorium-229 (Th-229), a byproduct of the uranium-233 (U-233) left over from the production of atomic weapons in the 1950s and 1960s. As a result, the supply was very limited.

As demand from radiopharmaceutical companies for Phase I clinical trial research increased, the need for Ac-225 surpassed the capabilities of the DOE's original production method. Yet the requests kept pouring into the DOE. The shortage was holding back research. According to an article published by The Journal of Nuclear Medicine, "The availability of α-emitters has slowed the successful development of radiopharmaceuticals for targeted alpha therapies (TAT)."

The DOE simply couldn't make enough Ac-225 to meet demand, because the supply of Th-229 was so limited. That led to the DOE creating an alternative production method, using a large particle accelerator to bombard Th-232 with protons. Because Th-232 is abundant in nature, the DOE now had a sustainable source for producing Ac-225.

While this method increases the supply, a byproduct is Ac-227 — which has a half-life of 21.7 years, compared to only 9.9 days for Ac-225. The long half-life of Ac-227 can create challenges for pharmaceutical companies and healthcare providers involving licensing, radiation safety protocols, and storage and handling. While the Ac-225 produced by this method has the Ac-227 impurity, pharmaceutical companies have few other viable options.

Creating the solution

How could more Ac-225 be produced without the potential for contamination from Ac-227? "We were aware that the stockpile of U-233 stored at DOE's Oak Ridge National Laboratory contained a sizeable quantity of Th-229. DOE's U-233 disposition contractor, Isotek Systems, LLC, was tasked to down blend the U-233 along with the Th-229. Working with the DOE, TerraPower and Isotek jointly stepped-in with a strategy that would solve the complicated and costly challenge of Th-229 extraction and save taxpayers a significant sum, while also providing the Th-229 needed to continuously produce Ac-225,” said Scott Claunch, President, TerraPower Isotopes.

With a clean supply of Th-229 secured, TerraPower Isotopes® sought the right strategic relationship to commercialize the solution. Speed to market is essential for creating an Ac-225 product without the Ac-227

"There are over 15 Ac-225 clinical trials in the U.S. currently, and clinical trials are taking place in multiple other countries, such as Germany, South Africa and India. There would be more trials, studying different types of cancer, if more Ac-225 was available. The current annual supply worldwide is under two curies. We need significantly more to sustain and create more clinical trials.”

— Olga Koper, Ph.D.
Senior Director of Business Development
Cardinal Health™ Nuclear & Precision Health Solutions
Tell me a little bit about your background, why you chose to become the Chief Medical Officer of Curium.

I’m a medical doctor and clinical pharmacologist by background, with over 25 years of professional experience in the pharmaceutical industry. I joined Curium as Chief Medical Officer in late 2021 – it is a great honor for me to join Curium – the world’s leading nuclear medicine company that is redefining the experience of cancer by improving the way cancer is diagnosed and treated. I was attracted to Curium because of its steadfast focus on providing life-changing diagnostics and treatment to millions of patients around the world, with recent successful clinical developments in nuclear medicine with radio-ligand diagnostic and therapeutic compounds in oncology to target different cancers.

This is a very exciting time for nuclear medicine and oncology in particular, and Curium is committed to continuous innovation in research and development. We are focused on what is important for improving the life of patients and their families. I’m proud to be a part of a company that is making a difference in disease diagnosis and treatment, as well as helping and supporting health care professionals in their diagnostic and treatment efforts every day.

Another very important aspect that attracted me to join Curium is that across research, development, and manufacturing functions, to name just a few, everyone is highly engaged, highly motivated, and extremely proud of their work to improve and save lives. The internal culture that values trust, respect, and personal development is what makes Curium unique – and I feel honored and proud to have an opportunity to contribute to this environment and be a part of Curium.

Tell me more about your experience at Curium

My experience at Curium so far has been incredible. The company’s legacy in developing and providing diagnostic imaging products world-wide, and the recent decision to make a much broader impact on patients by developing different new radioligand diagnostic and radioligand therapeutic compounds makes this an exciting time to be a part of Curium. It is this redefined purpose that is focusing everyone’s efforts at the company, with everyone committed to continuous innovation to redefine the experience of cancer through our trusted legacy in nuclear medicine. I am now an integral member of the Curium family, and I am honored to have an opportunity together with my team to contribute to Curium’s mission and purpose.

