NCI SBIR DEVELOPMENT CENTER

PRESENTS

WORKSHOP ON
FACILITATING THE DEVELOPMENT OF MOLECULARLY TARGETED RADIOTHERAPY

NOVEMBER 10, 2016

This hand-out contains

- Workshop Agenda
- Panelist Bio
- Attending Company Introduction
- NCI SBIR Funding Opportunities

NATIONAL CANCER INSTITUTE
SBIR
DEVELOPMENT
CENTER

WORKSHOP AGENDA

9:00 AM – 9:05 AM	**Welcome** Michael Weingarten, Director, NCI SBIR Development Center
9:05 AM – 9:15 AM	**Presentation of Radiation Research Program Vision** Dr. Vikram Bhadrasain, NCI Radiation Research Program
9:15 AM – 9:25 AM	**Introduction to Workshop Objectives** Deepa Narayanan, Program Director, NCI SBIR Development Center
9:25 AM – 10:45 AM	**Awardee Introduction** Each awardee organization will provide a quick introduction of the company/institution, technology, and current project.
10:45 AM – 11:00 AM	**BREAK**
11:00 AM – 11:45 AM	**Pre-clinical Considerations for TRT Technologies** Dr. Haleh Saber, Deputy Director, Division of Hematology Oncology Toxicology/ OHOP/CDER, FDA
11:45 AM – 12:30 PM	**Clinical Considerations for TRT Technologies** Dr. Amanda Walker, Medical Officer, Division of Oncology Products 1, CDER, FDA
12:30 PM – 1:30 PM	**LUNCH/NETWORKING**
1:30 PM – 2:15 PM	**Information about DoE's Isotope Program and Access to Isotopes** Dr. Marc Garland, Deputy Director, Department of Energy Isotope Program
2:15 PM – 2:30 PM	**BREAK**
2:30 PM – 4:30 PM	**Interactive discussion with the DOE & FDA** Moderated by Dr. Jacek Capala, NCI Radiation Research Program
4:30 PM – 4:45 PM	**Closing Remarks**

PANELIST BIO

Michael Weingarten

Director
NCI SBIR Development Center
National Cancer Institute

Michael Weingarten is the Director for the Small Business Innovation Research (SBIR) Development Center at the National Cancer Institute in Bethesda, MD. In this role, Mr. Weingarten leads a team of nine Program Directors who manage all aspects of the NCI SBIR & STTR Programs including a **portfolio of $136M** in grants and contracts annually. The SBIR & STTR programs are NCI's engine of innovation for developing and commercializing novel technologies and products to prevent, diagnose, and treat cancer.
Mr. Weingarten has implemented a set of key initiatives for optimizing the performance of the NCI SBIR Program at the NIH. These include the establishment of a new model at the NCI for managing the program – the SBIR Development Center.

Under Mr. Weingarten's leadership, the NCI SBIR Development Center has launched a range of new initiatives to facilitate the success of small businesses developing cancer-related technologies. Recent initiatives include the launch of the **NIH I-Corps™** pilot program in which teams of budding entrepreneurs engage in a hypothesis-driven approach to validate their proposed business models by conducting over 100 interviews with potential customers. Companies adjust their strategies based on direct customer feedback and analyze the information they collect to determine if there is a product/market fit. Other NCI SBIR initiatives introduced under Mr. Weingarten's leadership include the **NCI SBIR Investor Forums, the NCI SBIR Phase II Bridge Award**, and the workshop titled **Federal Resources to Accelerate Commercialization (FRAC)**. Thus far, NCI SBIR has held three investor forums that in total have facilitated the closing of investment deals with NCI-funded SBIR companies valued at over $300M. The NCI SBIR Phase II Bridge Award, which was launched in 2009, incentivizes partnerships between NIH's SBIR Phase II awardees and third-party investors and/or strategic partners to help small businesses bridge the funding gap between the end of their SBIR Phase II awards and the next round of financing needed to advance a promising cancer therapy or imaging technology.

Vikram Bhadrasain

Branch Chief
Radiation Research Program
National Cancer Institute

Dr Vikram received his medical degree from the University of Delhi and trained in radiation oncology at Memorial Sloan-Kettering Cancer Center in New York City. He subsequently served on the faculties of Memorial Sloan-Kettering, Cornell University Medical College and Mount Sinai School of Medicine. From 1992-2003 he served as Professor and University Chair of the Department of Radiation Oncology at the Albert Einstein College of Medicine and Radiation Oncologist-in-Chief at the Montefiore Medical Center in New York City.

