Navidea BIOPHARMACEUTICALS

Precise Identification of Macrophage-Mediated Diseases

August 2018

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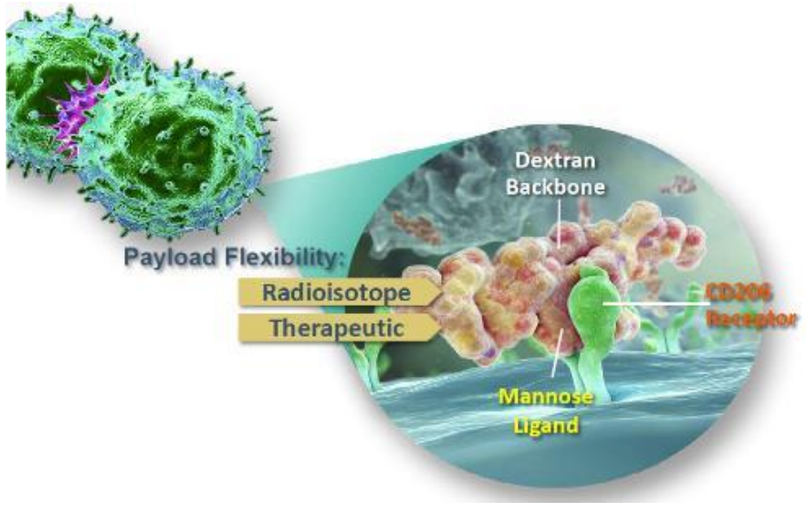
Our Technology



Target CD206 Activated Macrophage receptor

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

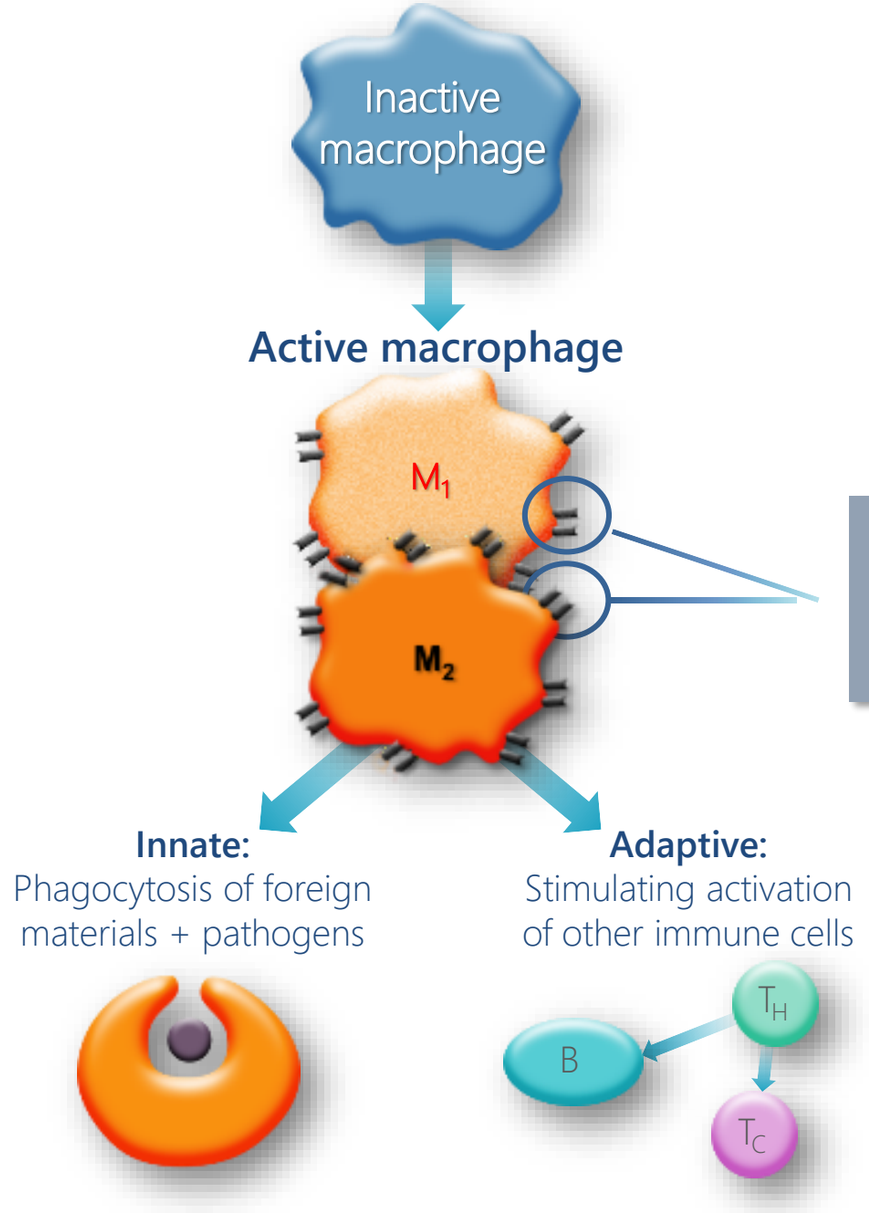
Navidea is marketing its Biomarker technology for use as a novel drug development tool in ongoing and future Oncology

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

The Role of Macrophages in Human Biology

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- 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**

Restructuring Relationship with Macrophage Therapeutics

Unlocking and enabling value creation at "NAVB" via the therapeutics franchise

Spinout Rationale

- Current structure severely hampers the ability to finance Macrophage Tx through traditional Venture Capital structure
- Minimal overlap between Diagnostic and Therapeutic focused institutional investors
- Macrophage Tx capital needs are significant relative to Navidea
- Minimize NAVB dilution to fund Therapeutic development

