Envisioning a world where disease can be precisely identified and treated

Jefferies Healthcare Conference
June 2015
**Forward-Looking & Regulatory Statements**

**Safe Harbor:** The private securities litigation reform act of 1995 (the Act) provides a safe harbor for forward-looking statements made by or on behalf of the company. Statements in this presentation, which relate to other than strictly historical facts, such as statements about the Company’s plans and strategies, expectations for future financial performance, new and existing products and technologies, anticipated clinical and regulatory pathways, and markets for the Company’s products are forward-looking statements within the meaning of the Act. The words “believe,” “expect,” “anticipate,” “estimate,” “project,” and similar expressions identify forward-looking statements that speak only as of the date hereof. You are cautioned that such statements involve risks and uncertainties that could cause actual results to differ materially from historical or anticipated results due to many factors including, but not limited to, the Company’s continuing operating losses, uncertainty of market acceptance of its products, reliance on third party manufacturers, accumulated deficit, future capital needs, uncertainty of capital funding, dependence on limited product line and distribution channels, competition, limited marketing and manufacturing experience, risks of development of new products, regulatory risks and other risks detailed in the Company’s most recent Annual Report on Form 10-K and other Securities and Exchange Commission filings. You are further cautioned that the foregoing list of important factors is not exclusive. The Company undertakes no obligation to publicly update or revise any forward-looking statements.

**Lymphoseek® (technetium Tc 99m tilmanocept) injection Indication and Important Safety Information**

Lymphoseek is a radioactive diagnostic agent indicated with or without scintigraphic imaging for:

- Lymphatic mapping using a handheld gamma counter to locate lymph nodes draining a primary tumor site in patients with solid tumors for which this procedure is a component of intraoperative management.
- Guiding sentinel lymph node biopsy using a handheld gamma counter in patients with clinically node negative squamous cell carcinoma of the oral cavity, breast cancer or melanoma.

**Important Safety Information**

- In clinical trials with Lymphoseek, no serious hypersensitivity reactions were reported, however Lymphoseek may pose a risk of such reactions due to its chemical similarity to dextran. Serious hypersensitivity reactions have been associated with dextran and modified forms of dextran (such as iron dextran drugs).
- Prior to the administration of Lymphoseek, patients should be asked about previous hypersensitivity reactions to drugs, in particular dextran and modified forms of dextran. Resuscitation equipment and trained personnel should be available at the time of Lymphoseek administration, and patients observed for signs or symptoms of hypersensitivity following injection.
- Any radiation-emitting product may increase the risk for cancer. Adhere to dose recommendations and ensure safe handling to minimize the risk for excessive radiation exposure to patients or health care workers.
- In clinical trials, no patients experienced serious adverse reactions and the most common adverse reactions were injection site irritation and/or pain (<1%).

Full Lymphoseek prescribing information can be found at: [www.lymphoseek.com](http://www.lymphoseek.com)
Investment Highlights

Lymphoseek® - FDA/EMA approved
- Sentinel Lymph Node detection: breast, melanoma and oral cavity cancers
- Lymphatic mapping in solid tumors (US only)

Acceleration of product revenue
- US label expansion Q4 2014; pricing leverage
- New US commercial strategy
- European approval Q4 2014 & partnership Q1 2015

Therapeutic applications based on Lymphoseek targeting backbone
- Macrophage Therapeutics, Inc. – independently-funded subsidiary
- Multiple diseases linked to activated Macrophages: Cancer, AI, ID, CV & CNS

New management and operational efficiencies
- Sharpened operational focus on Lymphoseek commercialization; and
- Net reduction in operating expenses
- Post $60 MM loan agreement, sufficient capital to cash-flow break even Q1 2016
Vision for Our Corporate Evolution

Product Development

Commercial Validation

Leveraged Pipeline

- Rheumatoid arthritis
- Tuberculosis
- Kaposi's sarcoma
- Cardiovascular diseases

Lymphoseek®
- Lymphatic Mapping
  - Breast cancer
  - Melanoma
  - Oral cavity (SLNB)