So what I hear you saying is that they have a culture that’s very supportive of its employees and they’re on the cutting edge of nuclear medicine with the history and experience and in the domain. Tell me more about your perspective on nuclear medicine innovations.

Innovations in nuclear medicine have been tremendously successful in the last few years, resulting in several new radio-diagnostic and radio-therapeutic products that have improved quality of life and saved patients’ lives. For oncology in particular, the radioligand diagnostic and therapeutic products are becoming game changers in both diagnosis and treatment of different tumor types – such as neuroendocrine tumors and prostate cancer. With new targets eligible for radioligand diagnosis and treatment of other radio-sensitive tumor types, over the next few years, we expect to see nuclear medicine and oncology having more radioligand diagnostic and therapeutic compounds developed and approved.

The current scientific and clinical development successes in nuclear medicine have broadened the strong collaboration of nuclear medicine, radiology departments,
Heart Failure Society Data Presented Shows 55% Shorter Length of Stay, 56% Lower Readmissions, and 86% Lower Heart Failure Mortality Utilizing Blood Volume Analysis (HSA-I131)

BY DAXOR, A SNMMI VALUE INITIATIVE PRINCIPAL MEMBER

Hospital systems and practitioners are looking for solutions which improve quality metrics, outcomes, reduce costs, and better the lives of patients. Blood volume analysis (BVA) applied as an early diagnostic provides significant value for providers and informs clinicians with critical information to manage and treat volume derangements, so patients get out of the hospital faster and have better results in terms of mortality and readmission.

Daxor’s innovative BVA-100® (Blood Volume Analyzer) utilizing HSA-I131 is the only diagnostic blood test cleared by the FDA to provide safe, 98% accurate, objective quantification of total intravascular blood, red blood cell and plasma volume compared to patient-specific norms. The test is based on the indicator dilution technique, the gold standard methodology for blood volume measurement and is administered at the bedside and sent to the lab to be processed. Today, BVA-100 tests are routinely performed for both inpatient and outpatient care with reimbursement by both public and private insurers. (Figures 1 & 2)

New data on the benefits utilizing BVA were presented at this year’s Heart Failure Society Meeting from key academic and clinical centers including Mayo Clinic and Duke Heart. Two studies addressed what hospital systems and practitioners are looking for that BVA technology addresses head-on - readmissions, mortality, and optimal resource use.

The study titled “Length of Stay After Blood Volume Analysis in Hospitalized Heart Failure” compared both hospital admission and discharge dates, allowing the calculation of pre- and post-BVA length of stay (LOS) for all patients. Those who received BVA-guided treatment on the day of admission to the hospital had a highly significant

Continued on page 11. See Heart Failure Society Data.
Efficient Patient Throughput Performing Cardiac PET Myocardial Perfusion Imaging with N-13 Ammonia in an Outpatient Office Setting: A Customer Experience

APRIL MANN, MBA, CNMT, NCT, RT(N), FSNM-TS, VP, CLINICAL DEVELOPMENT, IONETIX CORPORATION

Cardiac Positron Emission Tomography (PET) Myocardial Perfusion Imaging (MPI) has proven to be a powerful first line non-invasive imaging tool available to assess the extent and severity of coronary artery disease in patients with known/ documented as well as unknown disease. In addition, it provides the ability to perform myocardial blood flow (MBF) and reserve (MBFR) of the entire coronary circulation which has been demonstrated to be useful in the assessment of microvascular and triple vessel disease. The demand for patient access to Cardiac PET MPI continues to increase, and since 2012, there has been demonstrated growth in the physician office setting. (193% from 2010 to 2019). N-13 ammonia has the highest extraction and retention rates of the currently available FDA approved tracers, extraction near 100% at stress and rest, 0.95 – 0.99 and retention 0.50 – 0.90, respectively. In addition, it also has a high spatial and contrast resolution. These properties provide consistently high-quality diagnostic studies regardless of patient size and gender and more reliable MBF quantitation. However, until recently N-13 ammonia was not practical for use in the office setting or higher volume

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**Table 1:** Examples of standard and stacked rest/stress dose ordering for N13 ammonia to be used for stress/rest and stacked rest then stress Cardiac PET protocols at CIRA Miami, Florida.

