



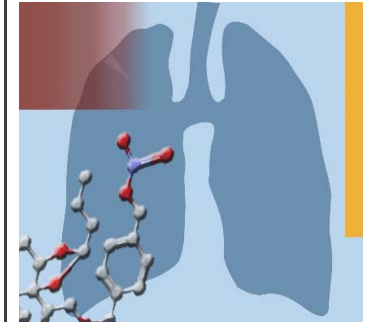
*Innovators in respiratory therapeutics*

# Corporate Presentation

**April 2009**

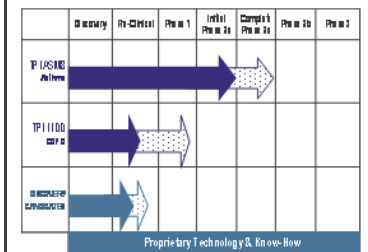
## Leading respiratory biotech

- Focused on developing novel and innovative drugs to treat respiratory diseases
- Unique multi-targeting approach against inflammation
- Leading company in the discovery & development of oligonucleotide drugs for respiratory diseases



## Advanced, innovative product portfolio

- Two drug candidates progressing in development
- Designed to address unmet clinical needs in asthma & COPD
- Targeting high growth, high value market segments



## Focused business strategy

- To advance compounds through Phase II, then partner for late-stage development and commercialization to leverage exit



## Privately-held

- Founded in 2000; raised C\$65 million in equity to date



**Mark Parry-Billings, PhD** Chief Executive Officer



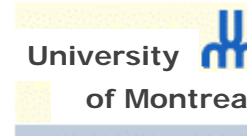
**Robert Boisjoli, CA** Chief Financial Officer



**Lisa Nolan, PhD** Chief Business Officer



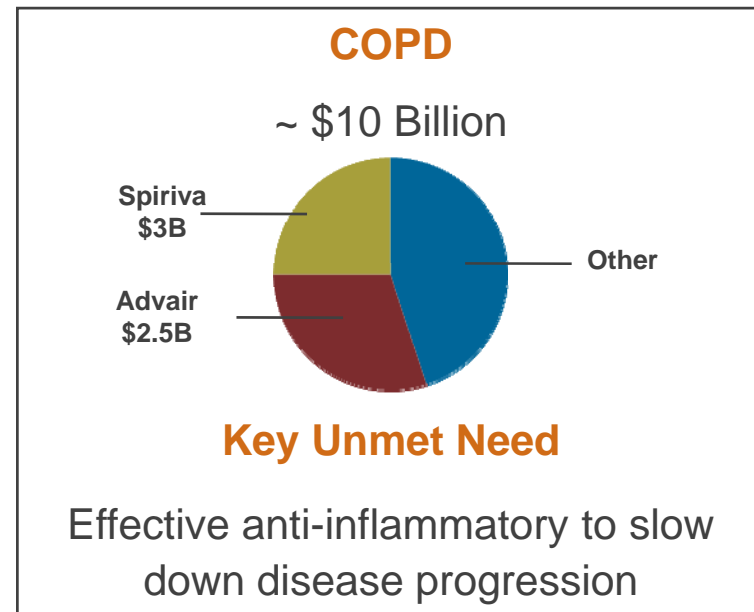
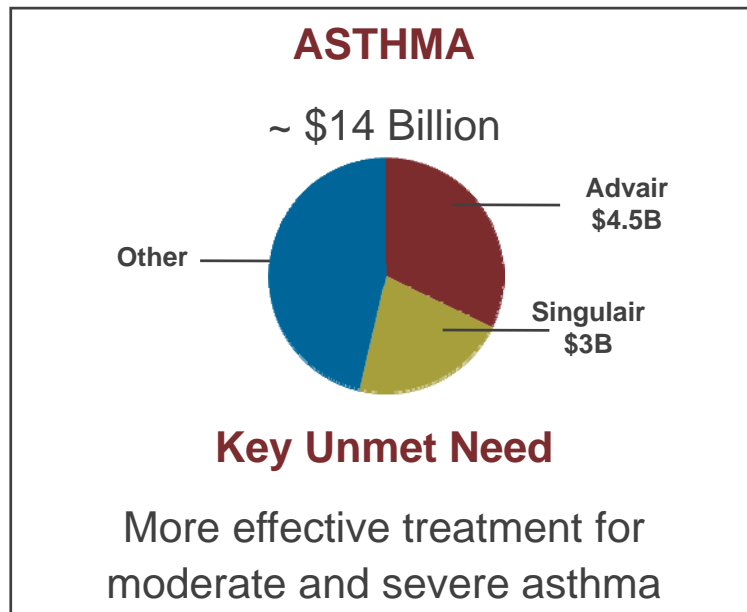
**Paolo Renzi, MD\*** Chief Medical Officer and Founder of Topigen