From 2003-2006 he served on the ACGME Residency Review Committee for Radiation Oncology. He has authored over 150 scientific publications and was listed as among the 1000 'Best Doctors in America' by American Health magazine, a Reader's Digest publication.

From 2002-2006 he worked at the International Atomic Energy Agency of the United Nations in Vienna, Austria, helping to establish or upgrade cancer therapy facilities in about 100 low and middle income countries, and founded the Program of Action for Cancer Therapy (PACT). In 2005 he shared in the Nobel Peace Prize awarded to the IAEA whose contribution to global cancer control was cited by the Nobel committee.

Since 2006 he has served as Chief of the Clinical Radiation Oncology Branch at the NCI, overseeing a portfolio of clinical research grants within the Radiation Research Program as well as assisting the Cancer Therapy Evaluation Program and the Coordinating Center for Clinical Trials with NCI's cooperative clinical trials groups program. He also continues his work on improving cancer prevention and control worldwide.

Deepa Narayanan

Program Director
NCI SBIR Development Center
National Cancer Institute

Deepa Narayanan is a Program Director in the Small Business Innovation Research (SBIR) Development Center at the National Cancer Institute (NCI), where she assists small businesses in securing funding for research and development of innovative medical devices with high commercial potential for cancer diagnosis and therapeutics. Deepa has extensive experience with the research, development and commercialization of scientific and medical instrumentation and molecular imaging agents. Previously she was the Director of Clinical Data Management at Naviscan, Inc. where she managed all aspects of clinical trials including FDA-regulated multi-center clinical trials for 510(K) clearance as well as phase IV post marketing studies. Prior to Naviscan, Deepa was a Scientific Associate with the Molecular Imaging laboratory at Fox Chase Cancer Center. Deepa is a certified Clinical Data Manager and has a Master's Degree in Biomedical Engineering from the University of Virginia and a Bachelor's degree in Biomedical Engineering from University of Mumbai.

Amanda Walker

Medical Officer
Division of Oncology Products 1, CDER
Food and Drug Administration

Amanda Walker is a Radiation Oncologist and Medical Officer in Office of Hematology Oncology Products in the Center for Drug Evaluation and Research (CDER) at the FDA. She holds a joint position as Adjunct Investigator in the Radiation Oncology Branch at the NCI where she specializes in the treatment of patients with CNS malignancies. She received her Medical Degree from Tufts University School of Medicine and her Undergraduate Degree from Indiana University. She currently serves as the Radiation Oncology Liaison in the Office of Hematology Oncology Products. She has a background in both clinical and bench research and has an interest in the regulatory issues surrounding the development of radiation oncology products as well as drugs to be used in combination with external beam radiation therapy.

Haleh Saber

Deputy Director
Division of Hematology Oncology Toxicology/
OHOP/CDER, Food and Drug Administration

Dr. Saber is the Deputy Director in the Division of Hematology Oncology Toxicology (DHOT). In this role she provides leadership for day-to-day activities, coordinates scientific research, and participates in oncology guidance development. Dr. Saber has extensive industry and regulatory experience. She served as a Subject Matter Expert assisting pharmaceutical companies worldwide in nonclinical drug development and served many roles at the FDA over 12 years, starting as a primary reviewer before becoming a Supervisory Pharmacologist in DHOT. Dr. Saber is recognized nationally and internationally for her efforts in establishing acceptable approaches in first-in-human dose selection for new classes of products. She has been the recipient of multiple CDER awards. Dr. Saber received her PhD in Biochemistry from Lehigh University and conducted her post-doctoral studies at Fox Chase Cancer Center.

Marc Garland

Deputy Director
Department of Energy Isotope Program

Marc Garland is the program manager for Isotope Program Operations and the Deputy Director of the DOE Isotope Program (DOE IP). As program manager for Isotope Program Operations, he is responsible for DOE IP programmatic issues and for the National Isotope Development Center (NIDC) which manages the business activities of the DOE IP (production, sales, and distribution of isotopes) which are carried out by the National Laboratory staff that constitute the NIDC.

