

# Invion Limited (ASX:IVX)

Clinical-stage life sciences company targeting chronic inflammation

# Invion: targeting inflammation

- > Global life sciences group in pharmaceutical drug development
- > Expertise and assets target chronic inflammation in two key areas of human health:
  - > inflammatory airways disease (respiratory disease)
  - > inflammation caused by autoimmune disease
- > Executive Directors with proven track record
  - > Dr Greg Collier, MD & CEO: former MD & CEO ChemGenex Pharmaceuticals (sold to Cephalon \$230M); 150+ peer reviewed publications; Roche Award for Excellence
  - > Dr Mitchell Glass, SVP R&D & CMO: 5 FDA-approved drugs, senior executive roles at AZ & GSK, Board certified pulmonary and critical care specialist
- > Growing a broad pipeline of drug assets that target improved patient outcomes and major commercial opportunities
- > Operations: Brisbane, Australia; Delaware, USA

# Invion's assets

## Respiratory

- > **INV102 (nadolol)**: a beta blocker (beta adrenergic biased ligand) currently used to treat high blood pressure, coronary chest pain (angina) and migraine, is being repurposed to treat chronic inflammatory airway diseases (e.g. asthma and COPD).
- > **INV104 (zafirlukast)**: a leukotriene receptor antagonist (LTRA) that reduces inflammation, constriction of the airways and the build-up of mucus in the lungs, is being developed as an inhaled therapy to treat asthma in adults and children.
- > INV102 & INV104 are the foundations of Invion's inhaled respiratory drug franchise

