



***Taking Therapeutic Control of the Immune System™***

BioFinance April 7, 2010

## The New Biotech Model . . . the Return of Innovation

“To return to health and vitality, the biotech sector needs to start . . . by focusing on three central strategies: first, create companies with leaner, more focused business models; second, fund more innovative and less incremental therapies; and third, capture value over the long term by engaging larger firms as collaborative risk-sharing partners earlier in the corporate life cycle.”

*Bruce L. Booth, partner with Atlas Venture, Nature Biotech. Aug. 2009.*

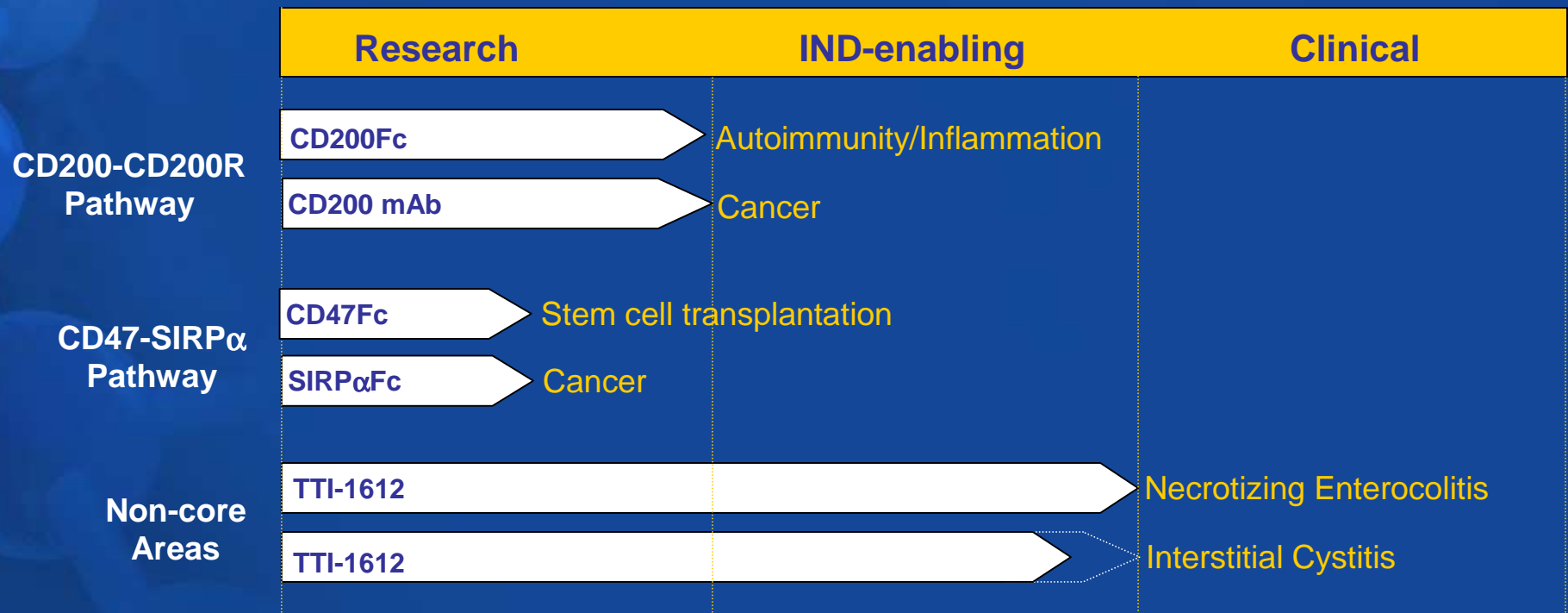
“More selective VC firms will place a greater emphasis on groundbreaking early-stage projects, while later-stage developers will face higher hurdles for gaining cash. I think there’s going to be a surprising shift to the big idea, science-based companies, sort of where we were 20 years ago.”