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Continued on page 13. See Efficient Patient Throughput Performing Cardiac PET Myocardial Perfusion Imaging.
Theranostics is a popular buzzword in nuclear medicine practice today, but it is far from being new. This combination radiodiagnostic and radiotherapeutic approach to patient management has been utilized by physicians for nearly 100 years. It has resurfaced over the past decade, as a renewed topic of interest, due to advancements in the fields of radiochemistry, medical physics, technology, and informatics, as well as isotope production. Fortunately, the combined progress made in these areas has resulted in the renaissance of a much more precise and revolutionary approach to patient management.

We at ITM understand the clinical value of this combination of imaging and therapy for patients and have been dedicated to the field since our inception, in 2004. Our headquarters neighbors the Technical University of Munich (TUM) and its FRMII reactor where the story of ITM was born. This knowledge-rich environment combined with our technical expertise allowed us to establish the first industry-scaled production line for non-carrier-added Lutetium-177 (n.c.a. Lu-177). Together, these factors bolster the fact that ITM talent and resources are truly the best industry has to offer and has allowed us to more than quadruple our production over the last 5 years to meet the growing needs of the theranostic marketplace.

Since 2004, we have grown exponentially, building a solid foundation and securing significant funding to ensure the dependability and sustainability of medical isotopes today and the growth of the market into the future. Specific examples of this include the recent announcement of an international collaboration between Bruce Power, Isogen, and ITM. Together we were fortunate to be the first to use the Isotope Production System (IPS) that irradiates targets to produce Lu-177 and is now equipped for commercial, industrial-scale production. Additionally, ITM will receive exclusive access to this new irradiation service, further expanding our capabilities of producing high-quality isotopes on a large scale. More recently, we completed the expansion of a new production line for our n.c.a. Lu-177 at our facility near Munich. This extension will allow us, once again, to multiply our production capacity to exceed the growing patient and physician's demand and further guarantee our uninterrupted supply of n.c.a. Lu-177 to our global partners and hospitals worldwide.

However, unleashing the full potential of theranostics requires the selection of the right pairing of therapeutic and diagnostic radionuclides. We recognize that there is not a single isotope that dominates either diagnostic or therapeutic applications and that the choice for the right pairing is dependent on several factors. Consequently, we continue to investigate different pairings, conduct our own research and monitor ongoing clinical research to make certain our future theranostic products address the unmet needs of patients.

As of today, we have identified the pairing of Gallium-68 for diagnostics and Lutetium-177 & Actinium-225 for therapy as the ideal pairing, based on our expertise, the industrial scale production capacity of these isotopes, and the clinical evidence.
15O-water myocardial perfusion imaging: a practical approach to simplifying the gold standard for approved clinical use

BY HENDRIK HARMS, PHD & MARK LUBBERINK, PHD, MEDTRACE PHARMA, A SNMMI VALUE INITIATIVE PRINCIPAL MEMBER

15O-water positron emission tomography (PET) is widely considered the scientific gold standard for quantification of myocardial blood flow (MBF). It has been used for the technical validation of what is now the invasive gold standard, invasive pressure measurements (De Bruyne et al Circulation 1994), as well as to validate MBF quantification with SPECT (Itô et al EJNMMI 2003) or cardiac MRI (Tomiyama et al JMRI 2015). It has shown excellent diagnostic accuracy when compared to the invasive gold standard, outperforming both SPECT and CT angiography in the PACIFIC trial (Danad et al JAMA Cardiol. 2017).

Despite this, 15O-water PET has seen mainly research use and is not FDA approved for clinical use. One reason for this is that 15O-water has historically been challenging to use. It requires an on-site cyclotron to produce 15O and a radiochemistry facility and chemist to produce 15O-water. As 15O-water behaves exactly the same as regular water and is not retained in the myocardial wall, late uptake images do not show any contrast between the heart muscle and the blood pool, and dedicated software is required to visualize MBF. Any industry partners interested in bringing 15O-water to market had to provide both an improved and automated synthesis and analysis approach, which makes 15O-water commercially challenging.