He received a B.S. degree in biology from the University of Washington, an M.S. degree in electrical engineering from Washington State University, and M.S. and Ph.D. degrees in nuclear engineering from the University of Maryland. He spent 18 years in nuclear facility operations and project management at the Hanford Site, was a faculty member in the nuclear engineering program at the University of South Carolina, and was at the Oak Ridge National Laboratory conducting research and development in radioisotope production, medical applications of radioisotopes, radioisotope power sources, and radiation detection and measurement before joining the DOE IP in September, 2010

Jacek Capala

Deputy Director
Division of Hematology Oncology Toxicology/
OHOP/CDER, Food and Drug Administration

Dr. Capala received his MSc in Medical Physics from Jagiellonian University, Krakow, Poland (1986), and PhD in Physical Biology from Uppsala University, Uppsala, Sweden (1991). From his experiences gained in the U.S., Dr. Capala received his DSc (docent) degree in Biomedical Radiation Sciences awarded by Uppsala University and an invitation to start a new BNCT Research Program at the Studsvik Neutron Research Laboratory in Sweden. During his time in Sweden, Dr. Capala established and led a National Consortium for mixed high- and low-LET radiation research. In addition, he coordinated two Phase II clinical trials of BNCT for GBM.

In 2004, Dr. Capala became the head of the Molecular Targeting Section, Radiation Oncology Branch of NCI Intramural Program. He initiated a multidisciplinary project to develop an individualized approach to treatment of cancer. His therapeutic strategy involved assessment of target presence and distribution in an individual patient, followed by optimized, target-specific drug delivery and early monitoring of tumor response by molecular imaging. His efforts resulted in new molecular probes for in vivo monitoring of HER2 expression in breast cancers either by PET or by near-infrared optical imaging and an US patent: Radiolabeled Affibody® Molecules. For therapy, his research team developed Affitoxin.

In 2007, Dr. Capala received the NCI Director Innovation Award and Federal Technology Transfer Award. His research accomplishments were featured in several press releases by NCI, NIH, the Society for Nuclear Medicine, and the American Association for Cancer Research, as well as articles in professional and popular journals and newspapers.

His research interests are indicated by more than 80 publications and several book chapters, including a wide spectrum of translational and clinical research from molecular imaging through targeted therapy to radiation oncology and medical physics. Dr. Jacek Capala has been a Program Director for the Division of Cancer Treatment and Diagnosis, Radiation Research Program since September 2011. His portfolio includes nanotechnology, nuclear medicine and image-guided, adaptive, and particle radiation therapy.

COMPANY INFORMATION

AKRIVIS TECHNOLOGIES, LLC

www.akrivis.com
Attendee: Joel A. BERNIAC, PhD, MBA, President, CEO & Co-Founder

Akrivis is a privately held biopharmaceutical company committed to the early detection, diagnosis and treatment of serious and life-threatening diseases based on its patented Z-TECT™ technology platform (called ADAPT™ for clinical applications). Z-TECT™ is in essence a proprietary and extremely versatile "pre-targeted carrier system" that provides key performance advantages in the following three areas: high signal amplification with high signal-to-noise ratios for (1) high sensitivity in vitro detection; and (2) high resolution in vivo imaging; and (3) pre-targeted delivery of high drug payloads specifically to targeted biomarkers, much like and Antibody-Drug Conjugate but with improved efficacy and safety profiles.

For diagnostic applications, the Z-TECT™ technology platform provides ultra-sensitive in vitro detection and high resolution in vivo imaging, with higher signal:noise ratios than competitors and most importantly without any specialized and expensive equipment since Z-TECT™ is entirely reagent-based. For therapeutic applications, the ADAPT™ technology platform provides higher efficacy (as a result of high drug payloads) and better safety (as a result of sequential targeting with less off-target drug delivery) than an ADC (Antibody-Drug Conjugate) approach.

Akrivis' focus is to expand the commercialization of its Z-TECT™-based best-in-class products for ultrasensitive in vitro detection (secondary and primary assays) and high-resolution in vivo imaging first for research-use-only (RUO) and then for clinical diagnostics. Akrivis is also engaged with pharmaceutical partners, Washington University School of Medicine, the Dana-Farber Cancer Institute and the NIH/NCI to evaluate its ADAPT™ technology platform for the sequentially targeted delivery of high payloads of chemo- and radio-therapeutic agents specifically to tumor cells.

