



Bringing targeted and safer therapies to market

# Tolera Therapeutics Inc

## Company Overview

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## Short Course Immune Induction Therapy (SCIIT)

*An industry trend employing rapid, specific, short-term modulation of the immune system using a therapeutic agent to induce T-cell non-responsiveness, also known as operational tolerance.*

T-cell  
Inactivation

Safe Mechanism  
of Action

### ***T-cell Disease Applications:***

- **Transplant induction (Tolera focus)**
- Bone marrow transplant
- Type 1 diabetes
- Multiple sclerosis
- Other T-cell mediated disease

*Wikipedia: [http://en.wikipedia.org/wiki/Short\\_Course\\_Immune\\_Induction\\_Therapy](http://en.wikipedia.org/wiki/Short_Course_Immune_Induction_Therapy)*

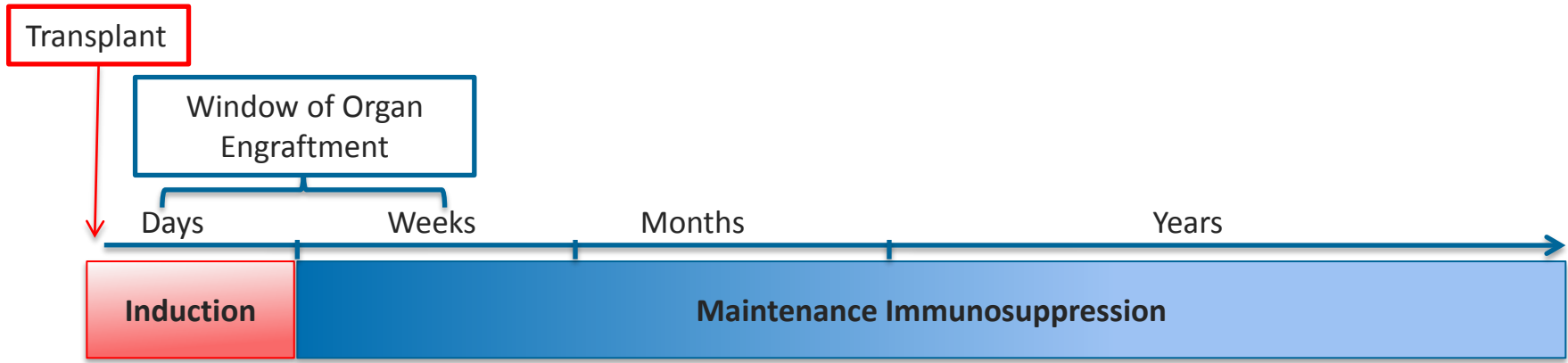
# Summary – Transplant Opportunity

- Highly profitable niche market - \$500 million
- Growing demand for induction drugs
- Single primary drug in market – Thymoglobulin
- No viable candidates in pipeline

**TOL101 in market  
changes competitive landscape**

**Significant value creation**

# Transplant Therapy Landscape



## Induction Agents

Thymoglobulin (rATG) Genzyme  
 Simulect (basiliximab) Novartis

**TOL101 (anti-TCR) TOLERA**

## Maintenance Immune Suppression Cocktail

**Primary**  
 Prograf (tacrolimus) Astellas  
 Neoral (cyclosporine) Novartis  
 Generic cyclosporine Sandoz

**New**  
 belatacept BMS

**Adjuvant**  
 CellCept (mycophenolate) Roche / Genentech  
 Myfortic (mycophenolate) Novartis  
 Rapammune (sirolimus) Pfizer  
 Zortress (everolimus) Novartis

**Corticosteroids**  
 Prednisone / Methylprednisolone

## Others

**Valcyte**  
 (valganciclovir)  
 Roche/Genentech

- Maintenance cocktail combines steroid with primary.
- Adjunctive therapy use varies by patient/site.
- Maintenance intensity (dosing) reduced over time.
- Patients usually weaned off steroids over time



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# Power and Growth of Induction Therapy

- Aging population has heightened the risk variables of transplantation (donors, recipients, quality of organ).
- Induction therapy has cut the rate of rejection by two thirds, and is a growing market.
- Induction therapy permits better engraftment, reduces use of toxic maintenance drugs.
- Induction therapy improves organ acceptance/function.
- Induction therapy holds potential for future implementation of tolerance induction strategies.