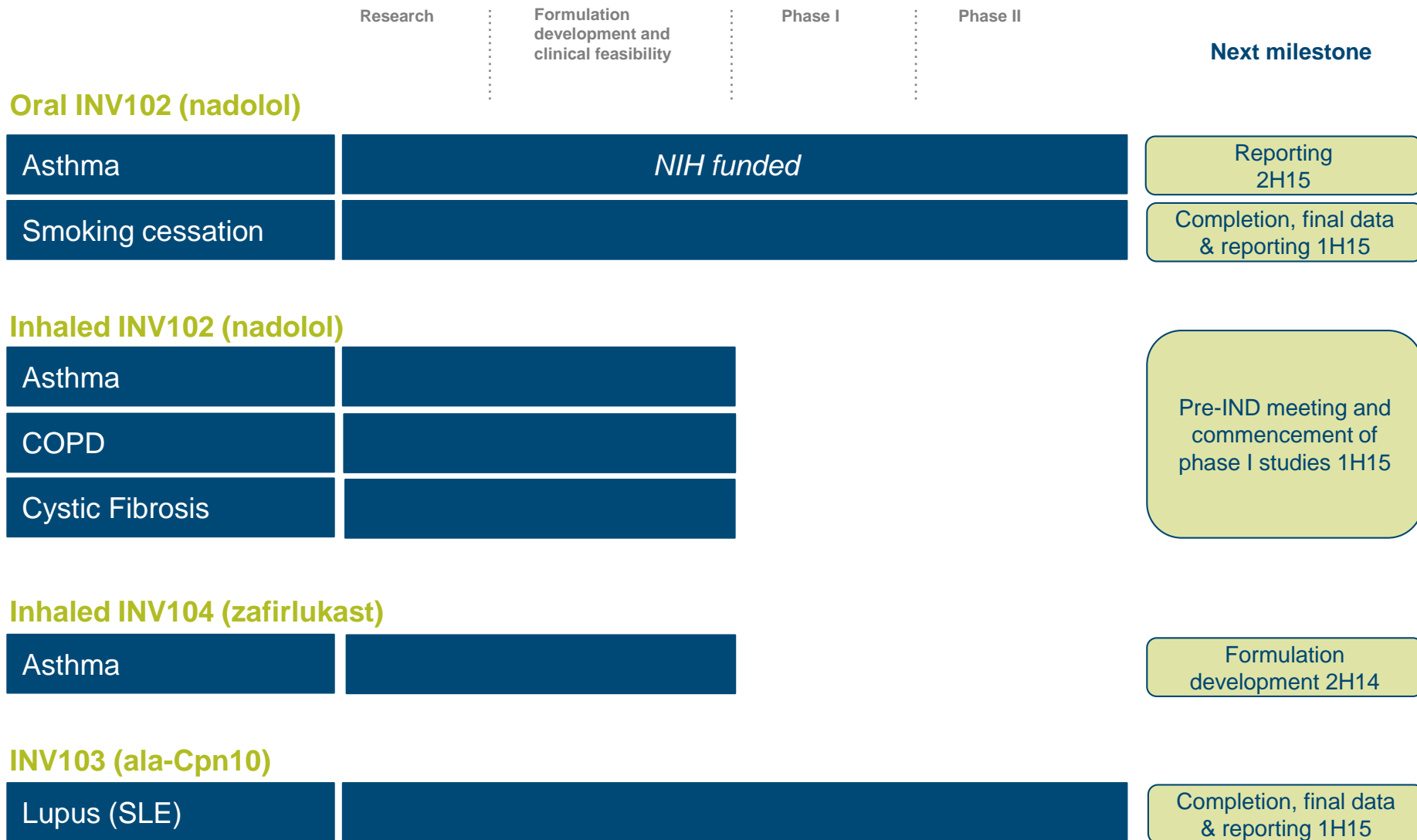
## Autoimmune

- > **INV103 (ala-Cpn10)**: a modified naturally occurring human protein and member of the Resolution Associated Molecular Pattern (RAMPs) family, hypothesised to maintain and restore immune homeostasis, is being developed to treat systemic lupus erythematosus (lupus or SLE).
- > Early partnering opportunity

# Strategic goals

1. Gain US FDA approval for **INV102 (nadolol)** as a treatment for cigarette smokers who repeatedly fail to quit
2. Demonstrate proof of concept for inhaled **INV102 (nadolol)** in the treatment of one or more diseases of the airway including severe asthma, COPD and cystic fibrosis
3. Demonstrate proof of concept for inhaled **INV104 (zafirlukast)** in the treatment of mild asthma and exercise-induced bronchospasm
4. Partner **INV103 (ala-Cpn10)** for further development in autoimmune diseases