CANCER TARGETED TECHNOLOGY

www.cancertargetedtechnology.com
Attendees: Beatrice Langton-Webster, PhD, CEO
Carolyn Anderson, PhD, Professor of Radiology, University of Pittsburgh

Cancer Targeted Technology (CTT) is a biotechnology company commercializing innovative small molecules that bind pivotal enzyme targets in cancer. CTT has created and patented a targeting scaffold that **recognizes the molecular target, Prostate Specific Membrane Antigen, with unexploited binding characteristics, making it unique among its competitors.** PSMA is an exceptional biomarker, expressed on close to 90% of prostate tumors with increased PSMA expression correlated with disease progression. Normal tissue expression is negative to low. CTT has engineered small molecule drugs to bind irreversibly to the PSMA target allowing them to stay at the tumor site and be rapidly internalized by PSMA-expressing tumor cells.

These targeting agents act as a platform to effectively and safely deliver a wide variety of diagnostic and therapeutic payloads. Along with prostate cancer, PSMA is also expressed on the new blood vessels of other solid tumors, including colon, liver, renal cell, and lung, providing a broad market for CTT's PSMA-targeted agents. ***Pipeline:*** 1. **CTT's first product is an innovative 18F-labeled PET diagnostic, CTT1057, for prostate cancer** that can be imaged within 2 hours. CTT1057 will specifically and sensitively detect cancer that has escaped from the prostate and distant metastatic disease including bone metastases with greater resolution than current standard of care. With the recent uncertainty introduced by the recommendation to drop the widely used PSA test, especially for metastatic prostate cancer, this market is wide open for new and more specific diagnostic tests.

CTT's PET agent is urgently needed to improve diagnosis and stratification of prostate cancer patients as it can be used to image both the location and extent of disease --something that all current urine and serum markers are unable to do. By affording more effective diagnosis and monitoring, imaging with CTT1057 will help inform

personalized treatment choices and regimens that can make a difference in disease progression. CTT has an approved IND and is targeting clinical trials in 2016. (Clinical Development, Phase I). 2. **CTT's targeted radiotherapeutic agent, CTT1403, will specifically deliver the radionuclide, 177Lu, to prostate cancer** with the goal of minimizing toxic side effects and more effectively treat metastatic disease. This agent could also be used against other tumors where PSMA is expressed (IND-enabling).

CELLECTAR BIOSCIENCES, INC.

www.cellectar.com
Attendee: Benjamin Titz, PhD, Senior Manager, Corporate Development and Strategy

Cellectar Biosciences, Inc., a Madison, WI-based biopharmaceutical company, is developing phospholipid drug conjugates (PDCs) designed to provide cancer-targeted delivery of diverse oncologic payloads to a broad range of cancers and cancer stem cells. Cellectar's PDC platform is based on the company's proprietary phospholipid ether analogs. These novel small-molecules have demonstrated highly selective uptake and retention in a broad range of cancers. Cellectar's PDC pipeline includes product candidates for cancer therapy and cancer diagnostic imaging.

The company's lead therapeutic PDC, CLR 131, utilizes iodine-131, a cytotoxic radioisotope, as its payload. It is currently being evaluated under an orphan drug designated Phase I clinical trial in patients with relapsed or refractory multiple myeloma. The company plans to initiate a Phase II clinical study to assess efficacy in a range of B-cell malignancies in the first half of 2017. Based upon pre-clinical and interim Phase I study data, treatment with CLR 131 provides patients with a novel approach to treating hematological diseases and may provide patients with an improvement in progression-free survival and overall quality of life.

The company is also developing PDCs for targeted delivery of chemotherapeutics such as paclitaxel (CLR 1602-PTX), a preclinical stage product candidate, and plans to expand its PDC chemotherapeutic pipeline through both in-house and collaborative R&D efforts.

EVO RX TECHNOLOGIES, INC.

www.evorxtechnologies.com
Attendee: Stephen Fiacco, CEO

EvoRx Technologies develops peptide therapeutics and radiopharmaceuticals to treat and diagnose disease with high unmet need. EvoRx uses a proprietary discovery platform to engineer EvoTides – drug like peptides that are resistant to proteolytic degradation are have antibody-like binding affinity and specificity.

Although antibodies have been used as “magic bullets” to deliver radionuclides specifically to tumors, their large sizes and long serum half-lives make them sub-optimal radiotherapy targeting agents. The large size of antibodies limits tumor penetration and speed of tumor uptake, thereby limiting access to the middle of tumors. Long serum half-lives of antibodies results in long circulation times and increased nonselective irradiation of normal organs and tissue. EvoTides are uniquely suited for use in targeted radiotherapy and have several advantages over existing approaches. First, EvoTides can clear from the body in a matter of hours, removing unbound radionuclide from circulation and decreasing nonspecific irradiation. Second, the much smaller size of EvoTides as compared with antibodies results in higher, faster tumor uptake. Third, EvoTides can be chemically synthesized under GMP conditions, and can specifically be functionalized with chelators for targeted radiotherapy, yielding a defined chemical product. Last, EvoTides incorporate these advantages while retaining antibody-like binding affinity and specificity.