Manocept™ Diagnostics

Macrophage Therapeutics

SLNB: 3 Tumor Types
- Lymphatic Mapping: All solid tumors

Scientific Fundamentals

Time

Value
Lymphoseek®: Evolution of FDA/EMA Approvals

- Breast Cancer
- Melanoma
- Oral Cavity
- All Solid Tumors (US Only)

Liver metastases

Lymphatic Mapping

SLNB

Q4 2014

Oral Cavity (SLNB)
Lymphoseek® Approval for Use in All Solid Tumors Represents a Large Market Opportunity

US Solid Tumor Incidences, 2014¹
Estimated Total: 1.2M

EU 28 Solid Tumor Incidences, 2014²
Estimated Total: 2.0M

Lymphoseek® Approvals
US Lymphatic Mapping
- All Solid Tumors (Oct. 2014)

1 ACS 2014
2 GLOBOCAN EU 28
Lymphoseek Revenue Targeting >130% Growth in 2015

Net Revenue to NAVB
Gross Margin

2013
2014

$- $500,000 $1,000,000 $1,500,000 $2,000,000 $2,500,000 $3,000,000 $3,500,000 $4,000,000 $4,500,000 $5,000,000
Lymphoseek® Clinical Value Proposition

Radical Neck Dissection

SLNB

Improve clinical practice and outcomes
- Enhance Results
- Increase Efficiency
- Reduce Morbidity

Assessment of Lymphoseek® as a Sentinel Lymph Node Detection Agent

<table>
<thead>
<tr>
<th>False Negative Rate</th>
<th>2.56% (p = 0.0205)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph Nodes Removed (average per subject)</td>
<td>Full Node Dissection: 38 Lymphoseek®: 4</td>
</tr>
</tbody>
</table>

1 Based on results from NEO3-06 clinical trial in H&N cancer
Getting Closer to the Customer

**Refocus Commercial Structure**
- Design commercial structure to meet growing customer needs
- Deploy an oncology sales force in Q1 2015
- Refocus and increase promotional activity

**Enhance Customer Engagement**
- Enhance customer segmentation and targeting
- Expand account targeting
- Engage oncology treatment teams and organizations to achieve adequate reach & frequency
- Drive patient education in partnership with advocacy groups

**Evolve the Brand**
- Leverage broader label to accelerate adoption
- Articulate full brand value proposition to oncology treatment team
- Exercise pricing leverage
- Capitalize on account re-order rate
## Future Directions Under Existing Label

**Lymphoseek® Lifecycle Management**

### Status

<table>
<thead>
<tr>
<th>Market Development</th>
<th>Indication</th>
<th>Phase</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Solid Tumors Lymphatic Mapping</strong></td>
<td>Solid Tumors Lymphatic Mapping</td>
<td>Phase 1</td>
<td>US FDA Approved: 2013 &amp; 2014</td>
</tr>
<tr>
<td><strong>Colorectal Cancer</strong></td>
<td>Investigator Initiated Pilot Study</td>
<td></td>
<td>Ongoing</td>
</tr>
<tr>
<td><strong>Kaposi’s Sarcoma</strong></td>
<td>Investigator Initiated Study – Grant-funded</td>
<td></td>
<td>Complete</td>
</tr>
<tr>
<td><strong>Comparative Study in Breast Cancer</strong></td>
<td>Head to Head patient study vs Sulfur colloid – Pain levels and performance</td>
<td></td>
<td>Complete</td>
</tr>
<tr>
<td><strong>Cervical Cancer</strong></td>
<td>Multi-center study - Grant-funded</td>
<td></td>
<td>Planned 2015</td>
</tr>
<tr>
<td><strong>Pediatric - Solid Tumor</strong></td>
<td>Multi-center study - Grant-funded</td>
<td></td>
<td>Planned 2015</td>
</tr>
<tr>
<td><strong>Anal/Rectal</strong></td>
<td>Single site study - Grant-funded</td>
<td></td>
<td>Planned 2015</td>
</tr>
<tr>
<td><strong>Endometrial Cancer</strong></td>
<td>Investigator Initiated Study</td>
<td></td>
<td>Planned 2015</td>
</tr>
</tbody>
</table>
Manocept™
Targeted Immunotherapies
Navidea Biopharmaceuticals