# Pipeline





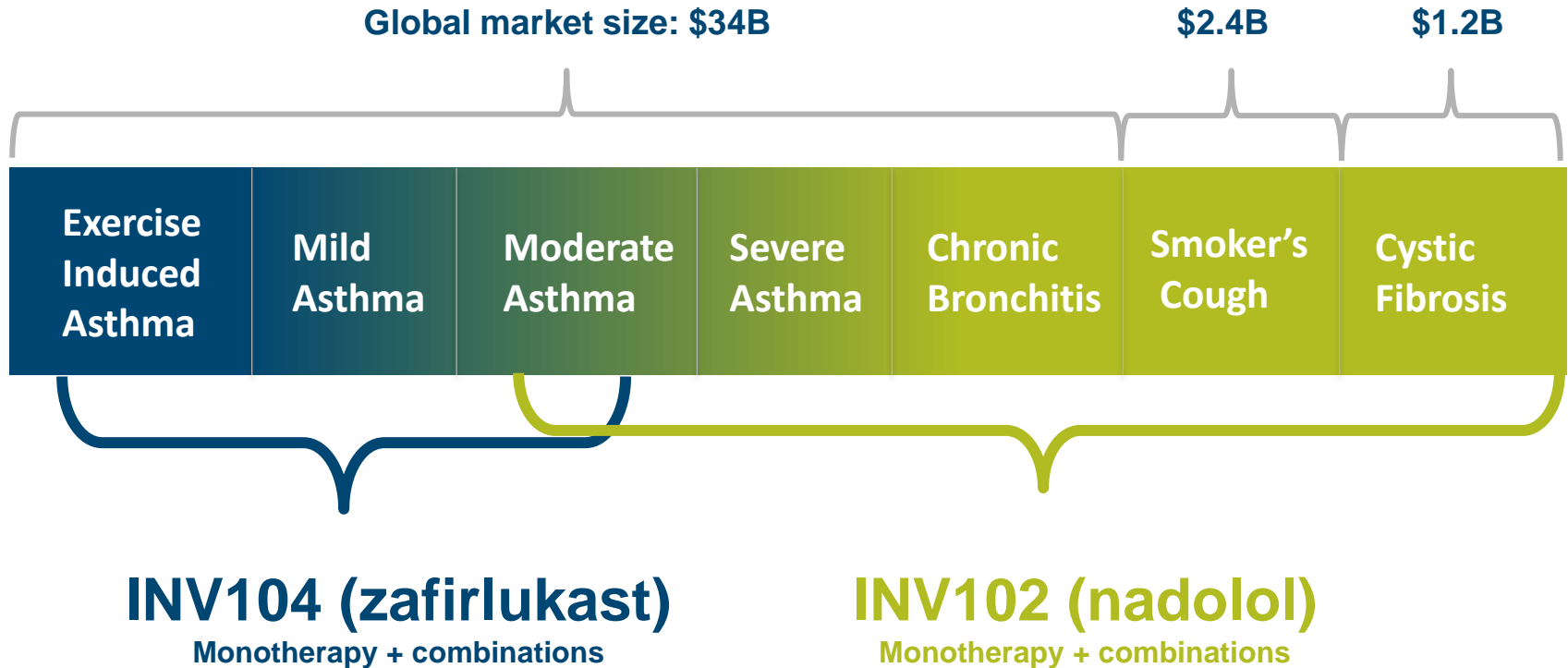
Targeting inflammation

## Targeting chronic inflammatory airway disease

INV102 (nadolol)

INV104 (zafirlukast)

# Spectrum of airway disease and opportunities

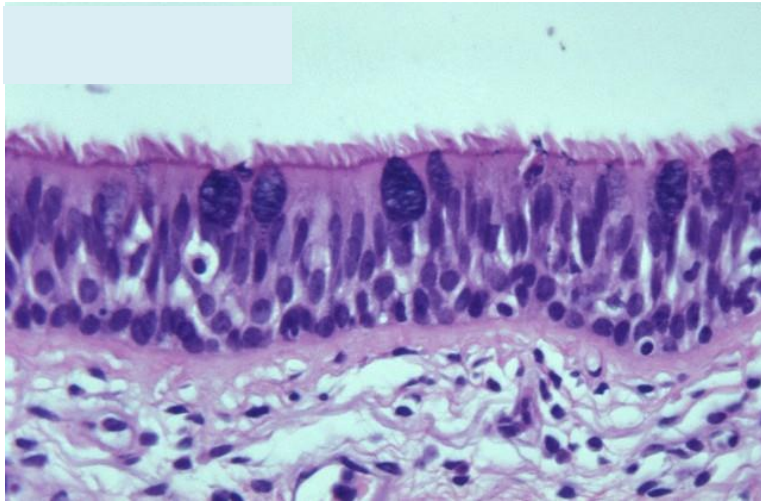


**INV104 (zafirlukast)**  
Monotherapy + combinations

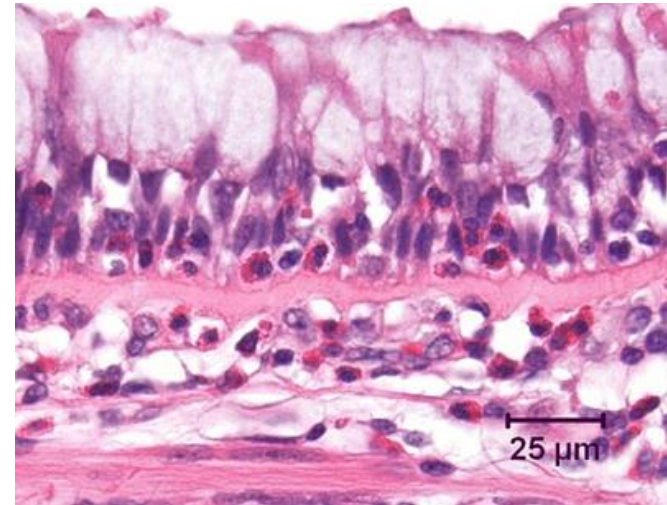
**INV102 (nadolol)**  
Monotherapy + combinations