We are developing a Her2-specific EvoTide for the treatment of trastuzumab and T-DM1 resistant cancers. While the successes of trastuzumab and T-DM1 have been exciting, some patients are resistant to Her2-directed therapies. Many patients resistant to anti-Her2 therapy retain Her2 receptor expression and could benefit from a Her2-directed targeted radiotherapy. Lastly, about one-third of patients who are treated with anti-Her2 therapies also develop brain metastases, and we believe that targeted radiotherapy with EvoTides can benefit this group with high unmet medical need.

HOUSTON PHARMACEUTICALS, INC.

Attendee: Rafal Zielinski., Research Scientist

Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal human malignancies with an expected 53,070 new cases and 41,780 deaths in 2016 in the US alone. This dismal prognosis is due to the fact that PDAC is highly resistant to all known anticancer therapies, it progresses with few specific symptoms, and at the time of diagnosis, it is found at an advanced stage with metastases to distant organs including liver. Thus, new efficacious therapies and compatible diagnostic agents are urgently needed.

Interleukin-13 receptor alpha 2 (IL-13RA2) is a monomeric receptor overexpressed in PDAC and other solid tumors but not in normal cells. Specifically, we and others found that IL-13RA2 is overexpressed in well over 60% of PDAC patients. Importantly, higher IL-13RA2 expression correlates with shorter survival and poor prognosis. These facts and our preliminary data strongly support development of an IL-13RA2-based theranostic platform for pancreatic cancer. In our approach we take advantage of tumor restricted expression of oncogenic form of IL-13RA2 receptor, availability of specific internalizing ligands to generate therapeutic/imaging construct that could delivery for radioactive isotope inside the cancer cell.

ICAGEN, INC.

www.icagen.com

Attendee: Douglas Krafte, Chief Scientific Officer

Icagen's technology is based on a proprietary x-ray fluorescence platform called XRpro that allows screening of large numbers of molecules in a bead-based format to identify agents which selectively bind different metals underphysiological conditions. These unique molecules can then be readily coupled to targeting vectors to direct to various cancer cells of interest. The nature of the system is modular such that the same agent may be coupled to different targeting vectors to allow the greatest flexibility. As such this platform has the potential to produce multiple new radiopharmaceutical agents with greater specificity and improved safety profiles compared to existing agents.

MODULATION THERAPEUTICS, INC.

www.modulationtherapeutics.com

Attendees: Mark L. McLaughlin, Ph.D, Executive Vice President
Lori Hazlehurst, Ph.D, President

Melanocortin 1 receptor (MC1R) is a highly specific biomarker for metastatic cutaneous and uveal melanoma. MC1R is expressed at 90% and 95% on patient tissue samples for those two diseases and its only detectable expression on normal tissues is behind the blood-brain barrier (BBB) and on monocytes. Fluorescent imaging based on the high affinity MC1R ligand (MC1RL) shows in vivo imaging at targeted tumor and no other accumulation except at the clearance organs. There is no significant permeation of the BBB and so there is no in vivo or ex vivo accumulation in the brain. We hypothesized that the high precision delivery based on MC1RL-MC1R interaction could be used to deliver and concentrate radiotherapy to cutaneous and uveal melanoma tumors and metastases with limited systemic toxicity. We had already shown that 225Ac-DOTA-MC1RL was easily prepared and that it had excellent in vitro stability in mouse, rat, and human serum. Our SBIR Phase I Contract-funded studies show that as expected there was minimal toxicity, biodistribution was only to the tumor or clearance organs, and no overt toxicity was observed upon pathology examine of the clearance organs, whereas 2 of 9 animals were cleared of tumors with a single dose of Ac-222-DOTA-MC1RL. Furthermore, in vivo efficacy has been shown against uveal melanoma tumor as well. In addition, PK and radiodosimetry studies have been completed in a Phase I contract that ends 10/21/2016

ONCOTAB, INC.

www.oncotab.com
Attendee: Rahul Puri, CEO

OncoTAb, Inc. was founded by a Mayo Clinic alumna, Dr. Pinku Mukherjee, with a mission to improve the quality of cancer care by addressing unmet cancer diagnostic and therapeutic needs. The technology platform on which these products are being developed is a patented monoclonal antibody (TAB004) that detects a tumor specific biomarker tMUC1, which is present in over 90% of breast cancer tissue. OncoTAb has a worldwide exclusive license to this technology platform.

