Precise Identification of Macrophage-Mediated Diseases
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.
Target CD206 Activated Macrophage receptor

Our proprietary activated macrophage targeting system is capable of identifying and measuring macrophage activity in-vivo.

Navidea is marketing its Biomarker technology for use as a novel drug development tool in ongoing and future Oncology.

**Tilmanocept combines:**
- Mannose ligand for binding CD206 receptors on activated macrophages  ✔ Seek
- Radioisotope  ✔ Identify
Macrophages and CD206 Receptors

Only Activated Macrophages express CD206

Macrophages are activated in multiple ways

Environmental Exposure
- Viruses
- Other infectious agents
- Drugs/chemicals
- Other (e.g. ultraviolet light)

Hormonal Effects
- Intrinsic and extrinsic
- Variable depending on disease

The mannose receptor, CD206, is only expressed on activated macrophages and dendritic cells (CD209)

Activated macrophages function in both innate + adaptive immunity
Macrophages are immune system cells that respond to tissue damage or infection.

Activated macrophages are stimulated by cytokines or bacteria to respond to invading or infected cells:

- Help clear infectious agents, repair damaged tissue
- Alter microenvironment to suppress or promote disease-causing cells
- **Have unique receptors that enable cellular targeting**
The Navidea Opportunity

Near term commercial opportunities and Macrophage valuation milestones

### Biomarker
- Ongoing discussion to utilize Tilmanocept in planned clinical trials
- Does not require additional approvals or reimbursement to generate revenue
- Applications: Cardiovascular, Cancer, RA, NASH, and Neuroinflammatory disease

### Clinical Diagnostics
- Rheumatoid Arthritis (Planned Ph3 Trial in 4Q18/1Q19)
- NASH Diagnostic to replace Biopsy (Completed Ph2)
- Cardiovascular imaging (Ongoing Ph2)

**Neuroinflammatory Diseases (generating proof of concept data)**

### Macrophage Tx
- Creating value at NAVB via passive stake in Macrophage Therapeutics
- Pursuing Orphan Disease with abbreviated regulatory pathway
- Multiple valuation milestones over the next 2 quarters
- Pursuing external partners and investors
Navidea Product Pipeline

Preclinical/Discovery Stage | Phase 1 | Phase 2 | Phase 3 | FDA-Approved
---|---|---|---|---
Solid Tumors Lymphatic Mapping, Sentinel Node Biopsy |  |  |  | FDA-approved in 2014, Sold to Cardinal
Rheumatoid Arthritis |  |  |  | Guidance from FDA expected by YE2018
Cardiovascular Diseases |  |  |  | Ph2 study ongoing at Mass General
Kaposi’s Sarcoma |  |  |  | Ph3 study expected completion by YE2018
NASH |  |  |  | Ph1 study
Alzheimer's, Parkinson's, MS |  |  |  | Generating data which should unlock exciting new Clinical Diagnostic and Biomarker
Our Pipeline: What’s New?

Detection & Monitoring of Neuroinflammatory Diseases

• Anticipate data indicating use of Tilmanocept as a Neuroinflammation diagnostic imminently
  • Initial data readout expected over next several weeks
    • Applications in Alzheimer’s, Parkinson’s, Multiple Sclerosis
    • Detection & Monitoring
• Clear unmet medical need for an early detection tool and biomarker for drug development
  • Ph2 results of Biogen’s BAN2401 highlight clear need for diagnostic and biomarker tool for Alzheimer’s drug development

Preclinical/Discovery Stage  |  Phase 1  |  Phase 2  |  Phase 3  |  FDA-Approved

Alzheimer's, Parkinson's, MS  |  |  |  |  Proof-of-Concept data expected within next several weeks

Sizeable addressable markets

Pipeline addresses unmet preventative screening needs

• Rheumatoid Arthritis FDA approval will pave the way for additional FDA approved clinical Diagnostics

• Will pursue both diagnostic and screening pathways for Cardiovascular disease

• Commercialization strategy will vary by indication
Corporate Overview
Targeting Activated Macrophages to Detect, Monitor and Treat Disease

Building off FDA/EMA-approved diagnostic product
Leveraging FDA approved Lymphoseek® to expand to more attractive clinical diagnostic end markets

Technology platform applicable to multiple disease states
RA, CV, Metabolic Diseases, Cancer and Neuroinflammatory Diseases

Targeting CD206 receptors on activated macrophages
Enables higher affinity and more precise non-invasive imaging

Business Strategy
Leveraging proprietary technology to create and maximize shareholder value through new products, collaborations, entities, and partnerships
Navidea Imaging Strategy