# The critical role of the epithelium in severe airway disease

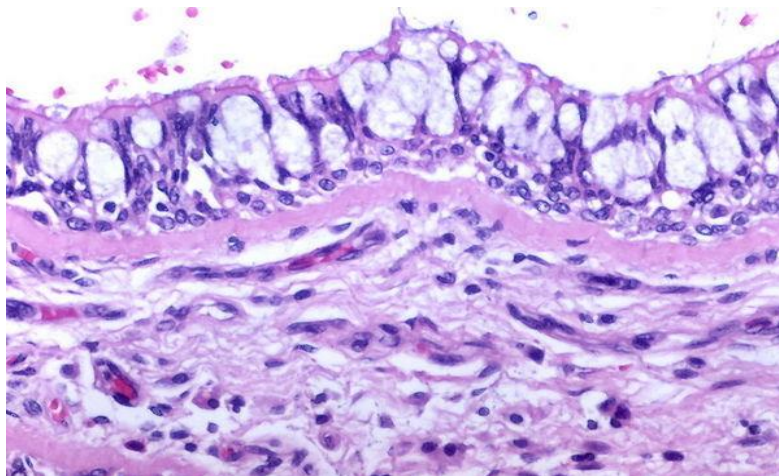
Normal respiratory epithelium



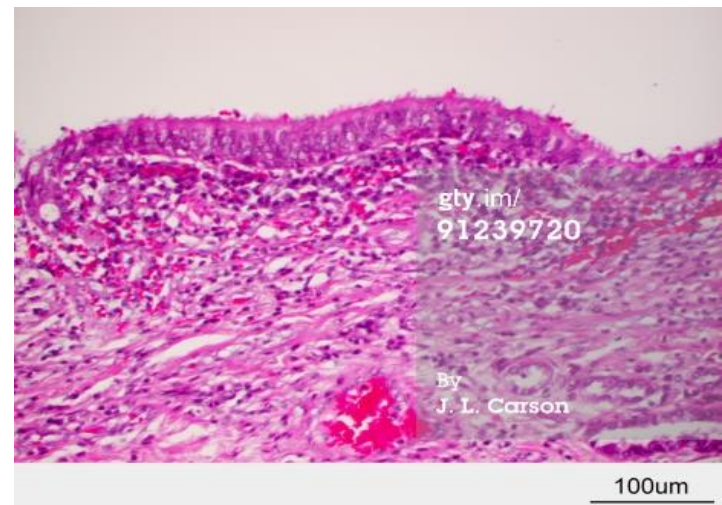
Severe asthma



Chronic bronchitis

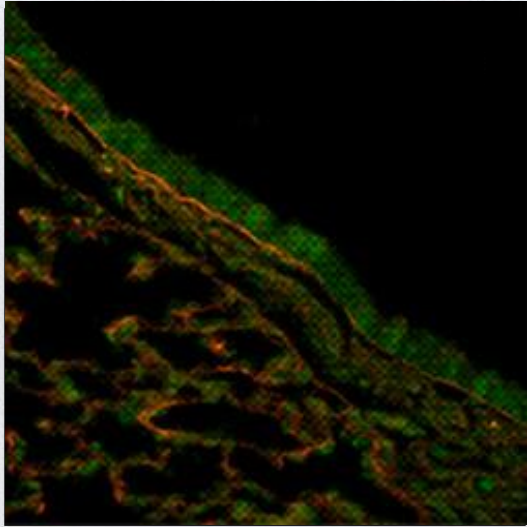


Cystic fibrosis

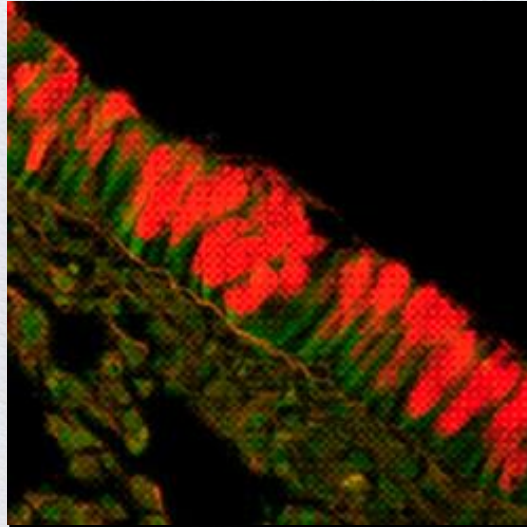




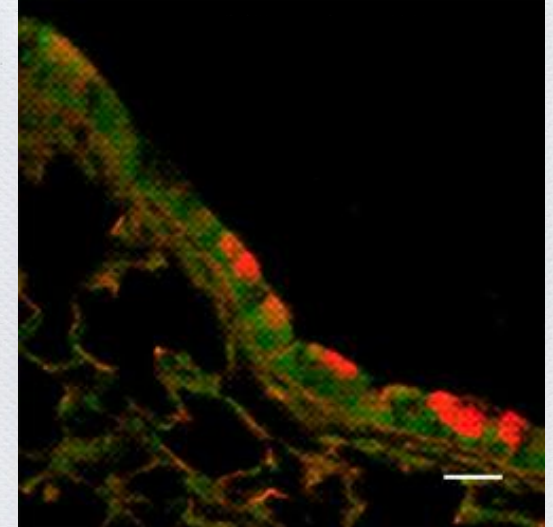
# INV102 reverses epithelial changes in pre-clinical studies



Control lung tissue



Lung tissue of 'asthmatic' mice: epithelial cells have been converted to mucus-producing goblet cells. No effect of alprenolol.