TAB 004 was developed using tumors expressing the altered form of MUC1 (US patent #8,518,405 and #909069) and recognizes the altered glycosylated epitope within the MUC1 tandem repeat sequence. This area is accessible for antigenic detection in tMUC1 but is blocked from antigenic detection in normal tissue MUC1 by large branches of glycosylation. Importantly, TAB 004 recognizes epitopes different from those recognized by other MUC1 antibodies, and has unique complementary determinant regions (CDRs) of the heavy and light chains.

OncoTAb is using TAB004 to develop a targeted radionuclide therapy for Triple Negative Breast Cancers (TNBCs). The tumor specific nature of this newly discovered antibody makes this an ideal molecule for targeted radiotherapy applications both for TNBC patients and eventually, in patients with other types of malignancies that express this MUC1 variant. We are in the process of fully humanizing this antibody and use innovative techniques developed by investigators at Duke (Drs. Vaidyanathan and Zalutsky) to: a) test the feasibility of labeling TAB004 with radioiodine, 131I; b) evaluate the binding affinity and internalization of 131I-labeled TAB004 in TNBC cell lines; c) determine bio-distribution of the product in mice; and d) assess long-term localization and radiation dosimetry in tumor bearing mice. Next, we propose to establish the therapeutic efficacy of 131I-labeled TAB004 in retarding growth and reducing the size of TNBC tumors in mice. Finally, we propose to initiate preliminary toxicity studies. The overarching goal of this Phase I proposal is to determine if TAB004 can be used for targeted radioimmunotherapy of TNBC. Successful completion will lead to Phase II activities focused on scaling up manufacturing and IND enabling studies in consultation with the FDA for a fast track approval.

ONCOTHERAPEUTICA, INC.

Attendee: Amin I. Kassis, CEO & President

Ideally, charged particle-emitting radiotherapeutic agents must (**1**) be efficiently and readily labeled with energetic particle emitters [e.g., **131I**, **90Y**]; (**2**) be stable within the circulation upon intravenous administration; (**3**) be taken up rapidly, specifically, and efficiently by the targeted tumor; (**4**) be retained for long periods by the tumor; (**5**) be minimally taken up and/or have a short residence within blood and normal tissues; (**6**) achieve high tumor-to-normal uptake ratios; (**7**) attain an intratumoral distribution that is sufficiently uniform to match the range of the emitted particles with the non-uniform intratumoral distribution of the radiopharmaceutical; (**8**) have an intratumoral concentration that will deposit [upon radionuclide decay] a tumoricidal dose in every targeted and non-targeted tumor cells; and (**9**) be readily labeled with a diagnostic photon/positron emitter and thereby formulating a **SPECT** [e.g., **123I**] or PET [e.g., **124I**] imaging radiopharmaceutical that (**i**) has the *exact same pharmacokinetics* as that of the radiotherapeutic [e.g., **131I**-labeled] agent, (**ii**) can identify those patients whose tumors are targeted by the radiotherapeutic agent [*patient stratification*], and (**iii**) will enable the calculation of the dose to be administered [e.g., mCi] that ensures the deposition of therapeutically effective doses to tumor lesions present in the patient being treated [*personalization of therapy*].

Onco**T**herapeutica, **I**nc. [**OTI**] is an early stage corporation dedicated to the development and commercialization of innovative proprietary radioidinated prodrugs for the treatment of cancer. **OTI** expects that its pre-clinical studies in tumor-bearing small animals will lead to the development of radiopharmaceuticals that will specifically target primary and metastatic cancerous lesions [e.g., prostate, lung, breast, and ovarian] and be therapeutically highly effective in any patient whose lesion(s) are confirmed to be targeted [post quantitative SPECT or PET]. OTI believes that its planned studies will *(1) substantially cut the costs associated with drug development, manufacturing, and marketing,*

(2) lead to the development of price competitive cancer therapeutics, and (3) reduce the death rates of men and women suffering and dying from these devastating diseases.