*David Mott, General Partner, New Enterprise Associates and former CEO, MedImmune Inc  
Mid-Atlantic Venture Association, Sep. 2009.*

## Trillium is Well Positioned for the “New” Era

- Innovative pipeline of proprietary preclinical biologics opportunities
- Strong immunology focus (autoimmune/inflammation & cancer)
- Demonstrated ability to execute business model and establish strategic partnerships
- Capital efficient with a lean infrastructure
- Defined growth & exit strategy

## 2010 Pipeline

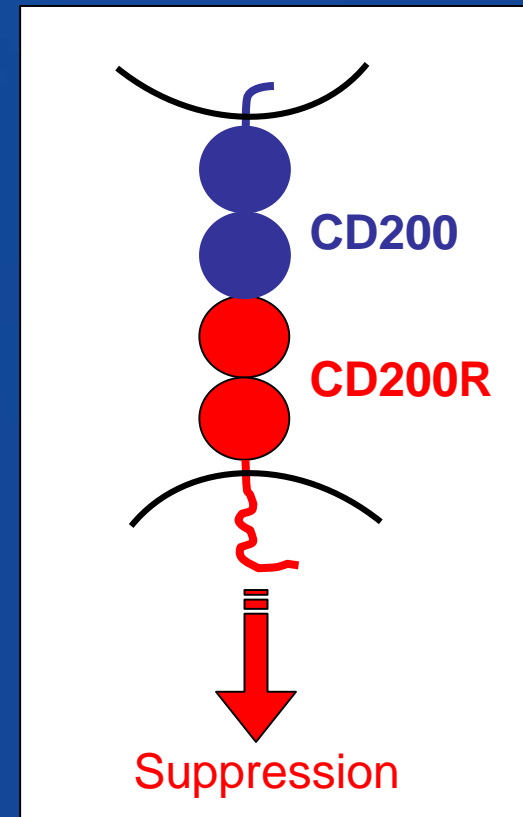


## Trillium's core focus – immunoregulation

- The immune system is a complex network regulated by both positive and negative signals
- There is growing interest in developing drugs that manipulate negative immunoregulatory pathways
- Trillium is focused on two important immunoregulatory axes:  
**CD200-CD200R** and **CD47-SIRP $\alpha$**
- Each pathway has two product opportunities:
  - Agonist to turn ON the pathway → suppression
  - Antagonist to turn OFF pathway → activation

## The CD200-CD200R immunoregulatory axis

- CD200R is expressed on myeloid cells
- Negative signal delivered by CD200
- Multiple suppressive mechanisms:
  - Inhibition of macrophage activation
  - Inhibition of mast cell activation
  - Modulation of dendritic cell function
  - Induction of regulatory T cells
- CD200 homologs encoded by viruses (viral immune evasion)
- CD200 over-expressed by many tumors (tumor immune evasion)



## CD200Fc program

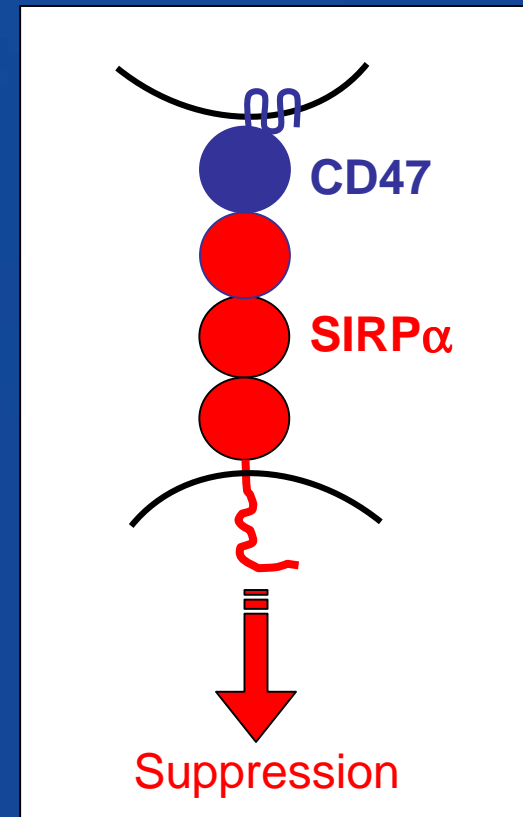
- CD200Fc is a soluble CD200R agonist
- Activates CD200-CD200R pathway to induce suppression
- *In vivo* efficacy demonstrated in numerous animal models:
  - Rheumatoid arthritis (CIA model)
  - Inflammatory bowel disease (TNBS, DSS models)
  - Multiple Sclerosis (EAE model)
  - Lung inflammation (influenza model)
  - Solid organ transplant rejection (allo and xeno models)
- Program licensed to major US biotech company