Manocept™ Technology
Targets Macrophages

FDA/EMA-approved Lymphoseek®
Solid Tumors Lymphatic Mapping
Sentinel Node: Breast, Melanoma,
Head + Neck Cancers

• Newly created, independently-funded Navidea subsidiary developing targeted therapies
• Therapeutic applications based on Lymphoseek targeting backbone
• Based on proprietary CD206 targeting Manocept platform technology
• R&D pipeline of targeted immunotherapies to treat macrophage-mediated diseases
What role do macrophages have in disease?
- Alter microenvironment
- Drive inflammation + metastasis
- Promote tumor angiogenesis

What is the purpose of macrophages?
- Repair damaged tissue
- Remove abnormal/tumor cells
- Quarantine harmful pathogens

Macrophage-involved diseases
- Cancer
- Auto-immune
- Infectious
- Cardiovascular
- CNS
Macrophages are a Validated Target

...But nobody has previously modulated the cell successfully

Targeting tumor-associated macrophages as a novel strategy against breast cancer
Yunping Luo,‡ He Zhou,† Jörg Krueger,§ Charles Kaplan,∥ Sung-Hyung Lee,∥ Carrie Dolman,∥ Dorothy Markowitz,∥ Wenyuan Wu,∥ Cheng Liu,∥ Ralph A. Reisfeld,∥ and Rong Xiang†
Department of Immunology, The Scripps Research Institute, La Jolla, California, USA; Key Laboratory of Laboratory Medical Diagnostics, Ministry of Education, Graduate School of Medicine, Shanghai University, Shanghai, China.

BRAF Inhibition Stimulates Melanoma-Associated Macrophages to Drive Tumor Growth
Tao Wang‡, Min Xia‡, Yingbin Ge‡, Clemens Krepler‡, Eric Belser‡, Alfonso Lopez-Coral‡, Xiaowei Xu‡, Gao Zhang‡, Rikka Azuma‡, Qin Liu‡, Rui Liu‡, Ling Li‡, Ravi K. Amaravadi‡, Wei Xu‡, Giorgos Karakousis‡,†, Tara C. Gangadhara‡,†, Lynn M. Schuchter‡,†, Melissa Lief‡, Sanika Khare‡,†, Nelly R. Halloran‡, Meenhard Herlyn‡, and Russel E. Kaufman‡
Clin Cancer Res; 2015

Macrophages in inflammatory multiple sclerosis lesions have an intermediate activation status
Vogel et al. Journal of Neuroinflammation 2013, 10:35

Targeting Tumor-Associated Macrophages and Inhibition of MCP-1 Reduce Angiogenesis and Tumor Growth in a Human Melanoma Xenograft
Silvina Gazzaniga1, Alicia I Bravo2, Angelo Guglielmotti3, Nico van Rooijen4, Fabricio Maschi5, Annunciata Vecchi6, Alberto Mantovani6, José Mordoh7 and Rosa Wainstok8
Journal of Investigative Dermatology (2007) 127, 2031–2041

How to Get from Here to There: Macrophage Recruitment in Alzheimer’s Disease

The role of tumor-associated macrophages in tumor vascularization
Guo et al. Vascular Cell 2013, 5:20

HPV16 Tumor Associated Macrophages Suppress Antitumor T Cell Responses
Ana Paula Lepique1, Katia Regina Perez Daghestani2, Iolanda Midea Cuccovia2 and Luisa Lina Villa1 Clínica Cncer Res July 1, 2009 15; 4391

Eradication of HIV-1 from the Macrophage Reservoir: An Uncertain Goal?
Viruses 2015, 7, 1578-1598; doi:10.3390/v7041578
Wasim Abbas1, Muhammad Tariq1, Mazhar Iqbal1, Amit Kumar3 and Georges Herbein4,5
Therapeutic Concept

Targeting activated macrophages

1. GPS
   - GPS = Mannose Moiety
   - ONE hardwired address i.e. activated macrophages

2. Missile
   - Missile = Tilmanocept backbone

3. Warhead
   - Warhead = Tc$^{99}$, other isotopes, Chemotherapeutics, immune-modulators, etc.
Macrophage Therapeutics: Multiple Therapeutic Opportunities