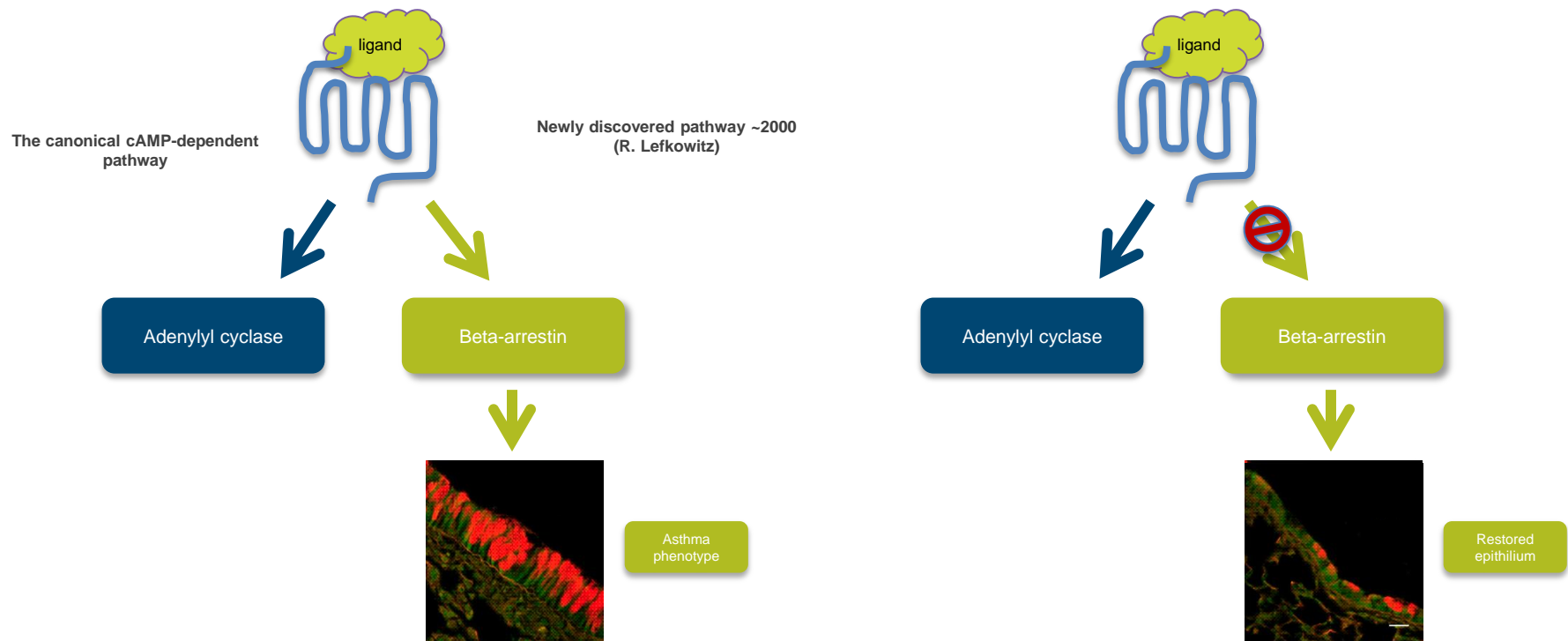


Lung tissue of 'asthmatic' mice **treated with INV102 (nadolol)** for 28 days: **restored epithelium**

Reference: Nguyen LP., et.al., 2011. Complementary anti-inflammatory effects of a  $\beta$ -blocker and a corticosteroid in an asthma model. Arch Pharmacol. 2011; Oct 2.

# INV102 reverses epithelial changes via inhibition of the beta-arrestin pathway

- > INV102 development is based on the science of Richard A. Bond PhD, Professor of Pharmacology, U Houston. In collaboration with nobel-prize winning Robert Lefkowitz, Dr Bond undertook studies on the spontaneous activity of G-protein-coupled receptors and compounds functioning as inverse agonists. Dr Bond's research has demonstrated that INV102 has been shown to inhibit the beta-arrestin signalling pathway.