Post Spinout Structure

- Navidea will maintain a passive ownership stake in Macrophage Tx
  - Depending on NAVB'S own financial needs MT shares will either be kept for access to capital to fund NAVB or distributed to shareholders at some future date
  - In any event progress at MT will translate to improved valuation in NAVB
- Macrophage Therapeutics BoD and potential institutional investors will hold controlling vote
  - Structure that mirrors typical Venture Capital investment

The Navidea Opportunity Post MT Spinout

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,vand Neuroinflammatory disease

Clinical Diagnostics

- Rheumatoid Arthritis (Planned Ph3 Trial in 4Q18/1Q19)
- NASH Diagnostic to replace Biopsy (Planned completion 4Q18)
- 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

Our Biomarker Approach

Biomarker: Overview

Near term commercial opportunity that obviates additional regulatory clearance

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

Biomarker addresses unmet need

Current Clinical Landscape & Monitoring Market Opportunity

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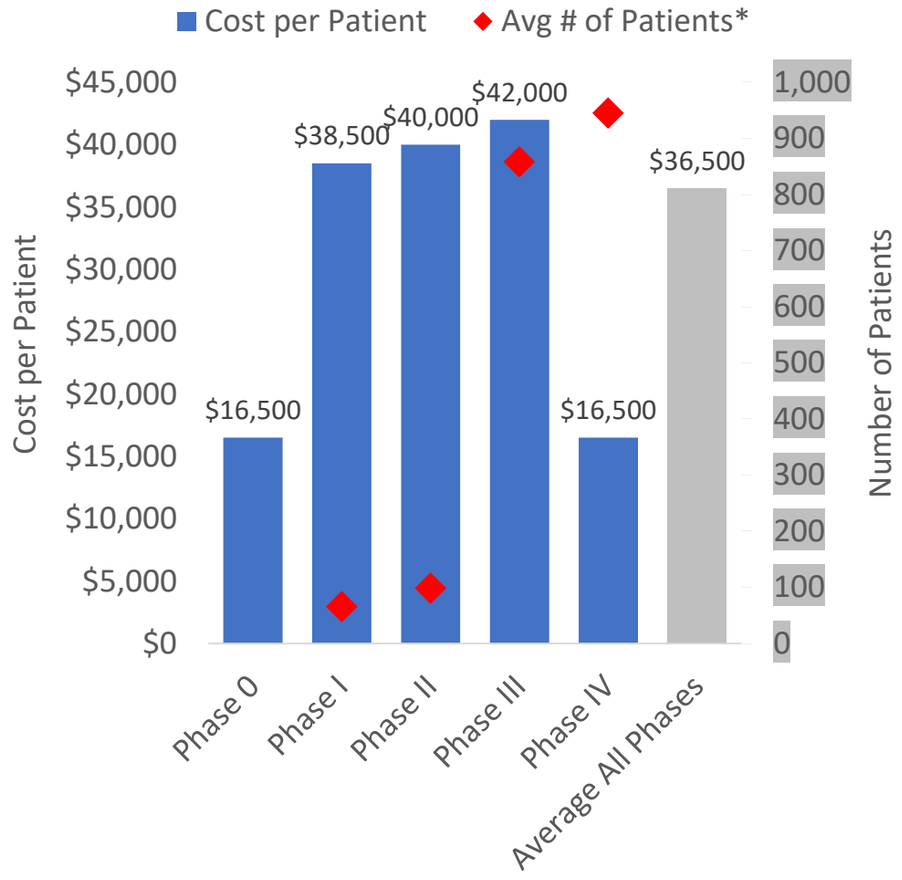
- Improvement in Savings for Clinical Trial Costs and Preventative Screening
  - *Average cost per patient in clinical trials today: $36,500*
  - *Site monitoring, recruitment and retention account for approximately one-third of trial costs*
- ***Focused recruitment and patient screening to optimize 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 expected in the future)
- 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