MedTrace Pharma A/S is a Danish company that aims to make 15O-water practically available. It currently has an automated manufacturing device under Phase 3 investigation (https://clinicaltrials.gov/ct2/show/NCT05134012) and is developing analytical software, aQuant. Its automated manufacturing device is in use clinically at Aarhus University Hospital in Denmark under regulatory exemption, where it has allowed a high patient throughput similar to that achievable with 82Rb (Hansen et al J Nucl Med 2021). As used under the regulatory exemption in Denmark, a rest and stress scan can be completed within 25 minutes, potentially allowing for more than 16 patients to be scanned during an 8-hour day.

The key to working with 15O-water is to convert the images of 15O-water radioactivity concentration into contrast-rich images of quantitative MBF. The aQuant software under development is unique in that it has the ability to segment the arterial and venous blood pools first, and the segmentation of the left ventricular wall is done later. The blood pool segmentation is fully automated and identifies all the cavities of the heart and the large vessels with full reproducibility. A three-dimensional display of these regions, presented to the user for confirmation, shows a region including the venous side of the heart and a region including the arterial side of the heart.

After confirmation, the segmented blood pool is used to generate quantitative images showing MBF instead of radioactivity concentrations, and the original 15O-water images are discarded. The MBF images are then automatically rotated to the standard cardiac view and segmented as is standard for other nuclear MPI techniques. The clinician is finally presented with the rotated images to allow for visual inspection of the MBF distribution. In addition, quantitative polar maps and the MBF values of the standard 17 segments of the heart are displayed, and regions with abnormal MBF values are automatically highlighted. As currently being developed, it is expected that the entire analysis

Figure 1. Prototype of the investigational automated 15O-water device (image on the left: A). As currently being investigated, it is placed adjacent to the scanner (B) and connected directly to a cyclotron (C), and is being studied to generate and inject well-calibrated doses under GMP conditions on-demand by the technologist (D).

(MSRF) to raise monies for innovative nuclear medicine research. In addition to the MSRF, which has raised over $3 million to date, we have an MSRF Study Section which will review full grant proposal applications and make funding recommendations to the Mars Shot Awards Committee. In addition, other R&D work includes:

Research and Discovery Initiatives
- Optimizing Readiness for Increasing Demand for Clinical RPT, SNMMI Designated Radiopharmaceutical Therapy Centers of Excellence. SNMMI’s Designated Centers of Excellence Program has launched with 48 applications received. To date, 21 comprehensive, 8 clinical, and 3 basic centers of excellence have been approved.

- Optimizing Readiness for Increasing Demand for RPT Clinical Trials, SNMMI RPT Dosimetry Certificate Program. SNMMI is launching a RPT Dosimetry Certificate for physicians, physicists, and technologists. The program will include didactic curriculum, online lectures, nuclear medicine and radiation oncology and practicums with on-site supervised and independent cases.

- Educational Initiatives for New Radiopharmaceuticals. SNMMI continues to create a library of online reader training modules for new radiopharmaceuticals. The modules consist of didactic training components including information on the molecule, patient preparation, dosing, imaging, and interpretation, followed by expert-led actual case

Radiopharmaceutical Therapy Centers of Excellence

**Approved Clinical Sites**
- ChristianaCare
- Excel Diagnostics and Nuclear Oncology Center
- Hoag Memorial Hospital Presbyterian
- Kettering Health Main Campus
- Northwestern Memorial Hospital
- ARA Theranostics Center
- St. Luke’s University Health Network
- Northwell Health

**Basic Therapy Centers**
- Beaumont Hospital Royal Oak
- Riley-Triple Cancer Center at Samsun Clinic
- Highlands Oncology Group

**Approved Comprehensive Sites**
- Stanford University - Stanford HealthCare
- Dana-Farber /Brigham and Women's Cancer Center
- Memorial Sloan Kettering Cancer Center
- SSM Saint Louis University Hospital
- M Health Fairview University of Minnesota Medical Center - East Bank Hospital
- The Ohio State University Wexner Medical Center - The James Hospital and Solove Research Institute
- Ahmanson Translational Theranostics Division, David Geffen School of Medicine at UCLA, UCLA Health Medical Center
- Duke University Health
- Emory University Hospital
- MD Anderson Cancer Center
- University of Pittsburgh Medical Center (UPMC)
- University of California, San Francisco
- Mayo Clinic
- Mount Sinai Health System
- University of Iowa
- University of Colorado Anschutz Medical Center
- Medstar Georgetown University Hospital
- University of Wisconsin - Madison
- UT Southwestern Medical Center
- Oregon Health & Science University
- New York-Presbyterian Well Cornell