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## Respiratory therapeutics: oral program

INV102 (nadolol)

# Oral INV102: emerging phase II clinical data

## Phase II asthma trial (NIMA): interim analysis

- > Randomised, placebo-controlled, 60 patient clinical trial in patients with mild asthma
- > High % of patients (> 90%) tolerated titration to maximum possible dose without severe adverse events
- > No pattern of cardiovascular or respiratory effects in patients during the four hours of observation required after each titration dose
- > Patients demonstrated no requirement to increase rescue medication usage – provided either as a short-acting beta-agonist (SABA) or as an anti-muscarinic agent
- > Next milestone: completion of enrolment 1H 2015

## Phase II smoking cessation trial: status

- > Randomised, placebo-controlled, 136 patient clinical trial in patients with chronic cough due to smoking who have failed to quit multiple times previously
- > Q4 2014 data will be released from sputum samples collected at baseline 4 and 8 weeks in early enrolled subjects
- > On target to complete enrolments in Q4 2014 and report final results 1H 2015
- > Data will underpin ongoing development of inhaled INV102 and support program for new drug application as an aid to treatment for smoking cessation
- > Next milestones: phase II interim data: Q4 2014 and End of Phase II meeting



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## Respiratory therapeutics: inhaled program

INV102 (nadolol) in asthma, COPD & cystic fibrosis