## CD200 mAb program

- CD200 mAb is a fully human antibody that neutralizes CD200 activity
- CD200 expression by cancer cells leads to suppression of anti-tumor immune responses and is correlated with poor clinical outcome
- CD200 mAb disrupts the CD200-CD200R immunoregulatory pathway allowing the immune system to overcome tumor cell-induced suppression
- *In vivo* efficacy demonstrated in NOD.SCID tumor model
- Program is being 50/50 co-developed with a major US biotech company

## The CD47-SIRP $\alpha$ immunoregulatory pathway

- SIRP $\alpha$  expressed on myeloid cells
- SIRP $\alpha$  binds CD47, a marker of “self”
- CD47 delivers a “do not eat” signal that suppresses macrophage function
- Emerging evidence that this pathway controls hematopoietic stem cell engraftment and protect cancer stem cells



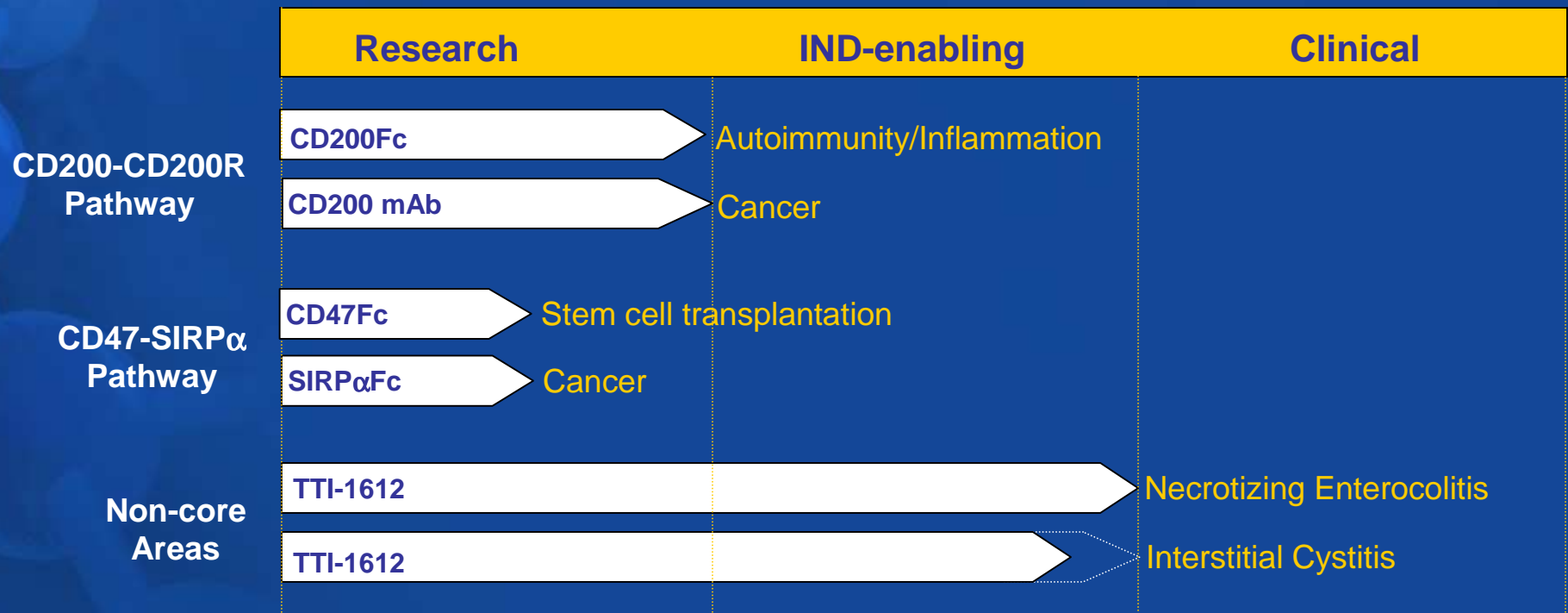
## CD47Fc program

- CD47Fc is a soluble SIRP $\alpha$  agonist
- Activates CD47-SIRP $\alpha$  pathway to suppress macrophages
- Primary indication: hematopoietic stem cell transplantation in cancer patients
- CD47Fc is designed to:
  - Improve stem cell engraftment
  - Accelerate blood cell recovery post-transplantation
  - Enable engraftment with lower doses of stem cells (e.g., cord blood)
- Program in research stage

## SIRP $\alpha$ Fc program

- SIRP $\alpha$ Fc is a soluble antagonist
- Blocks the CD47-SIRP $\alpha$  pathway to activate macrophages
- Primary indication: acute myeloid leukemia (AML)