Aberrant macrophages are associated with several major disease states

**Infectious Disease**
- In certain infectious diseases, the macrophage acts as an incubator for the proliferation of the ingested material
  - HIV, HPB, HPC, Ebola, etc.
  - TB, assorted drug-resistant bacteria

**Cancer**
- Cancer cells can modify the macrophage to create new cancer cells called tumor associated macrophages (TAMs)
- TAMs can enable enhanced blood vessel growth and release other tumor enhancing factors for an immunosuppressive microenvironment

**Inflammation**
- Often triggered by a foreign body, activated macrophages can stimulate excessive inflammation, resulting in autoimmune disease

**CNS**
- Activated macrophages can stimulate improper clearance of amyloid and cause the associated inflammation typically seen in Alzheimer disease and implicated in MS, Parkinson’s and other CNS diseases

**Cardiovascular**
- Lipid-containing macrophages can exacerbate atherosclerosis, an inflammatory condition
Macrophage Therapeutics, Inc.

Developing novel immunotherapies that target activated macrophages

- Manocept technology – platform for immuno-constructs that target CD206+ (and CD209+ dendritic cells) activated macrophages, TAMs and their microenvironment
  - Tilmanocept (FDA-approved scaffold of Lymphoseek®): proprietary synthetic glucose polymer ligand with ultra-high affinity for CD206 surface antigen ($kd = 3 \times 10^{-11}$) on activated macrophages and TAMs

- Lead compounds:
  - MT-1001: selectively induces apoptotic death of CD206+ activated macrophages and TAMs
  - MT-2001: inhibitor of the inflammatory process caused by overactive CD206+ macrophages
  - MT-3001: selective antibacterial construct (to eradicate granulomatous TB lesions/macrophages and other pathogens)

- Broad therapeutic applications for disease states resulting from aberrant behavior of activated macrophages
  - Rapid development paths to clinic for orphan, fast track indications
  - Preclinical proof-of-concept as a therapeutic (clinical validation of the Manocept technology for targeting/localizing activated macrophages)

- Strong IP estate

- Renowned SAB and experienced management team
Macrophage Therapeutics, Inc.
Developing novel immunotherapies that target activated macrophages

Lead programs:
- MT-1000 class: selectively induces apoptotic death of activated macrophages and TAMs
  - Does not impact on the large pool of tissue resident or bone marrow resident un-activated macrophages
  - Single agent to deplete the TAMs and thus profoundly impact on the immuno-suppressive properties of the tumor micro-environment
  - Essentially acts to reboot the malfunctioning innate immune system
  - Generic approach to target infectious agents that does not require customization
- MT-2000 class: inhibitor of the inflammatory process caused by overactive macrophages
  - Powerful anti-inflammatory compounds exist but their benefits are limited by their significant off target effects
  - By targeting one of the most powerful actors in excessive inflammation, MT-2001 can significantly boost the on target dose while reducing side effects of a proven, highly effective anti inflammatory agent
- MT-3000 class: drug delivery construct (to treat contents of the macrophage which the macrophage cannot eliminate on its own)
  - An example of using the property of the macrophage that it often acts as an incubator of infectious agents so that by targeting an effective agent vs. the infectious agent one can improve the potency while significantly reducing toxicity.

Additional compounds in development designed to take advantage of the ability to target the activated macrophage
- Macrophages are long lived cells
- Macrophages are malleable and can be redirected from a pathological state to a therapeutic state
- CD-206 internalizes so an excellent target for products that are designed to be active only inside a cell
- CD-206 recycles to cell surface so it can be used again if necessary i.e. suicide switch, etc.
Macrophage Therapeutics: Developing Classes of Immunoconstructs that Target Activated Macrophages and the Microenvironment

Classes of Immunoconstructs

Targeting Activated CD206+ Macrophages

- Inhibiting Inflammatory Activity
- Targeting Macrophage Contents
- Depleting Through Apoptosis
- Reprogramming Activity

Altering Activated Macrophage Function & Treating the Mechanism of Disease

*MT-2000 and MT-3000 class of constructs*

MT-1000 Class: Killing TAMs & Altering the Tumor Microenvironment to Enhance Immunotherapies

*MT-1000 class of constructs*
Macrophage depletion with liposomal agents that target all macrophages (active and inactive) failed due to toxicity.