(Continued on page 9. See Satoshi.)
reviews. The training is also offered in person with each participant reviewing full DICOM cases on an iPad, facilitated by an expert. Coming soon: an image library of amyloid cases with clinical background and findings in a fully functional image viewing and analysis software program.

Our ongoing efforts to raise awareness continue to gain traction through our Outreach program:

**Outreach Initiatives**

- **Patient Education & Advocacy.** SNMMI is working to deepen its already strong ties with the members of its Patient Advocacy Advisory Board (PAAB). Beginning in July, SNMMI leadership began participating directly in the group’s month calls to engage in a dialog and receive patient input and feedback on the Society’s initiatives and work products. SNMMI also has reached out to several PAAB-member groups to inquire about the possibility of adding nuclear medicine physician participation on their medical/scientific advisory boards. In addition, the Society continues to offer patient education through webinars, videos, factsheets, and other resources at www.discovermi.org, as well as in-person events such as Patient Education Day, held each year in conjunction with the SNMMI Annual Meeting, and Capitol Hill Days.

- **Outreach to Referring Physicians.** SNMMI LIVE Roadshows are back, providing multi-disciplinary CME education for referring physician. We’ve held a total of eight roadshows in 2022 drawing more than 400 attendees, on the topics of PSMA for prostate cancer imaging and therapy and movement disorder diagnosis. In addition, the Society has held outreach webinars on PSMA and Molecular Breast Imaging and is embarking on a new “Case of the Month” video series for the UroToday website.

- **Collaboration with other Societies.** SNMMI has submitted numerous proposals to present at societal meetings. Among the proposal acceptances are: 2022 Pediatric Endocrine Society (200+ attendees); NANETS (100+ attendees); the American Academy of Orthopaedic Surgeons (March 2023); and the American Association of Clinical Endocrinology (May 2023). In addition, the Society has provided several satellite symposia at relevant meetings, including the 2022 and 2023 San Antonio Breast Cancer Symposium, the 2022 ASCO-GI Cancers Symposium, and the 2022 American Urological Association Annual Meeting.

**Advocacy Initiatives**

As always, Advocacy for the field is a top priority. Legislatively we have worked hard on The Facilitating Innovative Nuclear Diagnostics (FIND) Act, federal research funding, CMS, FDA, coverage from the Insurance/RBM companies, and radiopharmaceutical supply issues. Highlights from our work include:

- **The Facilitating Innovative Nuclear Diagnostics (FIND) Act.** We currently have 39 co-sponsors in the House and 4 co-sponsors in the Senate, and SNMMI continues to host virtual meetings with congressional offices in the House and Senate. The Coalition is laying the foundation to attach the legislation to a larger “must pass” bill before Congress adjourns and simultaneously, also examining new regulatory options to present to CMS.

- **Regulatory Efforts: FDA.** The Quality and Regulatory Compliance Task Force Chairs, Dr. Cutler and Dr. Dick, met with the FDA to discuss hosting a follow up workshop on inspection management and regulatory considerations for PET drugs. The Task Force is working on submitting comments to the FDA on Draft Guidance to Expand Remote Regulatory Assessments.

- **Denial of Coverage from Insurance/RBM.** Together with ASNC, SNMMI wrote to AETNA regarding non-coverage policy for hybrid PET/CT. AETNA reversed their
and oncology departments, leading to the creation of theranostic centers focused on radioligand therapy and designed to utilize both diagnostic and therapeutic radioactive agents. From the medical equipment and medical products perspective, these theranostic centers are becoming centers of excellence in diagnosis and treatment of oncology patients using new innovative nuclear medicine technologies.