# Renal Transplant Market Need

- 1) Short course induction is generally accepted, and increasing – but over-suppression, increased complicating events evident
- 2) Thymo (off label) is uncontested standard-of-care
- 3) Thymo safety issues well known – tolerability, infusion reactions, infection rates, all managed at high cost, patient and organ risk - a significant industry and regulatory concern
- 4) There is a need for induction alternatives and pipeline

Doctors, regulators and drug companies are open to next generation therapies to move beyond Thymoglobulin

# Snapshot Transplant Induction Market

*US market only - 2008*

All Solid Organ - USA	Xplants Base Yr 2008	
Thymo	8,500	Significant uptake in kidney, but less used in other solid organ
<b>Simulect (Basiliximab)</b>	<b>4,000</b>	<b>Plateaued</b>
<b>Alternatives (Zenapax, OKT3, Atgam, Campath)</b>	<b>5,700</b>	<b>Available alternatives disappearing</b>
No reported induction	9,200	Induction use increasing
<b>Total</b>	<b>27,400</b>	

- Induction is proven to lower rejection and is growing globally
- Alternatives to Thymo in high demand
- Adoption of induction use continues to grow, driving market expansion

• Addressing just the Basiliximab and alternatives segment of the market is \$100M in the USA, excluding induction growth, Thymo, and rest of the world.

# Worldwide Transplant Induction Market Growing

## Base Case Transplant Induction Therapy

Worldwide	2012	2013	2014	2015	2016	2017	2018	2019
Potential induction market (\$M)	\$500	\$538	\$573	\$614	\$657	\$693	\$750	\$790

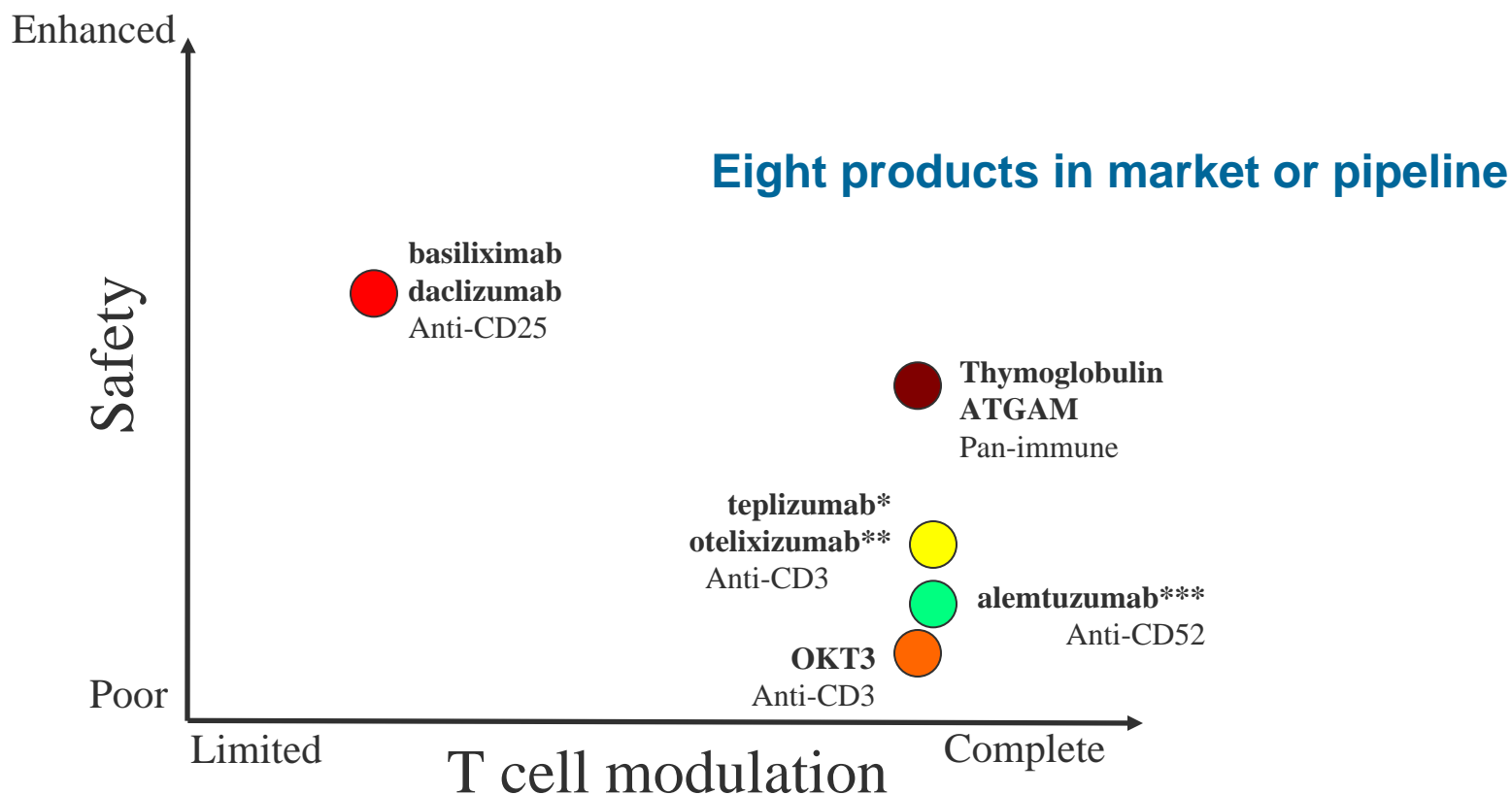
### Notes on Transplant Forecast:

- US represents just under half of worldwide transplants (~28,000 of ~65,000)
- Includes only base-case transplant antibody induction market, all organ transplants
- Excludes any upside for autoimmune applications, Type 1 diabetes, MS, etc.
- Excludes any upside for bone marrow, stem cell transplant applications

### Thymoglobulin / Sanofi (Genzyme):

- Estimated sales ~\$250M in 2011
- Financial filings report double-digit growth

# Early 2000's Competitive Landscape

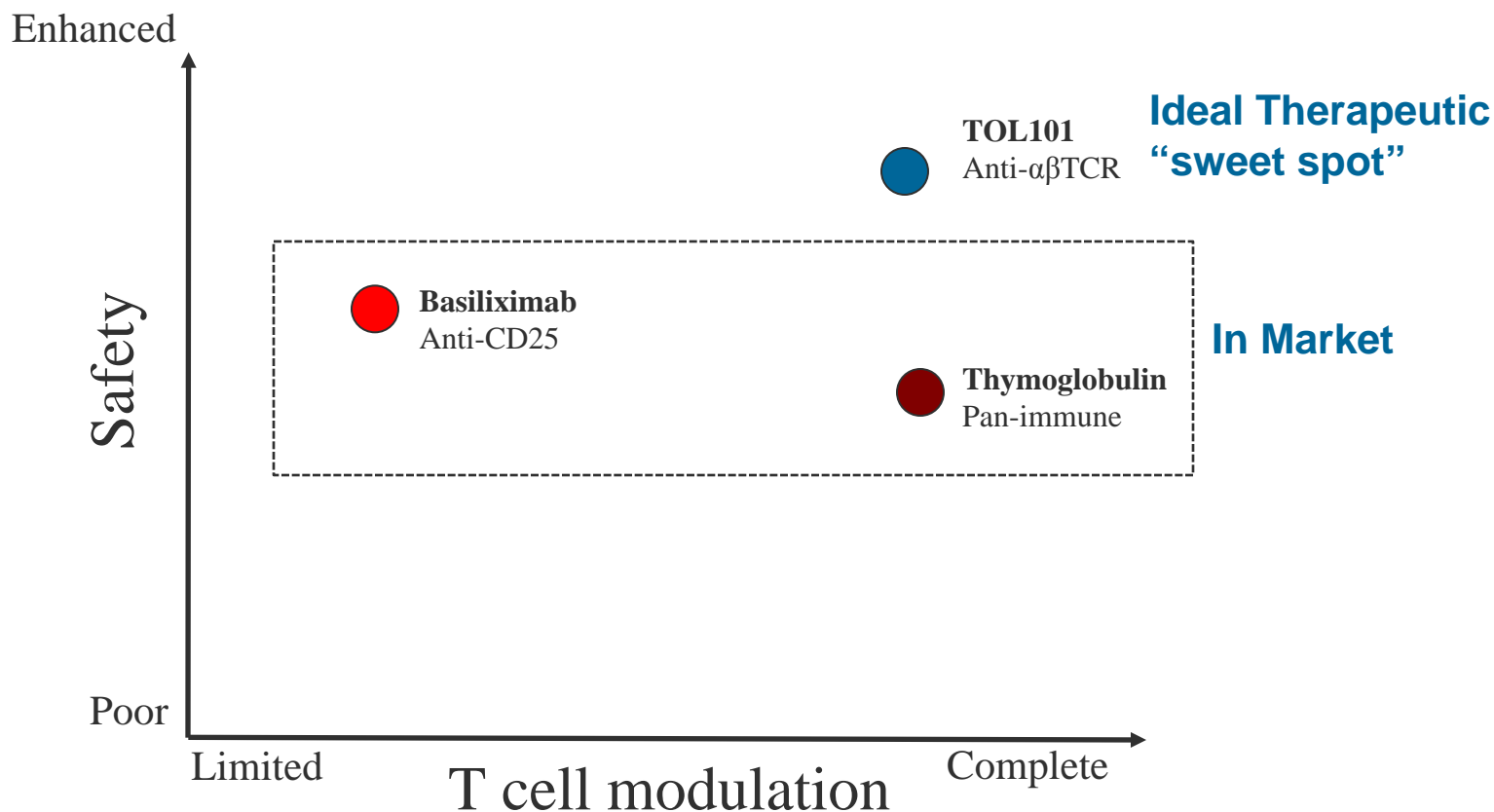


\* Teplizumab (Lilly/Macrogenics) failed to show efficacy for induction – likely due to narrow therapeutic index.  
Clinical trial halted Oct. 2010

\*\* Otelixizumab (GSK/TolerX) failed to show efficacy for induction – likely due to narrow therapeutic index.  
Clinical trial halted Mar. 2011

\*\*\* Alemtuzumab acquired by Sanofi/Genzyme – to be pulled from market and re-labeled / re-marketed for MS at \$60k per patient – no longer available to transplant.

# Today's Competitive Landscape



- **Highly toxic drugs departing market**
- **No credible pipeline in the industry**
- **Thymoglobulin use is off-label, with multiple risks to safety**

# TOL101 - Short Course $\alpha\beta$ TCR Antibody

*A novel technology with demonstrated safety benefits*

- **Novel:** T-cell targeting ( $\alpha\beta$ TCR) monoclonal leveraging unique mechanism of action
- **Effective:** Quickly and specifically down regulates the immune system
- **Safety Proposition:**
  - low/no cytokines
  - low immunogenicity
  - lower infection risk
  - lower cancer risk
  - rapid restoration of immune function
- **Expected Benefit:** Better tolerated - better overall therapeutic index

# Product Profile TOL101

*Induction is a growing market with few product alternatives*

Thymo – polyclonal with increasing safety issues  
but growing with no alternatives

**TOL101 Profile:** TOL101 is expected to be:

- **safer and better tolerated than Thymo**
- **as effective as Thymo** in preventing rejection
- **more effective than Basiliximab** in preventing rejection