INV104 (zafirlukast) in asthma

# Inhaled INV102: program status

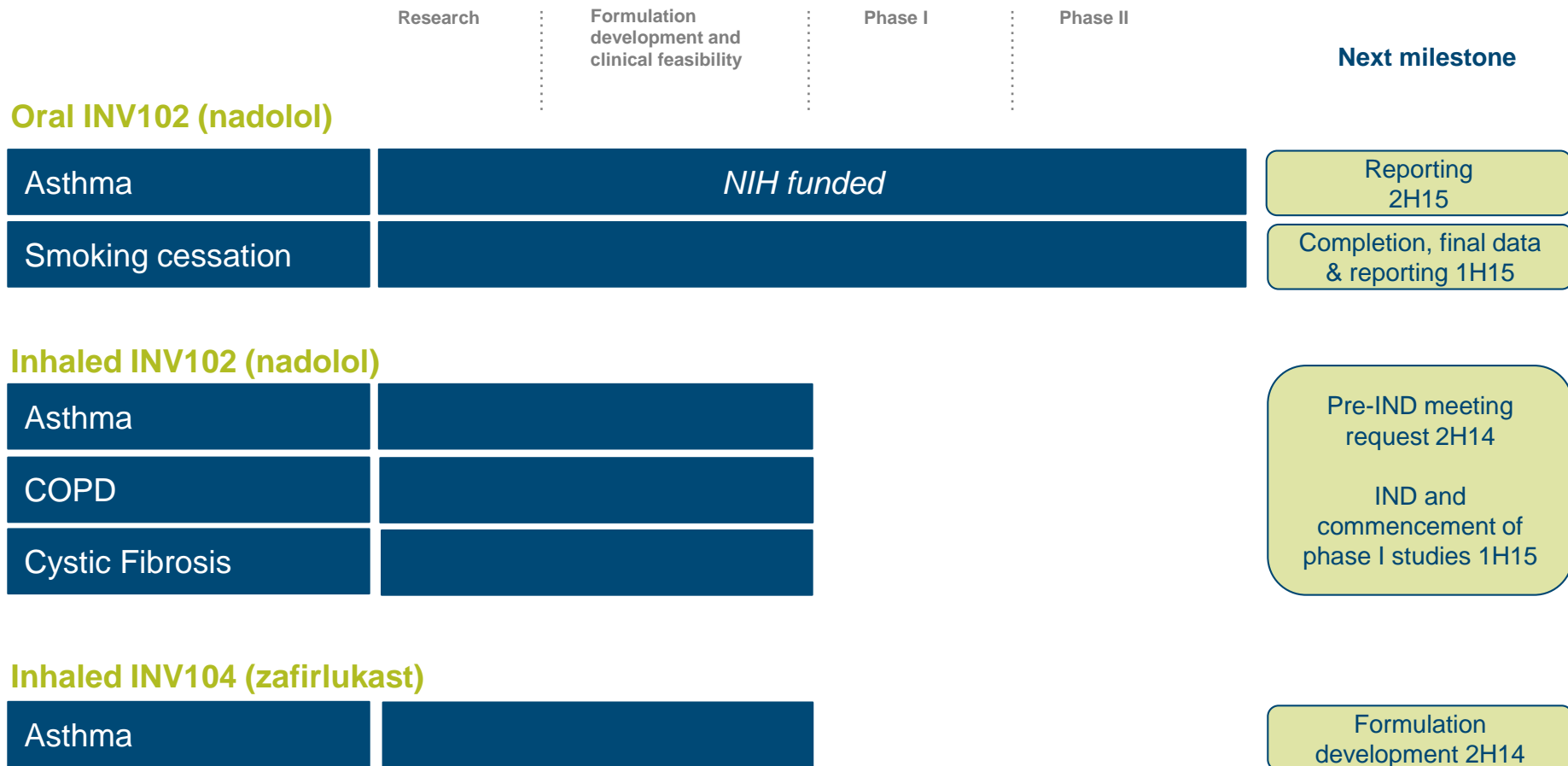


- > Collaboration with 3M Drug Delivery systems
- > Target outcome: proprietary formulation and device using 3M's proprietary pressurised metered dose inhalation (pMDI) technology
- > Collaboration encompasses manufacture for toxicology and phase I studies
- > Limited toxicology package using 3M formulation and device
- > Feasibility work: Stage 1 (method development and validation) complete. Stage 2 (product screening) work is nearing completion. Stage 3 (accelerated stability) anticipated to complete 1Q 2015.
- > Next milestone: Pre-IND request to be lodged 4Q 2014, with IND and commencement of phase I studies anticipated 1H 2015

# Inhaled INV104: program status

- > First inhaled non-steroidal anti-inflammatory drug for asthma
- > Ongoing collaboration to develop proprietary formulation and device
- > Largely risk mitigated development based on chemistry, inhaled toxicology and inhaled proof of concept studies conducted by ICI/ Zeneca under Mitchell Glass
- > Well defined CMC/TOX/ADME and safety profile: > 4M patients as oral Accolate (AZ)
- > 7 studies showed excellent prevention of asthma, cold air and exercise induced bronchospasm (EIB) without detectable drug blood levels
- > Next milestone: completion of formulation development and validation (2H 2014).

# Respiratory Pipeline







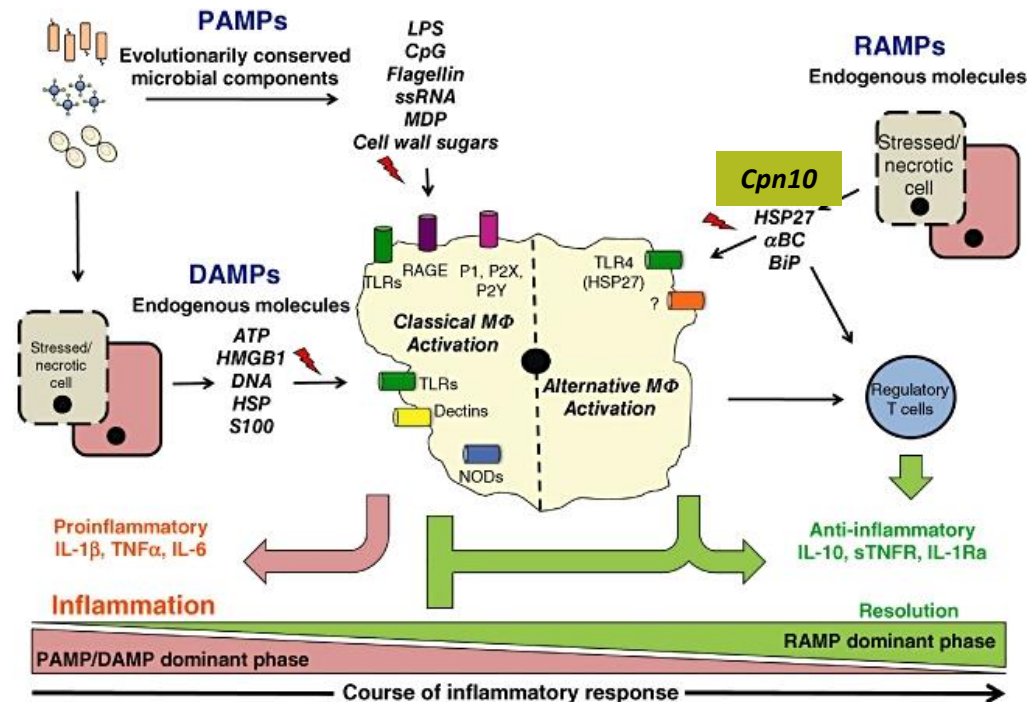
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Targeting chronic inflammation caused by  
autoimmune disease