Curium is supporting these new theranostic centers by providing specific products and radiopharmaceutical supply solutions, and we are fully dedicated to serve and fulfill the needs both in the nuclear medicine and oncology fields. We are also very closely collaborating with nuclear medicine and oncology specialists in clinical development of the new radioligand diagnostic and radioligand therapeutic compounds – with a few clinical Phase I/II and Phase III trials underway or in the planning stages.

**What are the clinical trials that you're running now and where do you see the most potential for advancements?**

We are continuously working on advancing our research and development in order to bring innovative radio-diagnostic and radio-therapeutic solutions to patients and health care professionals. The two clinical trials we have underway are focused on prostate cancer: ECLIPSE clinical Phase III trial is a multi-center, open-label, randomized trial comparing the safety and efficacy of 177Lu-PSMA I&T versus hormone therapy in patients with metastatic castration-resistant prostate cancer. This clinical trial is ongoing in the US and will be initiated soon in Europe. The second is SOLAR clinical Phase I/II trial. It is a multi-center, open-label, randomized Phase I/II study of 64Cu-PSMA I&T in patients with histologically proven metastatic prostate cancer. This trial is also ongoing in the US.

**So how would you define the difference between what other companies are doing in prostate diagnostics and therapeutics, ones that have been approved, and ones you are researching?**

Clearly, you’re using copper-64, but how else would you differentiate what you’ll be offering the market?

Because we are currently investigating these drugs, I’m not able to speak to how they compare to approved products already on the market. What I can tell you is that we are excited to be working on new potential treatment options that could give physicians and patients another choice when it comes to the way they manage disease. I can also say that we believe that these trials are an important milestone, and that they show Curium’s commitment to redefining the experience of cancer. As you noted, we are using copper-64 in our SOLAR trial, and we hope to be able to capitalize on its 12.7-hour half-life in a way that, if the product is approved, will allow us to establish a centralized supply and provide more flexibility in scheduling diagnostic procedures – both for patients and nuclear medicine healthcare professionals.

And what else do you see advancing besides treatments for prostate cancer and neuroendocrine tumors?

With the new ligands, both small molecules, peptides, antibodies and nano-antibodies targeting different receptors – either cancer stroma or cancer cells – as well as a new radioisotope, the opportunities to successfully use the radioligand technology for developing both radio-diagnostic and radio-

therapeutic solutions in oncology are enormous. This is particularly true for expanding into other radiosensitive tumor types, such as solid and hematological ones. However, there is still a lot of work to be done in the pre-clinical as well as in the clinical research and development to move this exciting radioligand technology forward to improve quality of life and save the lives of patients suffering from different types of cancer.

Curium is committed to continue developing nuclear medicine solutions and investing further in clinical research and development in oncology.

**You are in Europe. How would you describe what’s happening in Europe versus what’s happening in the US?**

Yes, I am based in Europe, but everyone who is involved in clinical development knows that developing new compounds independently from current technologies is a global effort. There are a few minor differences in US and European regulatory processes and regulatory review timelines up to approval, but in general they are very similar. From a nuclear medicine perspective, establishing theranostic centers in Europe may have started slightly earlier than in the US, but we have seen recently in the US a growing number of theranostic centers.

**So where do you see the field in five years?**

I believe the focus in the next five years will be on bringing current clinical development in nuclear medicine to the next level. We’ll see new approved products in oncology and non-oncology fields, see more established theranostic centers in the US, Europe, China, and Japan, and see more research and development of radioligand diagnostic and therapeutic...
compounds in different tumor types – in particular in underserved tumor types that do not have established standard of care and where there is high unmet medical need.

For your Phase III prostate cancer study, it looks like you’re going to do a dosimetry sub-study?

Yes, we are conducting the dosimetry sub-study within our ECLIPSE Phase III clinical trial to determine the radiation absorbed dose in metastatic castration-resistant prostate cancer patients. This is an integral part of our clinical development program in this patient population.

Any thought to increasing the initial doses? There was some research presented at our recent annual meeting that showed that hitting the tumors with a higher dose earlier on is better than giving the same dose across the same cycles, because they are less receptive.