×

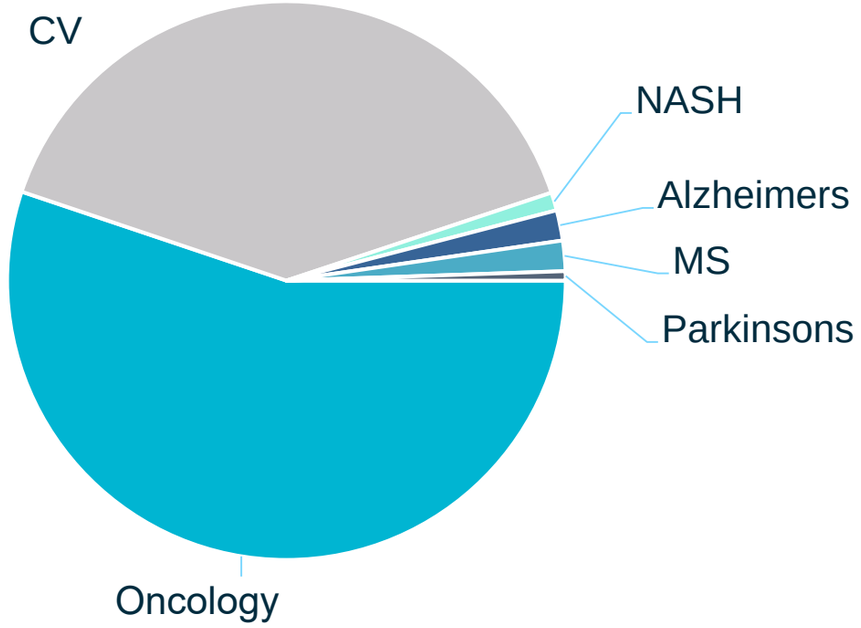
$5,000/dose

NAVB sales price

=

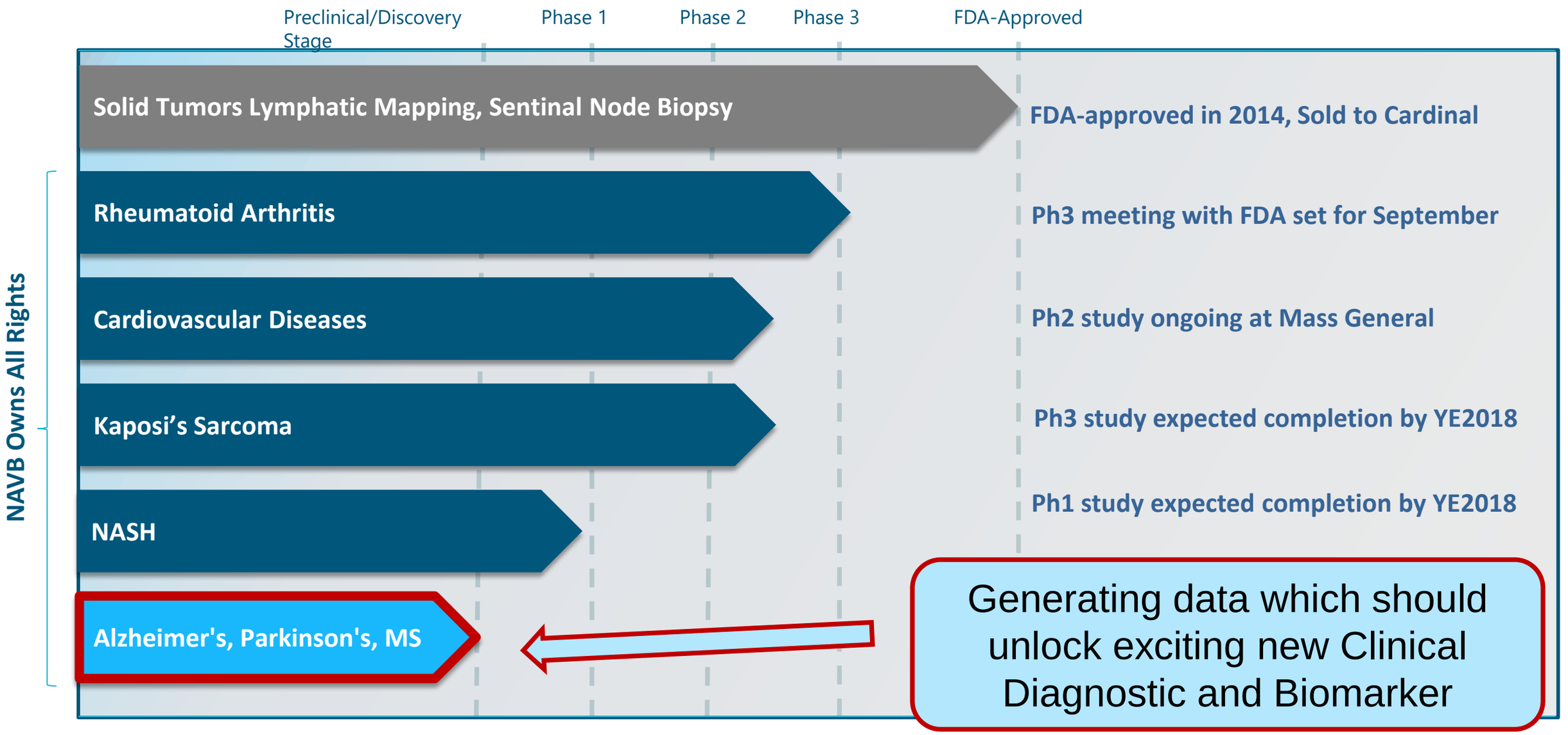
$2.5B

Potential revenue for research purposes *only*



Our Clinical Diagnostics Strategy

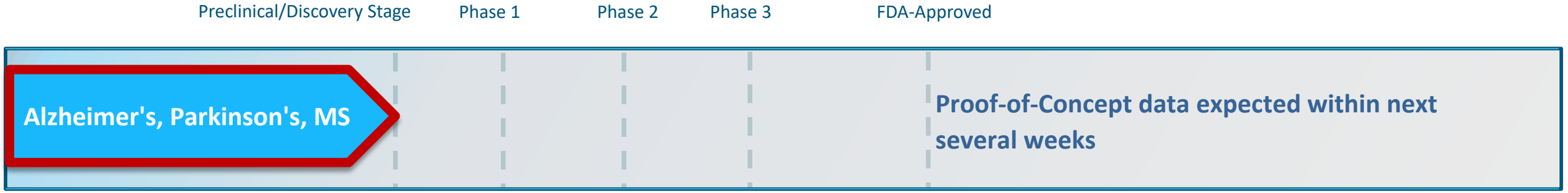
Navidea Product Pipeline



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

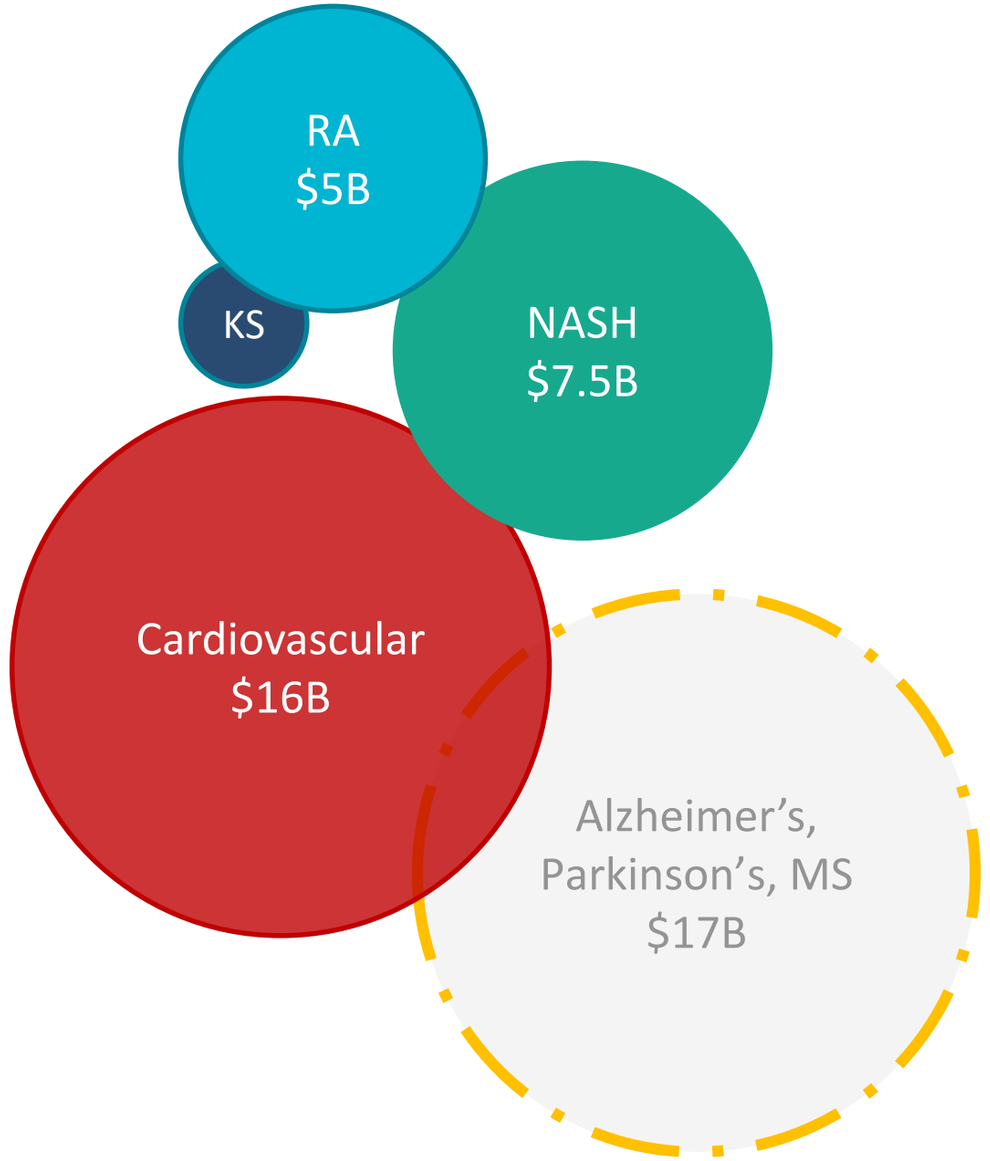


Brain Perivascular Macrophages Initiate the Neurovascular Dysfunction of Alzheimer Aβ Peptides. Circ Res. 2017 Jul 21;121(3):258-269. doi: 10.1161/CIRCRESAHA.117.311054. Epub 2017 May 17.

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

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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, NASH, 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