INV103 (ala-Cpn10)

# INV103 (ala-Cpn10): background and rationale

- > Modified naturally occurring protein
- > Intracellular function: prevent protein misfolding
- > Extracellular function: proposed as founding member of the Resolution Associated Molecular Pattern (RAMPs) family - a critical component of prevention of autoimmunity
- > Significant clinical data base > 250 patients
  - > demonstrated anti-inflammatory and immunoregulatory activity in multiple indications including RA, psoriasis
- > Strong pre-clinical data in lupus animal model
  - > reduced renal and circulating levels of key pro-inflammatory mediators (TNF- $\alpha$ , IL-6 and MCP-1) reduced CD4+ T cells and auto-reactive T cells and increased the number of activated DC (critical in the establishment of self tolerance)



Reference: Resolution-associated molecular patterns (RAMPs) in the acute inflammatory response. Inflammation initiates the over-expression and release of RAMPs, such as Cpn10 (Hsp10). These help limit and resolve the inflammatory responses via a variety of direct and indirect mechanisms. (Reproduced from Shields A.M., et. al., 2011, Clin and Exp. Immunology, 165, 292-300)

# INV103 phase II lupus trial: interim blinded data

- > Double-blind, randomised, placebo-controlled clinical trial in lupus patients. Up to 40 subjects in up to 5 cohorts (8 patients per cohort), increasing dose and increasing disease severity. Doses 10mg, 30mg, 100mg, 300mg
- > Data analysed from lower dose cohorts - 10mg and 30mg twice weekly dosing
- > Good safety demonstrated – no pattern of adverse events
- > Safety profile now supportive of concurrent testing of:
  1. higher doses – 100mg twice-weekly is a tenfold increase over previously tested highest doses; and
  2. patients with more severe disease – i.e. showing signs of renal impairment
- > Business development and partnering activities geared towards maximising potential commercial opportunities from emerging data
- > Next milestone: completion of trial and final data: 1H 2015

# Invion: key milestones next 12-18 months

## 2H 2014

- ✓ Interim data from NIH-funded phase II study of INV102 (nadolol) in asthma patients
- ✓ Interim data from phase II study of INV103 (ala-Cpn10) in lupus patients
- > Phase II interim data from oral INV102 (nadolol) study in patients undergoing smoking cessation
- > Pre-IND for inhaled INV102 (nadolol) as a potential therapy for asthma, COPD & cystic fibrosis

## 1H 2015

- > Completion and final data from phase II study of INV103 (ala-Cpn10) in lupus patients
- > Completion and final data from phase II oral INV102 (nadolol) study in patients undergoing smoking cessation
- > Completion of enrolment of NIH-funded phase II study of INV102 (nadolol) in asthma patients
- > Commencement of phase I studies of inhaled INV102 (nadolol)

## 2H 2015

- > Reporting on NIH-funded phase II study of INV102 (nadolol) in asthma patients
- > End of phase II meeting with FDA for INV102 (nadolol) in smoking cessation
- > IND for INV104 (zafirlukast) as an inhaled therapy for asthma
- > Initiation of phase II (proof of concept) studies for inhaled INV102 (nadolol) in COPD, asthma and cystic fibrosis
- > Initiation of phase II (proof of concept) study of INV104 (zafirlukast) in asthma



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## Summary

- ✓ 3 drug assets with multiple paths to market
- ✓ 3 FDA-regulated phase II clinical trials
- ✓ early partnering opportunity for INV103 (ala-Cpn10)
- ✓ two de-risked novel and proprietary inhaled respiratory assets
- ✓ collaboration with global partner on inhaled franchise
- ✓ experienced leadership team
- ✓ significant valuation drivers: 12-18 months

# Corporate snapshot

Sector	Life Sciences (Biotechnology)
Principal activities	Clinical-stage pharmaceutical drug development
Pipeline	3 drug assets, multiple clinical and pre-clinical programs
Operations	Australia & USA
ASX code	IVX
Share price (31-Oct-14)	\$0.053 (5.3 cents)
Shares on issue	~541M
Options on issue	~45M
Market cap (31-Oct-14)	~\$30M
Cash at bank (30-Sep-14)	\$1.8M
Anticipated cash inflows	\$0.79M (R&D tax rebate)
Executed funding agreement (10-Nov-14)	Up to \$17.4M over 24 months



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