RAD IMMUNE, INC.

www.radimmune.com
Attendees: David J Rickles MD, President
Glen Dahlbacka, PhD, Program Director, R&D

Rad Immune is a start up biotechnology company whose expert multidisciplinary management team is committed to fostering research and development in molecular targeted radiotherapy (formerly known as radio immunotherapy (RIT)). We plan to do this by directly introducing our unique biotechnology products to the cancer pharmaceutical industry; as opposed to relegating these radio-pharmaceuticals to further investment and development by the medical device oriented nuclear imaging industry. Our vision is that molecular targeted radiation therapy has significant untapped potential for offering effective, low toxicity drugs to the oncology market. Rad Immune is currently focused on developing therapies for melanoma and pancreatic ductal adenocarcinoma (PDAC). Our recent accomplishments include:

-Provisional Patent application on using Centrin1 as a target for diagnosis, imaging and therapy of pancreatic cancer has been filed in June 2016.
-Background Patent for anti-melanin targeted RIT licensed from Albert Einstein College of Medicine in 2016.
-Two publications on encouraging results of experimental melanoma RIT using 8C3 IgG to melanin have been submitted to the peer reviewed journals Immunotherapy and Melanoma Research.
-NIH Phase 1 SBIR Contract for Molecular Targeted Radiation awarded in October 2016.

RADIOMEDIX, INC.

www.radiomedix .com
Attendee: Izabela Tworowska, PhD, CSO

Radiomedix, Inc is a clinical stage biotechnology company, based in Houston, Texas, focused on innovative targeted radiopharmaceuticals for diagnosis, monitoring and therapy of cancer. The company is commercializing generator produced radiopharmaceuticals based on Gallium-68 chemistry for PET imaging and therapeutic (alpha and beta-emitter labelled) radiopharmaceuticals for targeted radionuclide therapy of cancer. RadioMedix has also established two service facilities for academic and industrial partners: cGMP Manufacturing Suite for human clinical trials and probe development and small animal Molecular Imaging Facility for evaluation of agents in animal models.

A peptide receptor radionuclide therapy (PRRT) using 177Lu/90Y labeled somatostatin analogs has been proven to induce objective response in 30-45% of patients with advanced/Progressive neuroendocrine tumors. The complete response to beta-emitter PRRT is rare. This is due to the fact that NETs are diagnosed at late stage of disease: the NETS patients with remissions could developed resistance to beta-radiation therapy that could be overcome by alpha-emitter-targeted therapy (TAT). The commercial potential of TA has been confirmed by recent introduction of Xofigo for therapy of bone metastasis in prostate cancer and remissions of NETS in patients undergoing therapy with [213Bi]DOTATOC and [255Ac]DOTATATOC. The TAT has a potential to revolutionize treatment of NETS whether applied alone or supported by beta-emitter PRRT. IT can significantly increase therapeutic efficient of PRRT without side effects on non-targeted normal tissues. In the proposed research, we will determine the commercial feasibility of [212]Pb-octreotate. . The objective of this Phase I SBIR is to 1) determine the feasibility of radio-synthesis of [212Pb] produced using AREVA Med high purity 212Pb generator; (2) Evaluate the pharmacokinetic, efficacy and toxicity of [212Pb]octreotate therapy in AR42J-xenographs; With success in these aims, we expect to advance our compound toward initiation of clinical studies and submission of NDA.

ROCKLAND IMMUNOCHEMICALS

www.rockland-inc.com

Attendees: David Chimento, Director Custom Services
Hiep Tran, President and CSO, Abzyme Therapeutics

In this proposed SBIR contract, Rockland Immunochemicals in collaboration with Abzyme Therapeutics and Dr. Carolyn Anderson (Department of Radiology, University of Pittsburgh), propose to develop and characterize a recombinant single chain bispecific antibody for pretargeted radioimmunotherapy or PRIT.

The clinical indication we are addressing is HER2 positive cancer. HER2-positive cancers test positive for a protein called human epidermal growth factor receptor 2 (HER2), which promotes the growth of cancer cells. Experts recommend that every invasive breast cancer be tested for the presence of HER2 because the results significantly impact treatment recommendations and decisions. Also new HER2 targeting molecules may offer option for treatment of trastuzumab resistant HER2 positive cancers.