- CD47 expression by AML leukemic stem cells leads to suppression of anti-tumor immune responses
- Program in research stage

## 2010 Pipeline



## Non-core programs – TTI-1612

- TTI-1612 is a recombinant soluble form of heparin-binding epidermal growth factor-like growth factor (HB-EGF)
- HB-EGF properties:
  - Induces cell proliferation (especially intestinal and bladder epithelial cells)
  - Anti-inflammatory
  - Anti-apoptotic
- TTI-1612 is being developed for:
  - Prevention of necrotizing enterocolitis (NEC) in premature infants
  - Treatment of interstitial cystitis (IC)

## Necrotizing enterocolitis (NEC)

- NEC is a devastating intestinal disease of premature infants
- Patients exhibit GI inflammation, bowel necrosis and sepsis
- Affects ~10% of very low birth weight (<1500 g) newborns
- Cause unknown; contributing factors include gut immaturity, inflammation, ischemia and enteral feeding
- No cure – treatment consists of medical support and surgery
- 30%-50% mortality rate; survivors frequently suffer long-term complications



## TTI-1612 NEC program

- TTI-1612 shows remarkable efficacy in animal models of NEC and intestinal ischemia/reperfusion injury
- TTI-1612 operates through multiple mechanisms:
  - Stimulates intestinal epithelial cell proliferation and migration
  - Decreases intestinal apoptosis
  - Decreases intestinal permeability
  - Decreases pro-inflammatory cytokine production
  - Increases mesenteric blood flow
- TTI-1612 can be administered orally
- IND in place for healthy adult volunteer safety study

