Corporate Overview
Q4 Update
Nov 2015
Highlights

2015

NEW CORPORATE IDENTITY / BRANDING
- WibiWorks Therapeutics → Commence
- Technology: STaRT™

MANAGEMENT TEAM
- Dr. Aline M. Betancourt: Founder & CSO
- Dr. Ruth S. Waterman: Co-Founder & CMO
- Thomas F. Isett: Co-Founder & CEO

CORPORATE STRUCTURING
- Delaware C-corporation
- CA certification
- MD certification

IP PORTFOLIO EXPANSION
- MSC1 cancer immunotherapy
- MSC2 inflammatory immunotherapy

MANUFACTURING & CONTROLS
- Process refinements
- Release assay(s) selected
- CDMO partner for lead PhI/II study

FIRST FDA PRE-IND SUBMISSION
- Lead indication:
  - Acute optic neuritis [AON]
  - MSC2 product: CMB-200
History

Idea
First to show (2007) that Toll-Like Receptors (TLRs) control immunomodulatory properties of mesenchymal stem cells (MSC) 1

SBIR Grants
First of two NIH grants for study of diabetic, painful neuropathy2 & rheumatoid arthritis (2010/2012)

START
MSC 1 & MSC 2 phenotypes characterized3 • Simulated Toll-like Receptor Technology (2010)

WibiWorks
Est. in San Diego (2012); MSC 1 shown to attenuate tumor growth and spread4

Tech Traction
START a "major event" in MSC immunomodulation4. Efficacy demonstrated in >7 disease models (2014)

Commence
Pre-IND submission: CMB-200 for acute optic neuritis (2015)


COMMENCE BIO TIMELINE
Our Vision

Cancer and inflammatory diseases can be optimally treated by rebooting patients' immune systems with a new class of medicinal stem cells: MSC1 & MSC2
• **Stimulated Toll-like Receptor Technology: STaRT**
  
  - **STaRT 41**: Stimulation of TLR4 to create the MSC1 phenotype
  - **STaRT 32**: Stimulation of TLR3 to create the MSC2 phenotype
Safety
MSC1 & MSC2 produced from naïve MSC populations:
Excellent safety profile
>20K patients safely treated

Uniformity
STaRT yields a homogeneous cell population
Improved potency/efficacy per cell dose

Homing
Greater migration capabilities
Improved biodistribution
Lower cell dose requirement

MoA
Multi-pronged effects
Targets innate and adaptive immune mechanisms
Immune system reboot

Simple Mfg
Simple priming step
Allogeneic bone marrow-, adipose-, or iPSC-derived cells
Low COGS

STaRT advantages
Phenotypic advantage: biodistribution

**Migration Capability**

STaRT provides >2x homing

**Biodistribution**

MSC 1 & MSC 2 avoid the lung trap

* Optimized mfg process

* Relative Change in Migration

MSCs MSC1 MSC2

* Optimized mfg process

**Biodistribution**

MSC 1 & MSC 2 avoid the lung trap
**Phenotypic advantage: Multi-pronged effect – MSC1**

### Anti-tumor mechanisms

**Dendritic Cell Therapies**
- e.g. Provenge

**Vaccines/TCell Therapies**
- IMA901

**mAb Checkpoint Inhibitors**
- Ipilimumab, Nivolumab, Tremelimumab, MK-3475

**αCD25, αGITR, Cy**
- Daclizumab, Basiliximab

**DC/ M1 macrophage**
- CD28-C80/86
- IL-12, IL-1, IL-23
- NK cells
- Th1 cells
- CTL
- IFN-γ, TNF-α, IL-17
- Mast cell degranulation
- TRAIL

**Pro-tumor mechanisms**

**CTLA-4-CD80/86**
- PD-1; PD-L1
- rDC/ M2 MF
- MDSC
- Treg cell
- IL-10, TG F-β
- RA
- CCL22/CXCL12
MSC1 efficacy: ovarian cancer immunotherapy

Cells migrate to the tumor site and...