The subject of doses and dosing schedules is extremely interesting. There are several clinical research attempts in Phase I/II clinical development stage as standalone or in combination with standard of care targeting different doses of different radioisotopes, as well as different dose schedules between treatment cycles. I believe this clinical research will offer new opportunities to

(p < 0.001) lower total LOS than controls (2.04 vs. 4.56 days) and significantly improved outcomes (lower 30-day readmissions and 365-day mortality).

“Shorter length of hospital stay has an enormous potential for hospital cost savings as hospitals receive a single block payment under DRG rules of reimbursement. All hospital systems are rated under this metric and seeking ways to improve it is one of the reasons we have adopted BVA locally,” stated Dr. John L. Jefferies, University of Tennessee Health Science Center, Memphis, TN.

A second study titled “Heart Failure Outcomes with Volume-guided Management in An Over-65 Population” showed that this cohort of patients experienced markedly better outcomes vs. controls for 30-day readmissions (12.0% vs 27.0%, P< 0.001), 30-day mortality (2.3% vs 11.8%, P< 0.001), and 365-day mortality (5.6% vs 36.8%, P< 0.001) rates.

“Understanding the impact of treatment decisions on outcomes for the over-65 population is of relevance to U.S. healthcare, as decisions made by the Centers for Medicare & Medicaid Services regarding reimbursement, outcome-based incentives and penalties applied to health providers, and indication guidelines have enormous impact on how healthcare is provided,” said John E. Strobeck, M.D., PhD, principal investigator.

By offering the Daxor BVA-100 blood test, your nuclear medicine department can provide safe, accurate, direct blood volume measurements to help clinicians provide optimal patient care, improving outcomes and reducing duration and cost of care.

Download the poster presentations by clicking on these links:

Length of Stay After Blood Volume Analysis in Hospitalized Heart Failure
Heart Failure Outcomes With Volume-Guided Management In An Over 65 Population

To learn more about blood volume analysis visit daxor.com.
Taking all these factors into consideration, we believe that the combination of these three radiometals exceeds the potential and clinical feasibility of all other candidates. Evidence of this is clear in the multitude of ongoing clinical trials utilizing these isotopes, as well as the new FDA-approved products coming to the market in the U.S.

While we will continue to leverage our expertise in GMP-scale production of medical isotopes and apply it to other emerging combinations to ensure the clinical value of our products, our interests and expertise lie far beyond our isotope production capabilities. ITM is also developing a proprietary portfolio and growing precision oncology pipeline. These product candidates are in various stages of clinical development and address a range of cancers such as neuroendocrine tumors, glioblastoma, prostate cancer, folate receptor α positive tumors like ovarian cancer or NSCL adenocarcinoma, as well as osteosarcoma and bone metastases. Ultimately, our main objective, together with our scientific, medical and industry partners, is to significantly improve treatment outcomes and quality of life for cancer patients, while at the same time reducing side effects and improving health economics through a new generation of theranostic pairs for precision oncology.

$^{15}$O-water myocardial perfusion imaging. Continued from page 7.

Figure 2 Parametric short axis and vertical and horizontal long axis images of MBF based on a $^{15}$O-water scan. The images resemble MBF calculated for every individual pixel.

Figure 3 Example of long-axis images in end-diastole and end-systole and a 3D rendering of the largest and smallest volume based on an early $^{15}$O-water image, taken 0–45s post injection.
laboratories due to space requirements and inefficient production related to older cyclotron technology and manufacturing processes not conducive to performing more rapid imaging protocols. Ionetix Corporation has created an innovative partnership solution and combined with the compact ION-12sc® cyclotron and integrated manufacturing process makes N-13 ammonia a reliable option for higher throughput physician offices or independent diagnostic testing facilities (IDTF).

Centers for Research and Imaging of America (CIRA) located in Miami, Florida is an IDTF focused on molecular imaging procedures with an emphasis in oncology, cardiology, neurological disorders, vascular diseases, and research. The site performs approximately 15 Cardiac PET MPI with MBF procedures daily on two PET/CT systems. Imaging is performed using a standard rest/stress or stacked rest then stress protocol with N13 ammonia, low dose rest (8mCi)/high dose stress (13mCi). Image processing for perfusion and MBF/MBFR is performed with INVIA 4DM® Premium software utilizing residual subtraction. The standard rest/stress protocol is completed in 25-30 minutes.