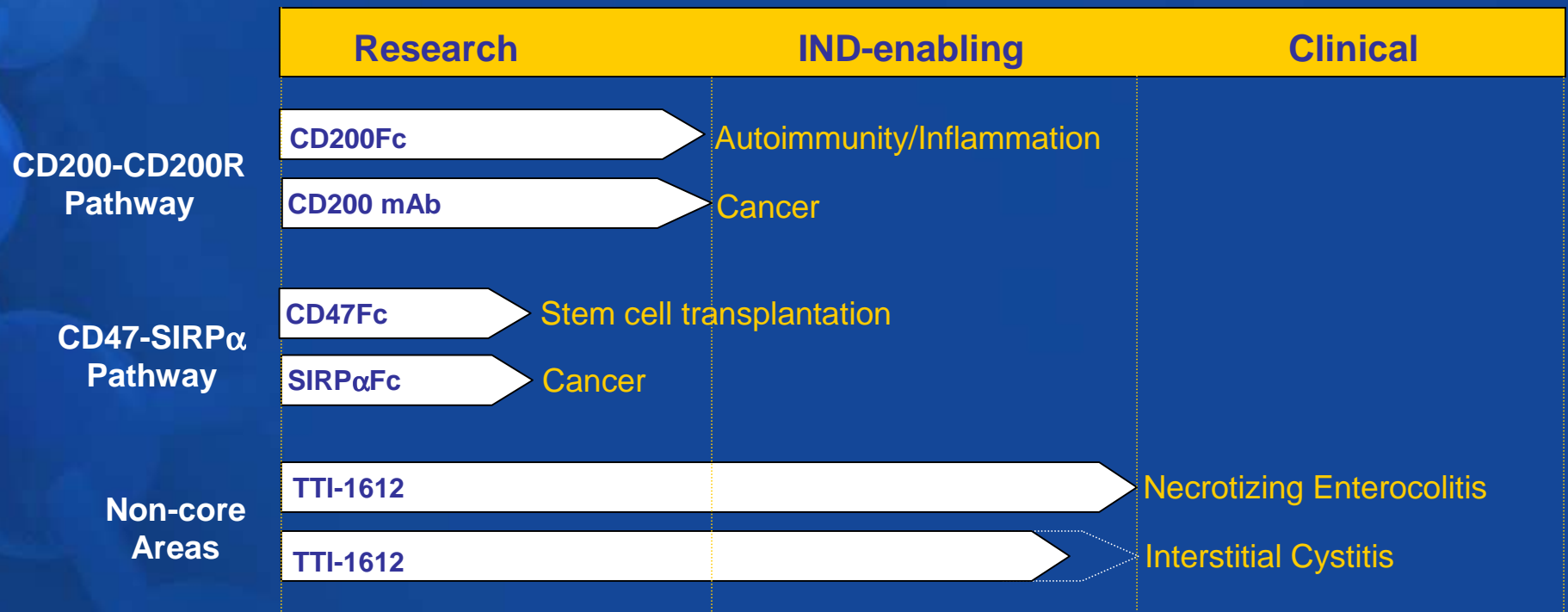
## Interstitial cystitis (IC)

- IC is a chronic bladder condition characterized by pain, urgency/frequency and nocturia
- Disease affects ~1 million people in the US (90% women)
- Patients often suffer with severe symptoms that impact sleep, work and social routines, and report lower quality of life than those with chronic renal failure
- Current therapies fail to adequately control symptoms in many patients
- Leaky bladder epithelium plays a major role in disease development
- IC patients have reduced urinary levels of HB-EGF, which may contribute to epithelial dysfunction

## TTI-1612 IC program

- TTI-1612 is being developed as a local (intravesical) therapy to correct the epithelial dysfunction in IC patients
- TTI-1612 stimulates the proliferation and reduces the permeability of IC bladder epithelial cells *in vitro*
- TTI-1612 normalizes the aberrant phenotype of IC bladder epithelial cells *in vitro*
- TTI-1612 stimulates the proliferation of bladder epithelial cells *in vivo* following intravesical administration
- Program is in “IND-enabling” phase (4 months from IND/CTA)

## 2010 Pipeline



## Capitalization

- \$5 million follow-on financing (Sept. 2008)
- \$9 million licensing revenues (2004-2010)
- \$13.5 million Series A financing (2003-2004)

## Major shareholders

- Vengrowth Advanced Life Sciences Fund
- Growthworks Canadian Fund
- BDC Capital

## Growth & Exit Strategy

1. Establish Trillium as a premier R&D company:
  - Broad pipeline of innovative, focused and synergistic biologics programs
  - Capture long-term value and risk-sharing through select partnerships
  - Maintain low G&A cost and lean infrastructure
  - Use preferred relationship with Toronto's immunology community to fuel pipeline
2. Trade sale to a larger public company:
  - Existing partner
  - Competitor
  - Clinical company seeking R&D capacity supporting development programs

## Trillium Investment Opportunity

1. Innovative pipeline of proprietary preclinical biologics opportunities
2. Strong immunology focus (autoimmune/inflammation & cancer)
3. Demonstrated ability to execute business model and establish strategic partnerships
4. Capital efficient with a lean infrastructure
5. Defined growth & exit strategy

## Contacts

**Niclas Stiernholm, PhD**

Chief Executive Officer  
Tel: 416-595-0627 x222  
niclas@trilliumtherapeutics.com

**Bob Uger, PhD**

Vice President, R&D  
Tel: 416-595-0627 x260  
bob@trilliumtherapeutics.com



*96 Skyway Avenue  
Toronto, Ontario, M9W 4Y9  
CANADA*