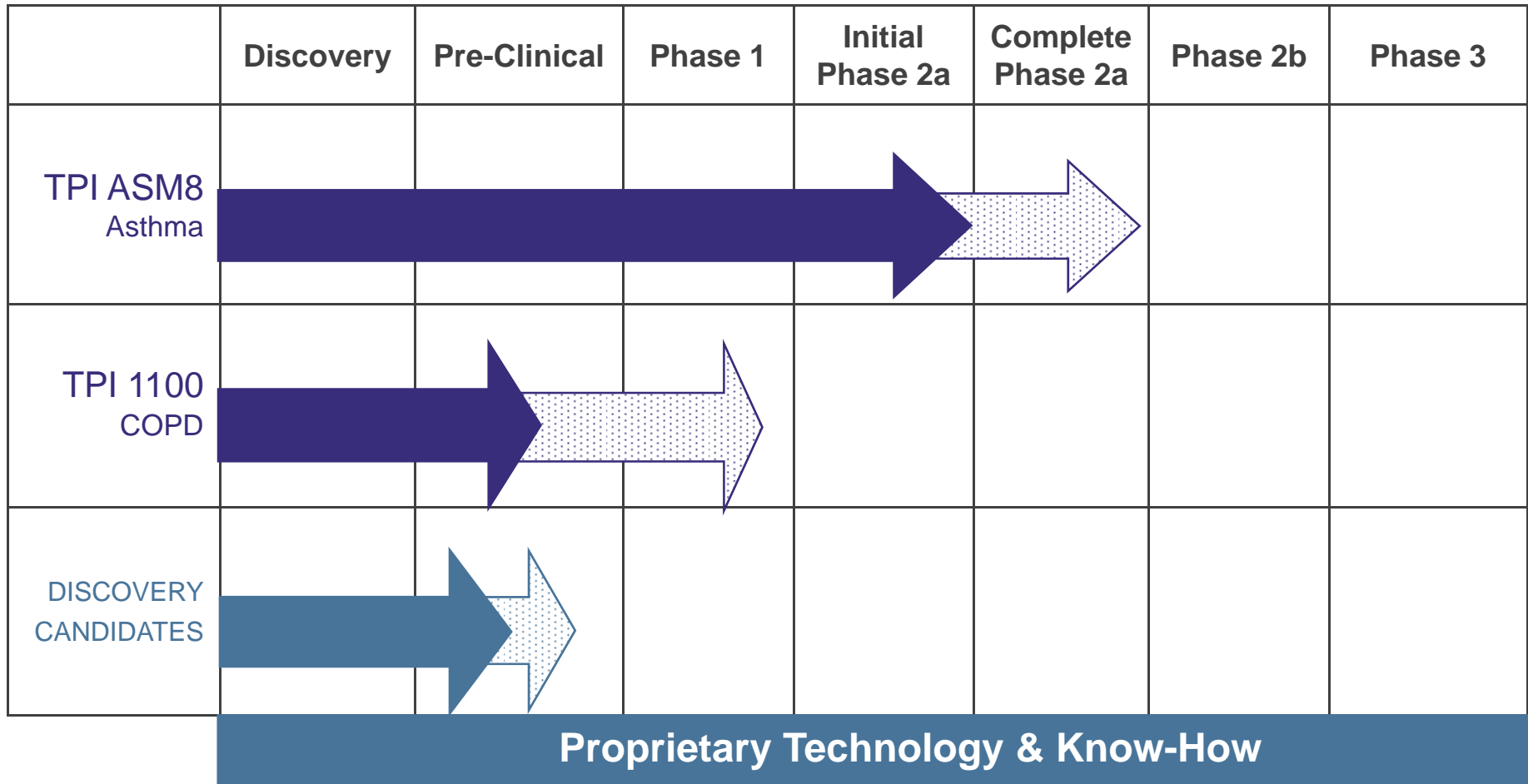


\* Part-time

Leading Therapy Classes by Global Pharmaceutical Sales, 2007		2007 SALES (US\$ BN)	% GROWTH YEAR-OVER-YEAR
1.	Oncologics	41.4	16.2
2.	Lipid lowering agents	33.7	-6.7
3.	<b>Respiratory Agents</b>	<b>28.6</b>	<b>12.3</b>