...reverse tumor growth with a single dose

- Efficacy observed at >500K cell dose (human bm-MSC1)
- In humans, expect infrequent IV dosing
Phenotypic advantage: Low dose

1. Naïve MSCs

Heterogeneity\(^1\) → Non-specific biodistribution: e.g. Lung\(^2\)

1.00M Naïve MSCs

50% loss → 0.50M

90% loss → 50K Naïve MSC

Estimate 99% phenotype induction efficiency with STaRP

0.99M MSC\(^1\) → 0.90M

10% loss → 900K MSC\(^1\)

Non-specific biodistribution→

- Cancer-selective, pro-apoptotic secretion of TRAIL
- Promotion of mast cell degranulation
- ↑ IL-6, IL-8, TNF-α, IFN-γ, IL-17
- ↑ Cytotoxic T lymphocytes, NK cells, M1 macrophage

18x more immunomodulatory cells at sites of immune dysfunction

2. Cell Stem Cell 2009, 5:54-63
3. Betancourt - no reported observations of bone marrow- or adipose-derived MSC lacking toll-like receptor 3 (TLR3) or 4 (TLR4)
Phenotypic advantage: Multi-pronged effect – MSC2

**Anti-inflammatory mechanisms**

- **IL-10, TGF-β, IDO, PGE2**
- M2 macrophage
- Treg cell

**Pro-inflammatory mechanisms**

- **TNF-α**
- **IL-6, IFN-γ, IL-17**
- **IL-1**
- Th17 cells
- CTLs
- Mast cell degranulation

**Standard Anti-inflammatory Therapies**
- e.g. NSAIDS, glucocorticoids, steroids, cyclosporins

**Anti-TNFα**
- Adalimumab, infliximab, etc.

**Anti-IL6**
- MoAb (tocilizumab)

**Anti-IL1**
- Anakinra, rilonacept, Xoma 052

**T cell targets**
- Abatacept, daclizumab

**Mast cell targets**
- Pemirolast, cromoglicic acid
MSC2 efficacy: multiple sclerosis immunotherapy

Cells improve clinical scores in EAE* model of MS...

...and deliver a complete response in 30% of subjects

- Restored myelin levels
- Improved motor function
- Relieved pain
- In humans, expecting infrequent IV dosing

* Experimental autoimmune encephalomyelitis

![Graph showing the improvement in clinical scores with MSC2 treatment]
Initial focus: multiple sclerosis

Large market: Therapeutic landscape suggests continuation of unmet medical needs

CD19/CD20/CD52

Interferons

S1P Receptor Modulators

Other Lymphocyte Targeting MOAs

Parenteral

Oral

Small Mol.

Biologic

^ Focused on SPMS and/or PPMS
Demyelinating AON: Often the first sign of multiple sclerosis [MS]

**Healthy**

- Optic nerve inflammation
- Myelination
- Nerve signal

**AON**

- Optic nerve inflammation
- Myelination
- Nerve signal
Demyelinating Disease

- Up to 75% of MS patients have at least 1 episode
- Damage to the retinal ganglion with pain and loss of visual acuity

Many Unmet Needs

- Pain relief, but no notable affect on progression of multiple sclerosis

CMB-200

- For first unilateral AON event
- IV administration
  - Low dose (10M cells)
  - High dose (50M)
  - Repeating (5x10M)

Safety & Efficacy

- Primary: Adverse events
- Secondary:
  - Visual acuity/color vision
  - Visual analog pain scale
  - Thickness: Retinal nerve fiber layer; retinal ganglion cell & inner retinal lexiform layer

CMB-200: Treatment + potential as an MS vaccine
Human therapeutics
- MSC 1 cancer platform
- MSC 2 inflammatory disease platform
- Combo therapeutics: Cell migration capability

Veterinary therapeutics
- MSC 1 cancer platform: e.g. FLV
- MSC 2 anti-inflammatory: e.g. COA

Research / Biofabrication
- Basic / Applied
- Biofabrication – 3D Bioprinting

Low cost manufacturing options
- Bone marrow-derived MSCs, low dose
- Adipose-derived
- iPSC-derived
Commence Bio: objectives

- **Pre-IND → IND**: CMB-200
- **Partner**: MSC1 (Veterinary)
  - MSC1 RUO Cells
- **Launches**: MSC2 RUO Cells
- **IP**: Continue portfolio expansion
- **Financing**: Seeking $6M
  - CMB-200 + other
- **Team**: Build out mgmt, SAB