CIRA has over 20 physician groups providing stress test supervision. The complexities of the physician coverage schedule are a key driver of protocol selection and makes efficiency a priority. The standard rest/stress protocol is performed when the physician coverage window is more flexible, and the stacked rest then stress protocol is performed when physician availability necessitates optimization of protocol times. Use of the stacked protocol allows for maximization of physician time while keeping the patient procedure time minimal. The Ionetix solution and integrated N13 ammonia manufacturing process allows for timely dose production and flexibility in protocol selection resulting in efficient patient throughput as well as physician and patient satisfaction (Figure 1).

The Ionetix solution is an innovative partnership offering clinical and operational expertise in Cardiac PET MPI with N13 ammonia. The small footprint requirement (less than 1000 square feet) of the ION-12SC® cyclotron is conducive for on-site production in all facilities, and the integrated manufacturing process allows for dose production in as little as ten minutes provided to the laboratory in a 5ml shielded syringe ready for patient injection®. The overall results are a convenient, efficient, and reliable supply of N-13 ammonia even in high patient volume laboratories and an alternative high quality PET tracer for use in these Cardiac PET Imaging programs.

REFERENCES

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**Increasing the supply of generator derived Ac-225. Continued from page 2.**

imurity. “We selected Cardinal Health because they had the end-to-end capabilities we needed for production and distribution,” Claunch said.

The collaboration of TerraPower and Cardinal Health is on a path to create 75 to 100 times more Ac-225 than was available before, without the Ac-227 impurity, for clinical trial research. The plan is for Cardinal Health to begin FDA non-Current Good Manufacturing Practices (cGMP) production by 2023 and cGMP by 2024.

For more information, please visit our website [http://cardinalhealth.com/theranostics](http://cardinalhealth.com/theranostics).

REFERENCES
Satoshi. Continued from page 9.

non-coverage after receiving our detailed letter. SNMMI SME’s met with eviCore jointly with ASNC regarding coverage of MBF and met with AIM/Anthem on coverage for PSMA PET for initial staging. Letters have been sent to eviCore, Cigna, and United Healthcare for appropriate coverage of PSMA PET.

At the 2022 Annual Meeting, VIIA committee members suggested the following Quality Practice topics: RaPTR+PLUS and RaPTR; Radiopharmaceutical Therapy Centers of Excellence; Include personalized dosimetry in the RPT Center of Excellence program; Create and provide ongoing diagnostic training; White paper best practices for radiopharmaceuticals; Color-coded system for radiopharmaceuticals; Develop pathways for oncology treatment with molecular imaging and report deviations from the pathway; MIPS Quality Measures; Define standards for drug manufacturing and image acquisition; Eliminate institutional controls for data sharing; Create a virtual mentor group for technologists. Most of these suggestions are underway. Highlights include:

- **MIPS Quality Measures.** To support the quality measures development initiative, SNMMI created a new Task Force that will work on creating innovative, practical, and comprehensive measures for the nuclear medicine specialty. SNMMI submitted two quality measures were submitted to CMS for implementation in 2024: Comparison of Somatostatin Receptor (SSTR) PET Imaging to Conventional Imaging (Computed Tomography [CT] / Magnetic Resonance Imaging [MRI]) to identify de-differentiated NET, and Somatostatin Receptor (SSTR) PET Imaging scan prior to Lutathera for patients with Neuroendocrine Tumors (NET).

SNMMI just completed a strategic plan and all the work of the VI continues to be priorities of SNMMI membership, industry partners, and other stakeholders. In 2023 and beyond, we will double down our focus on theranostics and capacity building for radiopharmaceutical therapies, increase education and outreach about nuclear medicine, advocate for physicians and non-physicians with a strong focus for advocacy of reimbursement, target hospital administrators as new stakeholders. The future is bright as the role of nuclear medicine within the healthcare economy grows.

Interview of Sakir Mutevelic MD, Chief Medical Officer. Continued from page 11.

adjust the dose, dose schedules, and even enable us to extend treatment cycles and allow radioligand therapies re-treatment tailored to specific tumor types. It is indeed an exciting time for all of us in nuclear medicine and specifically those utilizing nuclear medicine solutions in oncology.
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