Image M1 or M2 Mediated Disease

**Dose it**

Same for all indications

**Image it**

Focus the camera on area of interest

3 hour image RA

High Resolution Imaging
Cardiovascular Disease

Potential diagnostic and screening opportunity with large addressable market

Detect High-risk Plaque

- Fat droplets in arteries induce cytokine release
- Cytokines recruit monocytes, which convert to macrophages
- Activated macrophages are potential markers of cardiovascular disease

NIH Grant with MAJOR HOSPITAL

- Phase I study completed under existing IND evaluating imaging and detection of vulnerable plaque
  - Published J Infection Diseases 16 Jan 2017: Application of a Novel CD206+ Macrophage-Specific Arterial Imaging Strategy in HIV
- Additional Phase 2 study underway
Quantifiable Inflammation Score
Computer Read of CV images Creates Quantitative Inflammation Score

Compiled 2D/3D Imaging

Computer Generated Score of CV Images

- Mean CD206+ macrophages/mm
- Percent aortic volume with high-level tilmanocept uptake

HIV-infected vs. Non-HIV-infected subjects

P=0.0002
P=0.009
Clinical Diagnostics Catalyst Calendar
Clinical Diagnostics Catalyst Calendar

- **Phase 3 RA dossier submitted to FDA**
  - 3Q-2018

- **FDA Response Expected by YE2018**
  - 4Q-2018

- **Completion of Phase 1**
  - 1Q-2019

- **Robust Neuroinflammation Dataset expected**
  - 2Q-2019

- **Completion of Phase 2 Trial**
  - 3Q-2019

- **Data Evaluation & Potential Publication of Ph2**
  - 4Q-2019

- **Proof of Concept Neuroinflammation Data Expected**
  - 3Q-2018

- **Biomarker Update w/ FDA (Sep 2018)**
  - 4Q-2018

- **Completion of Phase 3 YE18**
  - 1Q-2019

- **Phase 3 RA meeting scheduled w/ FDA (Sep 2018)**
  - 3Q-2018

- **Data Evaluation & Potential Publication of Ph1**
  - 3Q-2019

**Phases and Milestones**

- **Rheumatoid Arthritis**
- **Kaposi Sarcoma**
- **NASH**
- **Cardiovascular Disease**
- **Neuroinflammation**

**Key Events**

- **Phase 3 RA**
- **Biomarker Update**
- **Completion of Phase 1**
- **Completion of Phase 2 Trial**
- **Data Evaluation & Publication**

**Timeline**

- **3Q-2018**
  - Phase 3 RA dossier submitted to FDA
  - FDA Response Expected by YE2018

- **4Q-2018**
  - Biomarker Update w/ FDA (Sep 2018)
  - Completion of Phase 3 YE18

- **1Q-2019**
  - Phase 3 RA meeting scheduled w/ FDA (Sep 2018)
  - Completion of Phase 1

- **2Q-2019**
  - Robust Neuroinflammation Dataset expected
  - Completion of Phase 2 Trial

- **3Q-2019**
  - Data Evaluation & Potential Publication of Ph2

- **4Q-2019**
  - Completion of Phase 2 Trial
  - Data Evaluation & Potential Publication of Ph1
Our Biomarker Approach
Three Key Attributes of our Biomarker Approach

(1) Clear unmet need to reduce clinical trial cost burden

(2) No additional regulatory requirements to generate commercial revenue

(3) Potential revenue opportunity for NAVB is significant
Improvement in Savings for Clinical Trial Costs and Preventative Screening

• Average cost per patient in clinical trials today: $36,500
• Site monitoring, recruitment and retention account for approximately one-third of trial costs

Focused recruitment and patient screening to optimize trial outcomes and minimize SAE’s and reduce overall patient mortality

• Ongoing patient monitoring and dose optimization
• End of trial scanning for outcomes
• Cut overall spend and time to market

Patient enrollment numbers reflect oncology trials
Source: ClinicalTrials.gov
Biomarker limits regulatory hurdles

Selling into clinical trials obviates need to obtain additional regulatory clearances

Regulations permit selling Tilmanocept to Biopharmas & CROs for use in registered clinical trials
  • US and Europe (Japanese approval imminent)

Potential CRO partners have cited FDA approval and superb safety profile as key selling points

Data generated through biomarker approach will help accelerate regulatory pathway for future clinical diagnostics
Biomarker revenue opportunity is robust

Potential to integrate Tilmanocept into thousands of clinical trials

>500,000
Patients currently being recruited for FDA registered clinical trials in applicable disease areas

$5,000/dose
NAVb sales price

$2.5B
Potential revenue for research purposes *only*

Oncology
CV
NASH
Alzheimers
MS
Parkinsons
Macrophage Therapeutics
Passive equity stake in spin out
Therapeutic Concept

**Selectively targeting Activated Macrophages**

Platform for immuno-constructs that preferentially target CD206+ (and CD209+ dendritic cells) activated macrophages

1. GPS
   - Mannose Moiety
   - With One Hardwired Address - CD206 Activated Macrophages

2. Delivery
   - Manocept™ Backbone

3. Payload
   - Chemotherapeutics
   - Immune-modulators
   - Tc⁹⁹
   - Other Isotopes
Arthritis
• Results report clear statistically significant anti-inflammatory activity with no apparent significant clinical signs relating to off target effects.