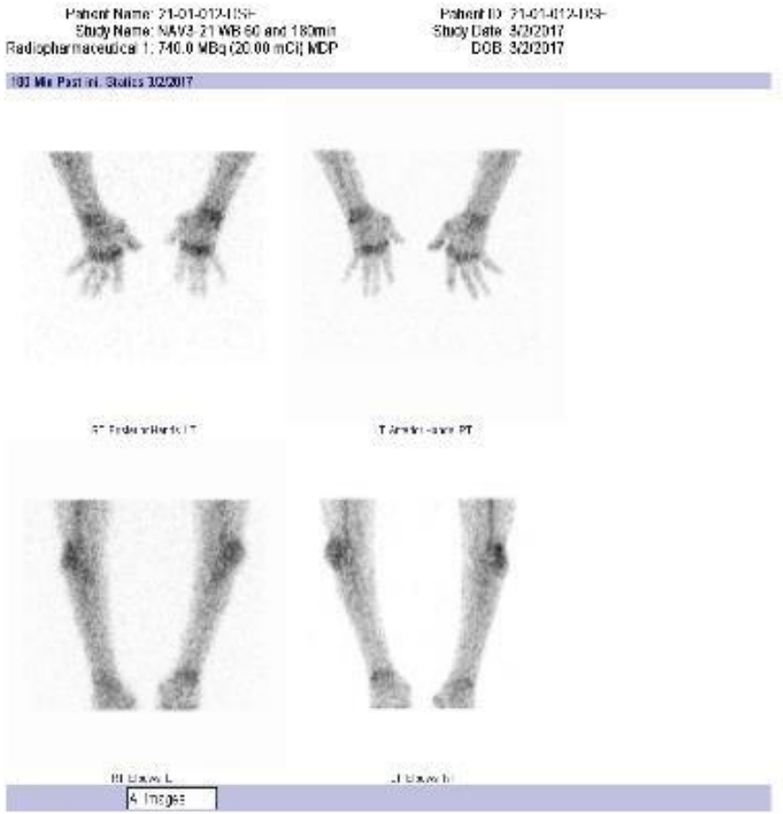
Dose it

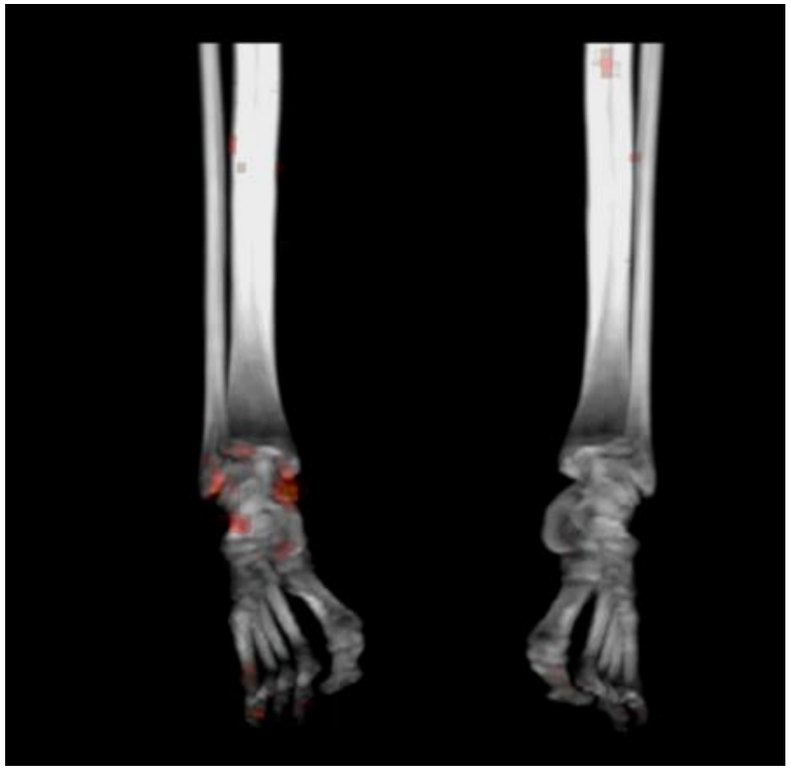
Same for all indications

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

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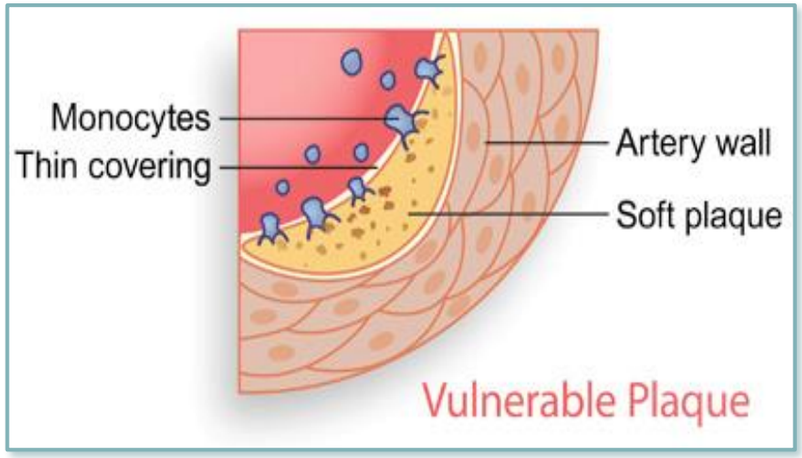
Detect High-risk Plaque

- 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 MGH 1811 MASSACHUSETTS GENERAL 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 Application of a Novel CD206
- **Additional Phase 2 study underway**