Source: IMS Health Incorporated





\*Dotted arrows indicate progress to end 2010

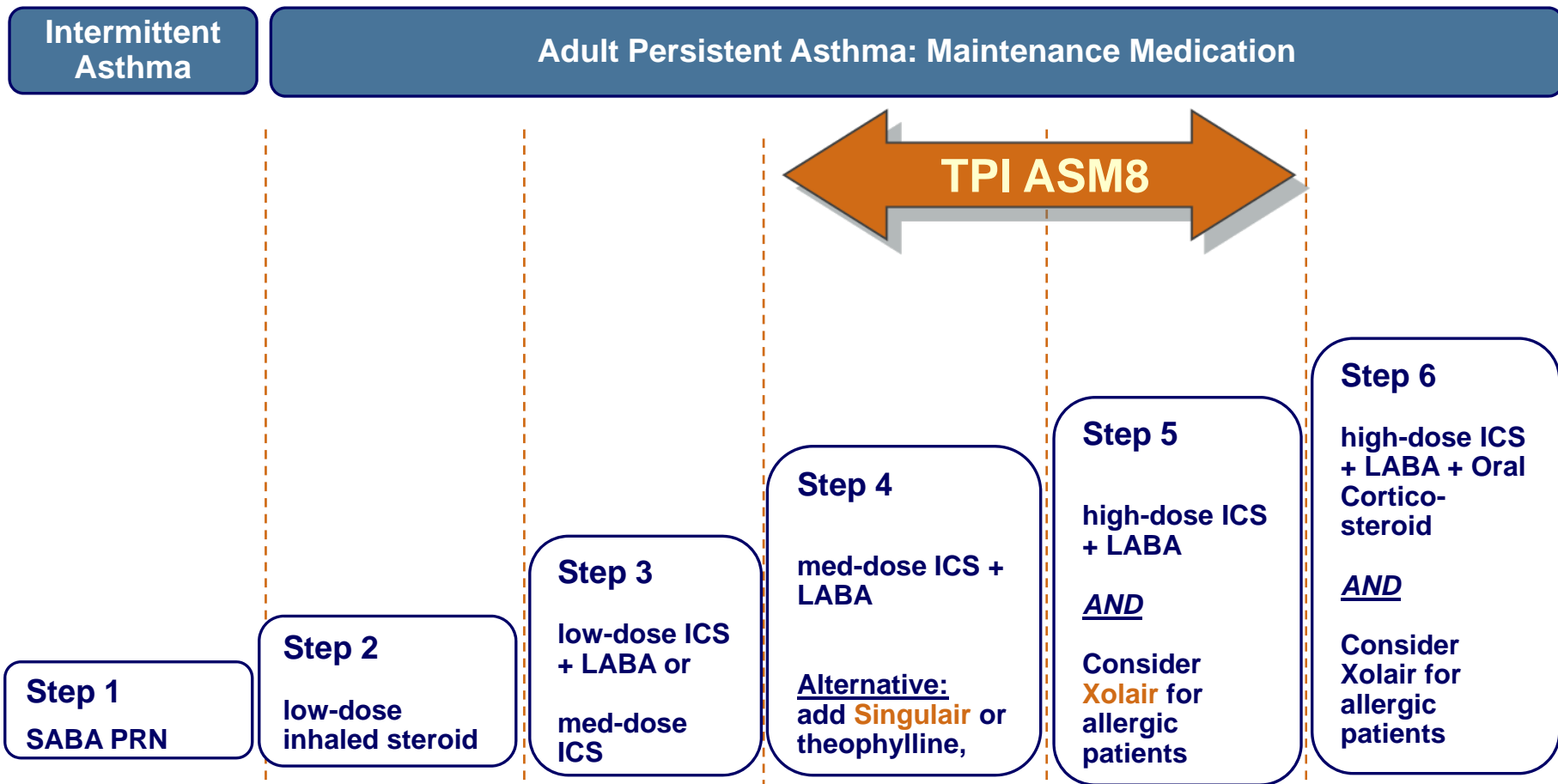
## PROFILE

- Inhaled anti-inflammatory
- Novel mechanism of action
  - Targets CCR3, IL-5, IL-3, GMCSF
- Indication: moderate / severe asthma
- Once-daily dosing