Asthma
• Results show a decrease in all three pro-inflammatory markers evaluated that are secreted by disease causing macrophages that successfully demonstrates an anti-inflammatory effect. Study repeated by large pharma collaborator with comparable results with different mix of pro-inflammatory markers.

NASH
• Results demonstrate statistically significant reduction in NASH related inflammation
• No evidence of damage to resident liver macrophages called Kupffer cells or other liver damage
• Three doses of MT1002 tested in NAFLD-NASH model and 1 dose of MT 2002 and MT 1002 tested in NASH fibrosis model

Neuro-inflammation
• Krabbe Disease: Data from the definitive naturally occurring animal model the Twitcher mouse.
  1. Evidence that we can normalize morphology of macrophage by converting from M1 to M2
  2. Enabled normal weight gain
  3. Significantly reduced or eliminated disease progression for time period evaluated so far
  4. Awaiting pathology data on brains to confirm protective effect and BBB permeability.

Cancer
• Results showed an immediate effect on the rate of tumor growth and in the slower growing tumor the inhibition in tumor growth rate remained throughout the duration of the study
• Synergy demonstrated with addition of a targeted antibody resulting in the ability to reduce the dose of the companion antibody
• This offers the potential for lower side effects, reduced resistance and dramatically lower cost
MT 2000: Macrophage Tx Lead Candidate

Activated Macrophage targeted steroid

**MT-2000: An activated macrophage targeted steroid**

- Designed to inhibit inflammation caused by overactive macrophages
- Converts pro-inflammatory M1 Macrophages to anti-inflammatory M2 Macrophages
- Receptor mediated delivery improves efficacy and eliminates off target toxicity
Recently generated pre-clinical data points to accelerated FDA pathway

Restructuring relationship with Macrophage Therapeutics

Why Now?

• Pre-clinical study just recently provided promising data in the treatment of a rare orphan Neuroinflammatory Disease
  • MT has selected this approach for identifying its Lead Indication and Lead Candidate
    • Provides an accelerated pathway to regulatory milestones and approval
    • Significantly limits capital needs to generate first-in-human data
  • MT has significant capital needs that must be addressed to bring any product to market
    • Current corporate structure limits MT’s ability to raise capital
  • MT has hired leading regulatory consultants to pursue Orphan Drug Designation and potential Pediatric Rare Disease Priority Review Voucher
Rare Pediatric Disease Voucher

Potential source of non-dilutive capital for MT and NAVB

Rare Pediatric Disease Voucher

• Potential to provide both MT and Navidea with non-dilutive capital
• MT plans to submit Rare Pediatric Disease Qualification package to the FDA by YE2018
  • Have hired leading CRO

Last 5 Rare Pediatric Disease Vouchers have sold for >$100 mn

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<th>Company Awarded Voucher</th>
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<th>Date Sold</th>
<th>Sale Price ($)</th>
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<td>Sanofi</td>
<td>May-15</td>
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Rare pediatric orphan disease with unmet medical need

Macrophage Tx Lead Indication

- Lysosomal storage disease resulting in myelin damaging neuro-inflammation
  - Disease diagnosed at 6 months old, typically fatal by 2-3 years
- MT is currently exploring the utility of MT-2000 class (anti-inflammatory)
  - We anticipate:
    - FDA Orphan Drug Designation (ODD)
    - Qualification of a Rare Pediatric Disease Priority Review Voucher
- Pending FDA ODD & Voucher qualification MT will pursue this indication first
  - MT will explore follow-on neuro-inflammatory diseases
Krabbe Disease will prove three key therapeutic traits of MT-2002

(1) Crosses Blood Brain Barrier

(2) Anti-inflammatory

(3) Non-enzymatic clearance of toxic metabolites

Proving these attributes will open the door to blockbuster neuroinflammatory indications…(and systemic inflammatory indications)
Krabbe: Proof of Concept for Neuroinflammation

Krabbe Disease will prove three key therapeutic traits of MT2000

1. Parkinson’s
2. Multiple Sclerosis
3. Devic’s Disease

Neuro-Inflammation

1. Goucher Disease
2. Niemann-Pick Disease
3. Fabry’s Disease

Lipid Storage Diseases
Thank you

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