Quantifiable Inflammation Score

Computer Read of CV images Creates Quantitative Inflammation Score

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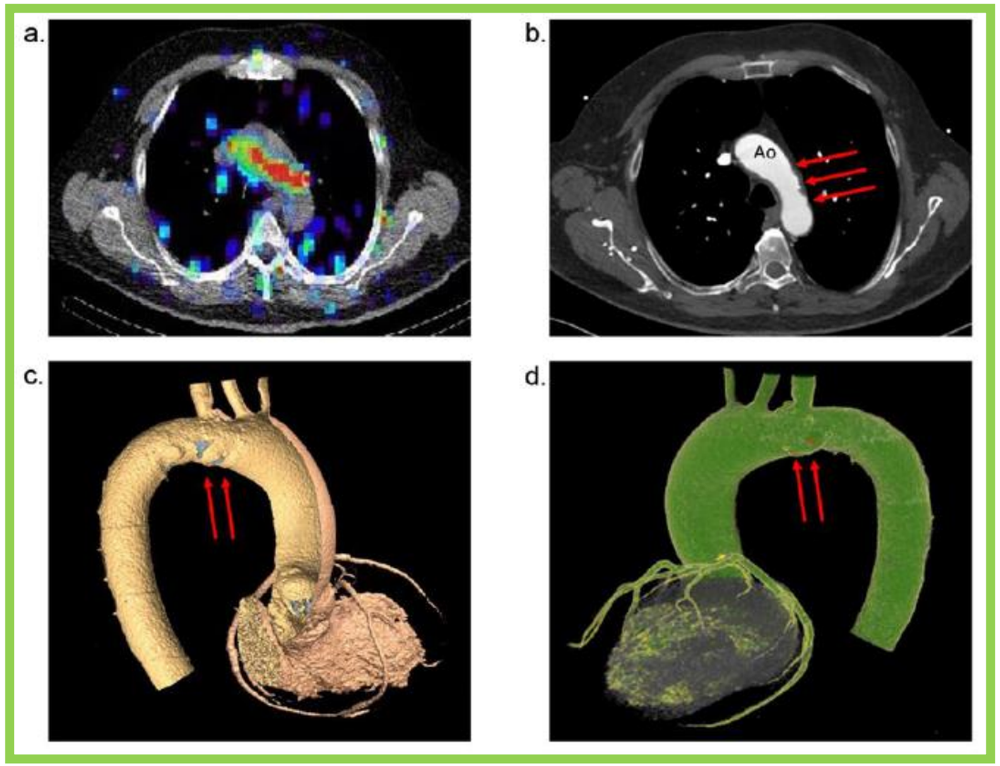
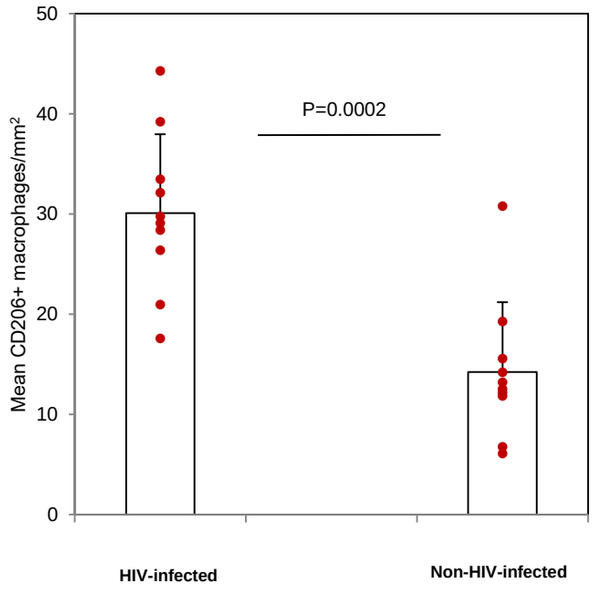
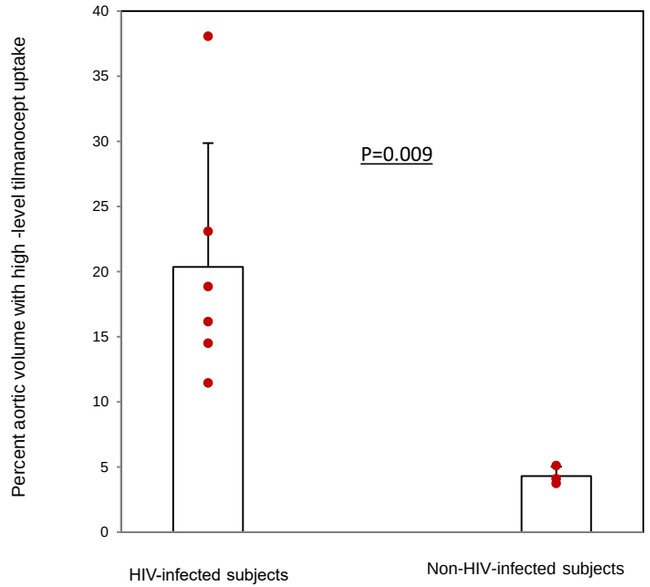
Compiled 2D/3D Imaging