**Manocept Radio-isotope Imaging**

Source: AACR 2015 Poster #5026
Tumor-associated targeting with Manocept: HIV-associated Kaposi’s sarcoma as a model system; M. McGrath et al; UCSF

**PEG-LD Liposomes Radio-isotope Imaging**

Source: Oncology; Pegylated Liposomal Doxorubicin: Scientific Rationale and Preclinical Pharmacology. Review Article; October 01, 1997; Francis J. Martin, PhD.
Strategies to Target the Critical Disease Causing Macrophage

Blocking endogenous macrophage specific activating agents – some early promise but also suffers from excess toxicity or lack of efficacy due to difficulty with selectivity and dosing regimens.

Stimulating macrophage activation by administration of macrophage activating agents – toxicity due to lack of specificity and significant off target effects.

Targeting specific compounds produced by over active macrophages, i.e., VEGF, TNF, MMP’s, IDO, etc.
Scientific Advisory Board

Siamon Gordon, MB, ChB, PhD
Emeritus Professor of Cellular Pathology, Sir William Dunn School of Pathology, University of Oxford, Oxford, UK

Mark I Greene, MD, PhD, FRCP
John Eckman Professor of Medical Sciences Vice Chair of Pathology, Division of Immunology and Experimental Pathology, Univ. of Penn. School of Medicine, Philadelphia, PA

Michael S. McGrath, M.D., Ph.D.
Professor, Departments of Laboratory Medicine, Pathology, and Medicine, University of California San Francisco

Thomas J. Rosol, D.V.M., Ph.D.
Professor, Veterinary Sciences, Ohio State University; Senior Advisor, Life Sciences, University Office of Technology Commercialization and Knowledge Transfer, The Ohio State University; Special Assistant to the Vice President for Research, The Ohio State University

Eric Rowinsky, M.D.
Chief Medical Officer & Head of Research and Development, Stemline Therapeutics

Larry S. Schlesinger, M.D.
Chair, Department of Microbial Infection and Immunity, Director, Center for Microbial Interface Biology, The Ohio State University

David Sidransky, MD
Professor of Otolaryngology – Head and Neck Surgery, Professor of Oncology, Professor of Pathology, Professor of Cellular & Molecular Medicine, Professor of Urology, and Director, Head and Neck Cancer Research, The Johns Hopkins University

Kenneth C. Williams, Ph.D.
Professor of Biology, Boston College
Corporate Overview and Vision
## Financial Highlights

<table>
<thead>
<tr>
<th></th>
<th>(MM)</th>
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<tbody>
<tr>
<td><strong>Total Revenue</strong></td>
<td></td>
</tr>
<tr>
<td>For the quarter ended</td>
<td>$2.1</td>
</tr>
<tr>
<td>March 31, 2015</td>
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<tr>
<td><strong>Lymphoseek® Revenue</strong></td>
<td></td>
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<tr>
<td>For the quarter ended</td>
<td>$1.8</td>
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<td>March 31, 2015</td>
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<tr>
<td>**Available Cash (Pro</td>
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</tr>
<tr>
<td>Forma)**</td>
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<tr>
<td>Balance</td>
<td>$22</td>
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<tr>
<td>Includes $18 MM from May</td>
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<tr>
<td>11 CRG loan</td>
<td></td>
</tr>
<tr>
<td>Does not include access</td>
<td></td>
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<tr>
<td>to additional ~27MM</td>
<td></td>
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<tr>
<td>remaining under Platinum</td>
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<tr>
<td>line of credit</td>
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<tr>
<td><strong>Capital Position</strong></td>
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<tr>
<td>(as of March 31, 2015)</td>
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<tr>
<td>Common Shares Outstanding</td>
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<tr>
<td>Conversion Shares,</td>
<td>26.8</td>
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<tr>
<td>Warrants &amp; Options</td>
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<tr>
<td>Fully Diluted Shares /</td>
<td>177.5</td>
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<tr>
<td>Equivalents</td>
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</tbody>
</table>
2015 Corporate Milestones

- $10 to $12 Million in 2015 Lymphoseek sales
- 50,000 + Lymphoseek procedures in 2015
- Manocept™ diagnostic and therapeutic pipeline expansion