## **TOL101 Market:**

New alternative in growing market

~ 20% growth per year

Replace alternatives in market

~ \$200 million immediate  
revenue opportunity

Safer alternative changes sentiment on Thymo

~ take 1/2 – 2/3 share

Safer induction option expands use across all organ types, led by kidney

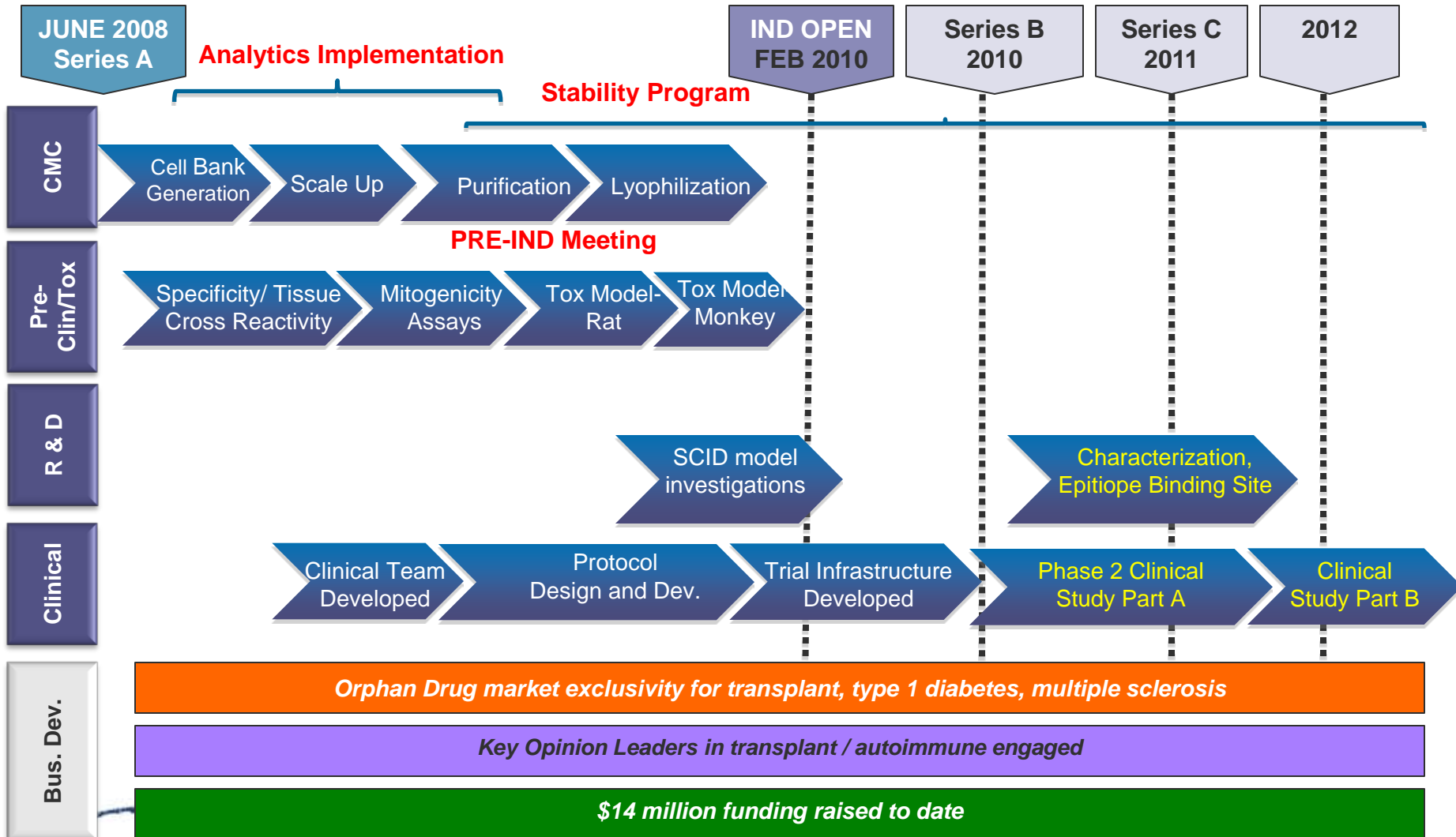
Basi – IL2 lacks targeted efficacy, declining share

# Path to Market: Goals, Time and Cost



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# Significant Progress Made To Market Entry



## Phase 2 – Part B

### Establish safety profile and competitive position vs Thymo

- *On standard transplant endpoint (event-free survival)*
- *Sufficient patient population and dosing to establish safety index*
- *Competitive positioning opportunities vs Thymo:*
  - *Drug tolerability*
  - *Reduced infusion reactions, fewer interrupted infusions*
  - *Easier dosing (peripheral vs central lines)*
  - *Lower cytokine release*
  - *Broader therapeutic index*

## Phase 3

### Registration trial – file BLA

- *Get to BLA filing / market approval by shortest path possible*
- *Standard transplant endpoint (event-free survival)*
- *Active comparator Thymo or basiliximab or both (tbd)*

# Value Generation Options

## TODAY

- Establish safe dosing, Tcell modulation
- Prove path to market, competitive to market leader

### Comparables

Macrogenics

> \$1B deal with Lilly (hOKT3)

TolerX

> \$760 M deal with GSK (hOKT3)

SangStat

> \$700 M acquisition by Genzyme (Thymoglobulin)

## VALUE DRIVERS – TOMORROW

- Get TOL101 into market / BLA
- No market pipeline ~ \$500 million plus available

## STRATEGIC OPTIONS

- Strategic partner (2011, 2012)
- Pharma acquisition (2012 -)
- Market approval / IPO

- Highly profitable niche market - \$500 million today
- Growing demand for induction drugs
- Single primary drug in market - Thymoglobulin
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**TOL101 in market  
changes entire competitive landscape**

**Significant value creation**