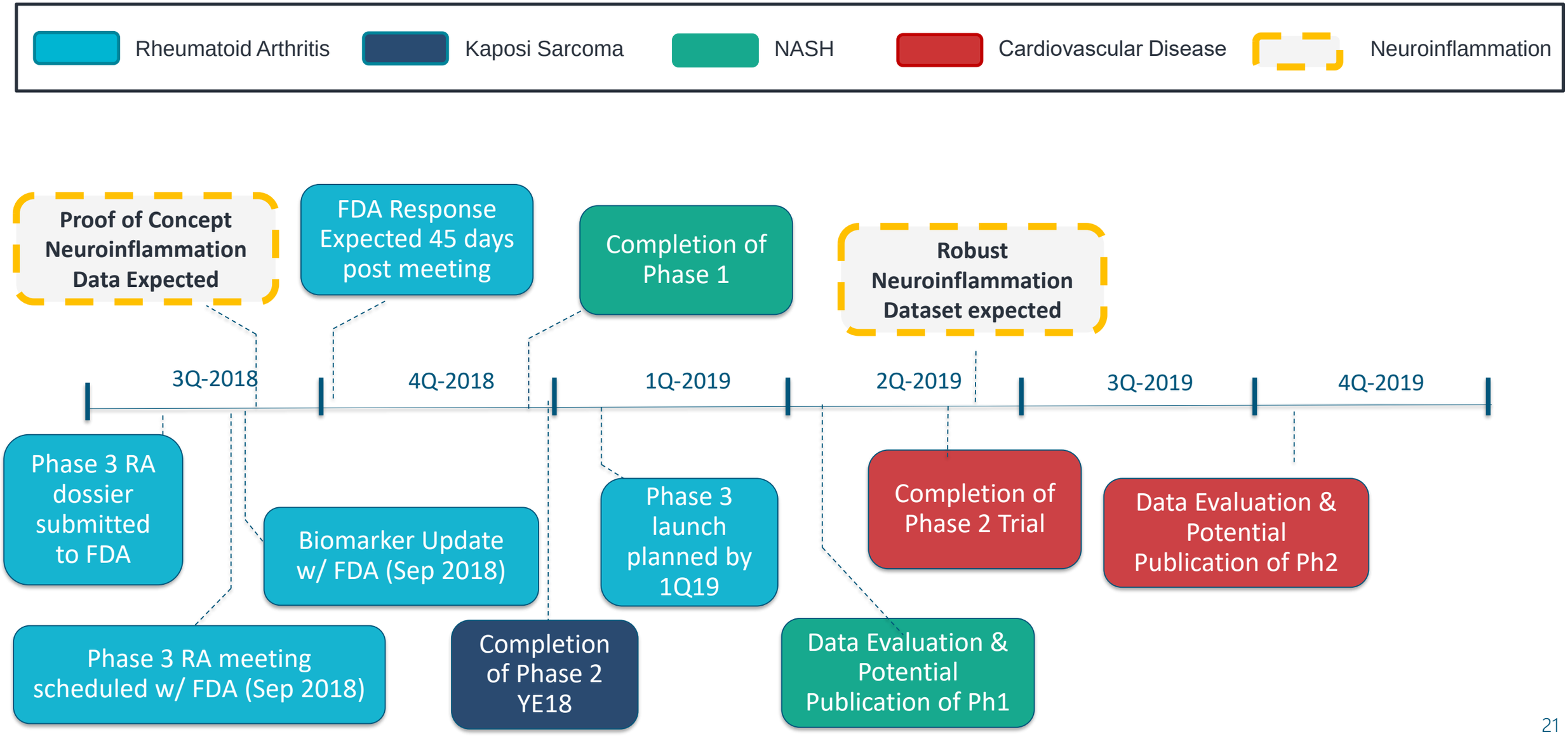
Computer Generated Score of CV Images





Clinical Diagnostics Catalyst Calendar

Clinical Diagnostics Catalyst Calendar



Restructuring Relationship with Macrophage Therapeutics

Pathway to Create Value for “NAVB”

Therapeutic Concept

Selectively targeting Activated Macrophages

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

1 GPS	2 Delivery	3 Payload
		
Mannose Moiety With One Hardwired Address - CD206 Activated Macrophages	Manocept™ Backbone	▪ Chemotherapeutics ▪ Immune-modulators ▪ Tc^{99} ▪ Other Isotopes

Preclinical Models Validate Macrophage Strategy

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

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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

Restructuring relationship with Macrophage Therapeutics

Recently generated pre-clinical data points to accelerated FDA pathway

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

Company Awarded Voucher	Voucher Acquirer	Date Sold	Sale Price ($)
Spark Therapeutics	Jazz	Apr-18	$110 mn
Ultragenyx	Novartis	Dec-17	$130 mn
BioMarin	Undisclosed	Nov-17	$125 mn
Sarepta	Gilead	Feb-17	$125 mn
Asklepion Pharma (Retrophin)	Sanofi	May-15	$245 mn

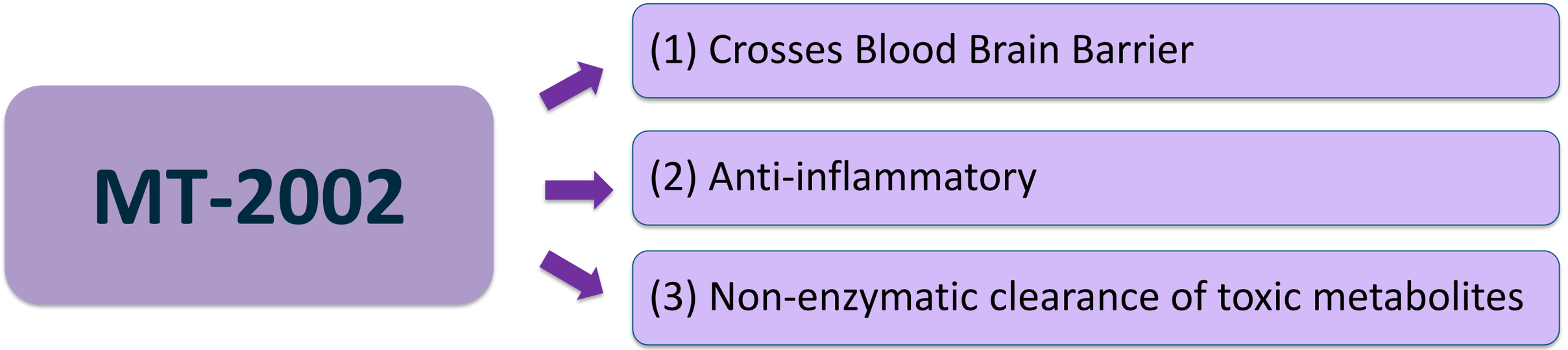
Macrophage Tx Lead Indication

Rare pediatric orphan disease with unmet medical need

- 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: Proof of Concept for Neuroinflammation

Krabbe Disease will prove three key therapeutic traits of MT-2002



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

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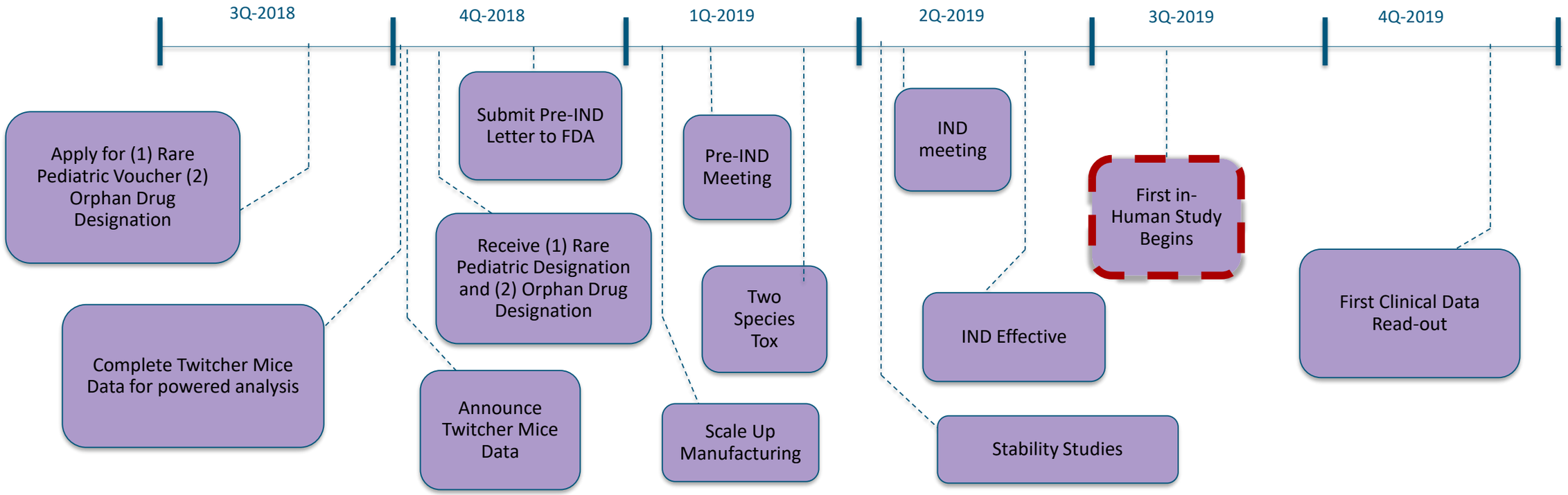
Neuro-Inflammation	1.Parkinson's 2.Multiple Sclerosis 3.Devic's Disease
Lipid Storage Diseases	1.Goucher Disease 2.Niemann-Pick Disease 3.Fabry's Disease