## DEVELOPMENT

- Two phase 1 studies completed
  - 38 subjects treated
  - “Clean” safety profile
- Two phase 2a studies completed
  - 35 patients treated
  - Preliminary proof-of-concept in first study
- Robust formulation
  - Nebulized solution with no special formulation/ delivery required
- Path forward in phase 2a clinical and toxicology program defined



The National Asthma Education & Prevention Program Expert Panel Guidelines, 2007

SABA=short-acting beta agonist, ICS=inhaled corticosteroid, LABA=long-acting beta agonist

### TPI ASM8 was effective at low (~200 µg) lung dose

- Inhibited target gene expression
- Inhibited influx of inflammatory cells
- Inhibited the early and late asthmatic response (FEV<sub>1</sub>) after allergen challenge

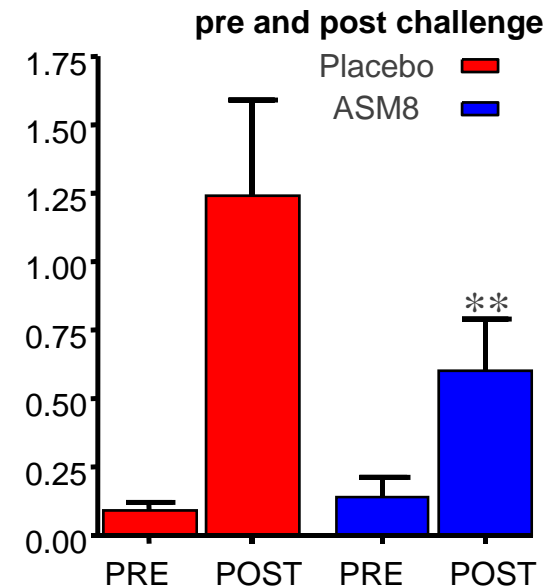
### TPI ASM8 was safe and well tolerated

- With low (<1%) systemic exposure

### First study to demonstrate:

- Efficacy in application of RNA silencing targeting drug in lung disease
- Support for multi-targeted approach

### SPUTUM EOSINOPHILS CELL COUNT (x10<sup>6</sup>cells/ml)



Gauvreau, et al. Am J Respir Crit Care Med 2008;2:952-958

### PROFILE

- Unique dual PDE 4 & PDE 7 inhibitor
- Inhaled once-daily
- Indication: COPD ± Asthma
- Systemic exposure is minimal following inhalation; expect significant safety advantages vs small molecule PDE inhibitors
- Potential for greater efficacy through dual PDE 4/PDE7 inhibition

### DEVELOPMENT

- Compelling pre-clinical data
  - Potential for greater potency with oligonucleotide and PDE4/PDE7 approach
- Robust formulation
  - Nebulized solution with no special formulation/delivery required
- Clinical and toxicology program defined



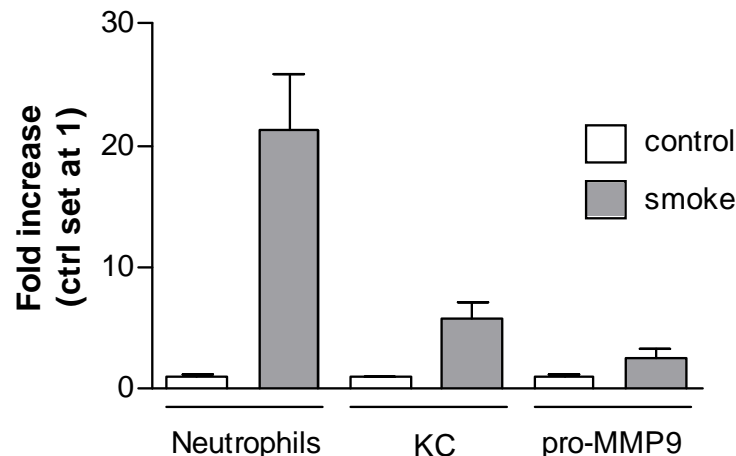
- Prevalence estimated at 41 million in the USA and EU
- Prevalence predicted to grow at 1-2%/annum due to expanding epidemic of smoking, aging population and improved diagnosis
- Very high unmet need for novel anti-inflammatory drugs to:
  - Impact the underlying inflammation and improve prognosis
  - Reduce exacerbations and hospitalizations
  - Inhaled corticosteroids do not impact disease progression in COPD