The prototype molecule with consist of a sdAb-based bispecific that can target both digoxigenin and HER2. The single chain bispecific delivery vehicle a single chain bispecific 30 kDa sdAb-sdAb produced as a linear fusion in a bacterial system. The bispecific sdAb-sdAb will consist of two arms - one binds to a cancer target HER2 and another binds to a payload delivery component, digoxigenin. In PRIT, the therapeutic will be administered in 2 stages to systemically to localize the tumor. Initial administration of the empty bispecific sdAbs allows for accumulation at the tumor site. Subsequent administration of a DIG-radionuclide payload allows for rapid accumulation at the pre-targeted HER2 tumor, and allows for rapid clearance of uncaptured payload radionuclide.

Our plan is to produce 2 novel high-affinity camelid single domain antibodies. One against the HER2 cancer biomarker and a second against digoxigenin (DIG), where DIG is a non-human molecule that can be used to target a radionuclide payload to the prelabeled HER2 tumor. The Anti-DIG and anti-HER2 VHH molecules will be humanized and subsequently reformatted into bispecific DIG and HER2 antibodies as a linear fusion. We will measure the recombinant bisepcifc HER2/DIG molecule for HER2 tumor accumulation, in-vivo clearance and its ability to capture DIG-fluorescent dyes of bispecific sdAbs for pretargeted therapy will be investigated in cancer xenograft murine animals. In collaboration with Dr. Anderson's group at the University of Pittsburgh, the ability of bispecific sdAbs to capture DIG-radionuclides (Ga-68 and Lu-177) will be evaluated.

SIBTECH, INC.

www.sibtech.com

Attendee: Joseph Backer, PhD, CEO

SibTech, Inc. is privately held company in Brookfield, CT, focused on developing novel protein-based therapeutic and imaging agents targeting receptors for vascular endothelial growth factor VEGFR-1 and VEGFR-2. These receptors play different yet critical roles in several diseases, including cancer, atherosclerosis and other cardiovascular maladies. SibTech is using company's proprietary technology for site-specific conjugation of therapeutic and imaging “payloads” to targeting proteins. Using this technology, SibTech is developing a family of radiopharmaceuticals and imaging tracers that are based on re-engineered VEGF, named scV, for targeting and imaging VEGF receptors. A novel radiopharmaceutical, scV/Lu proved to be effective in primary orthotopic and metastatic breast cancer models and is currently in late pre-clinical/early clinical development.

Considering different roles of VEGFR-1 and VEGFR-2, SibTech has recently developed first-in-class VEGFR-1 and VEGFR-2 selective versions of scV targeting protein and is exploring their potential as 177Lu radiopharmaceuticals, as well as their use as 89Zr and 18F PET and 99mTc SPECT tracers.

SibTech is currently funded via SBIR Fast-Track grant and SBIR Fast-Track Contract from NCI for two clinical trials at Johns Hopkins University for the first 177Lu radiopharmaceutical and the first 18F PET tracer based on scV.

SibTech has established a wide network of collaboration with leading academic and industrial groups (Stanford U, John Hopkins U, Memorial Sloan-Kettering Cancer Center, Columbia U., University of Massachusetts, German Cancer Center, Vienna Medical University, Uppsala University, GE Healthcare. GlaxoSmithKline), which resulted in a consistent stream of joint publications and grants.

To date, SibTech has experience only with converting its scientific findings into commercial research reagents or custom services. With oncoming clinical trials, SibTech plans a search for corporate partners for clinical development of novel radiopharmaceuticals and imaging tracers.

VIEWPOINT MOLECULAR TARGETING, LLC

www.viewpointmt.com
Attendee: Frances L. Johnson, M.D., CMO

Viewpoint Molecular Targeting has developed the first “theranostic” product for metastatic melanoma. Theranostic refers to a radiopharmaceutical drug that is a therapeutic agent that can be modified for use as a diagnostic companion product. Viewpoint aims to commercialize a proprietary-IV-injectable radiopharmaceutical drug that targets radiation to melanoma cells by binding to a cell surface receptor (melanocortin receptor subtype 1; MCR1) that is highly expressed in metastatic melanoma cells, but is virtually absent in all other cells in the body. The radiopharmaceutical can be labeled with an imaging isotope for SPECT/PET imaging and with a therapeutic radionuclide for therapy.

Based on non-invasive imaging scans that predict quantitatively the pharmacodynamics, clinicians can dose the right amount of therapeutic, for the right patient, at the right time. Subsequently, driving targeted treatment to each patient’s tumor. Better outcomes for melanoma care may be achieved as historically, radiopharmaceutical therapies have been highly efficacious and have had lower toxicities over conventional therapies.