Macrophage Catalyst Calendar

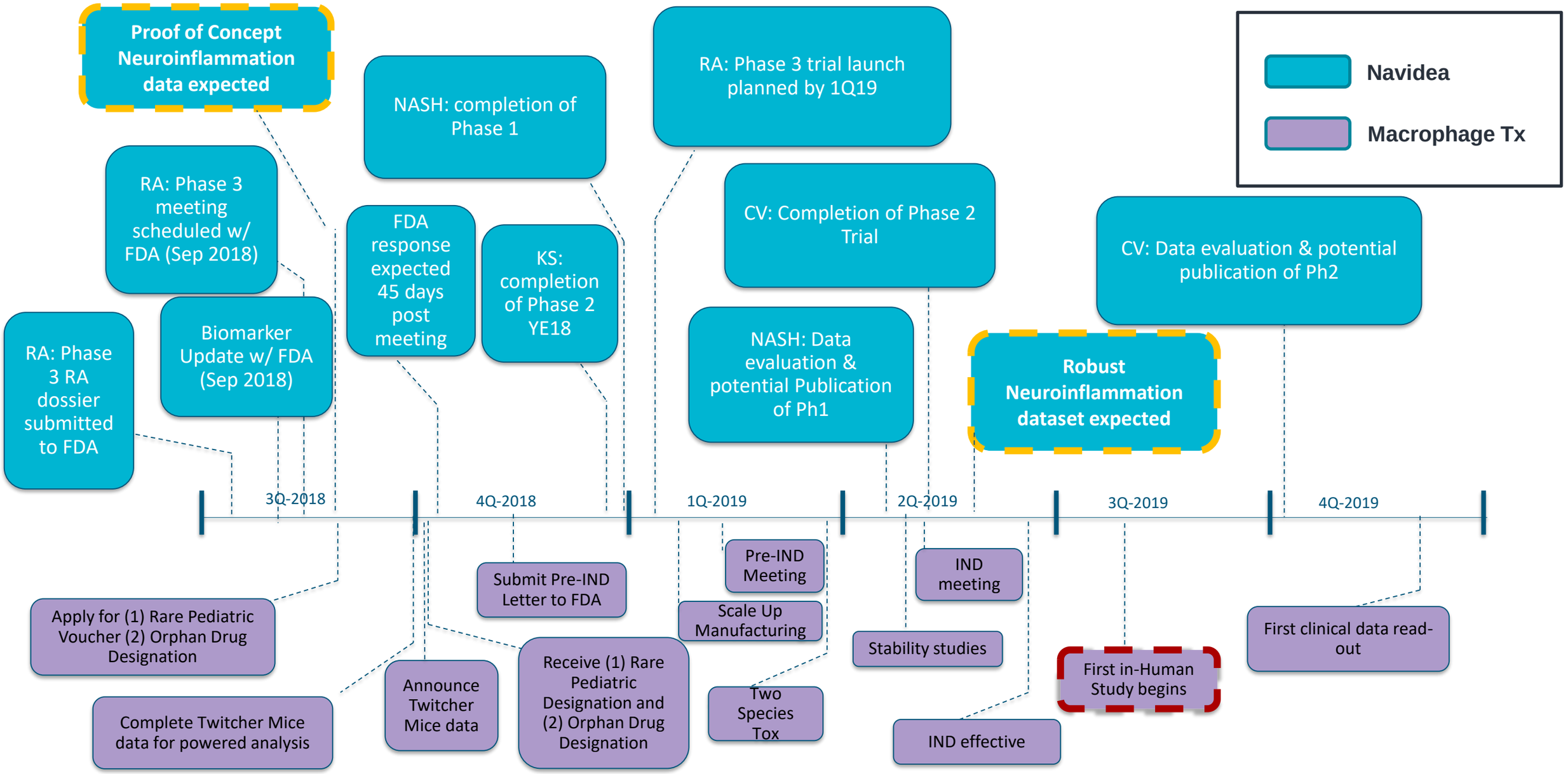
Multiple opportunities to create value over the next 15 months

Orphan indication provides accelerated regulatory pathway

- Provides numerous potential valuation catalysts to create value for Macrophage Therapeutics
- Value creation at Macrophage will directly translate to **value creation for "NAVB"**



Exciting next 15 months for Navidea and MT



End of Phase 2 Meeting with FDA

Timeline

- July 11th – Meeting Request Sent to FDA
- August 9th – Briefing Book Sent to FDA (Includes questions)
- Late September – 90 Minute Meeting with FDA
- Will be utilizing KOLs for the meeting with the FDA
- Up to 45 days post-meeting – Receive meeting minutes with actions and agreements from FDA
- Q1 2019 – Commence Trial post FDA guidance

Thank you

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Contact Details

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