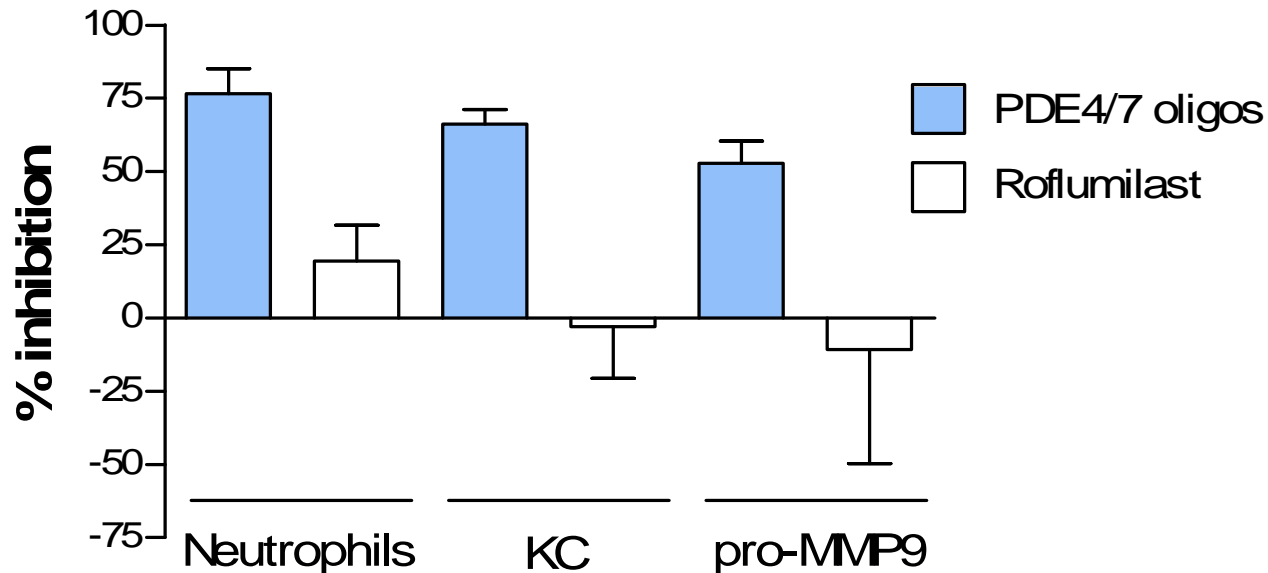
*“The argument is that corticosteroids are the wrong anti-inflammatory for COPD and I think it is o.k. to use them as a placeholder, but hopefully we will get some better anti-inflammatories coming along and we will be able to replace them.”*  
**COPD Specialist, US, Topigen KOL Research, 2008**

*“In COPD, if the goal is to improve FEV1 and reduce exacerbations, then this would be interesting because there is no current therapy that addresses these issues.*

**Pulmonologist, Europe, KOL Interviews, 2008**

- **PDE4/7 Oligo**, 0.2 mg/kg, once every 2 days (4 treatments), inhaled
- **Roflumilast**, 5 mg/kg, daily (4 treatments), oral
  - Daxas™ (Nycomed) successfully completed Phase 3 (2008) in COPD
- **Smoke challenge (4 days) induces**
  - Recruitment of key inflammatory cells (neutrophils)
  - Increase in key neutrophil chemoattractant (KC, = murine IL-8)
  - Increases in proteases involved in lung remodeling (MMP9)





- **Inhaled oligo has more potent anti-inflammatory activity compared to roflumilast (oral).**
  - Efficacy of PDE4/7 oligo (0.2 mg/kg) achieved at a dose 25-fold lower than roflumilast (5 mg/kg) (n=16-21 animals per group)
  - PDE4/7 oligo also inhibited the release of key cytokines that are responsible for inflammation and breakdown of lung tissue in COPD.

Fortin et al, American Thoracic Society Conference 2008

- Oligonucleotide discovery capability
  - Drug design
  - In vitro and in vivo screening & optimization
- Proprietary chemistry
  - DAP (2-Amino 2 Deoxyadenosine)
  - Modified base
- Key performance attributes
  - Potency
  - Tolerability
- Series of valuable applications
  - Respiratory products
  - Platform to generate new candidates in multiple indications

