

Invion Limited (ASX:IVX)

Clinical-stage life sciences company targeting chronic inflammation



Targeting inflammation

Disclaimer

This presentation has been prepared by Invion Limited (Invion or the Company) solely for its use at presentations to be made by the Company. The information contained in this presentation is an overview and does not contain all information necessary to make investment decisions. Although reasonable care has been taken to ensure that facts stated in this presentation are accurate and that the opinions expressed are fair and reasonable, no representation, expressed or implied, is made as to the fairness, accuracy, completeness or correctness of the information and opinions contained in this presentation and no reliance should be placed on such information or opinions. This presentation does not constitute an offer, invitation, solicitation or recommendation with respect to the purchase or sale of any security in the Company nor does it constitute financial advice nor take into consideration your investment objectives. This presentation contains or may contain forward-looking statements that are based on management's belief, assumptions and expectations and on information currently available to management. All statements that are not historical, including those statements that address future operating performance and events of developments that we expect or anticipate will occur in the future, are forward looking statements. Although management believes these forward looking statements are fair and reasonable you should not place undue reliance on these statements.

Invion: targeting inflammation

- > INVION: 3 drug candidates in development
 - > INV102 (nadolol): beta blocker being repurposed to treat asthma, COPD, cystic fibrosis, and smoking cessation failures
 - > INV104 (zafirlukast): inhaled anti-leukotriene that reduces inflammation, constriction of the airways, and the build-up of mucus in the lungs
 - > INV103 (ala-Cpn10): modified, naturally occurring human protein shown to reduce interleukin-6 (IL-6), a key inflammatory marker of autoimmune disease
- > 3 FDA-regulated phase II clinical trials currently underway



Management team with proven track record

Invion's management and board have significant experience repurposing drugs for new markets, and guiding drugs through FDA regulatory and approval processes.

Greg Collier, PhD., Managing Director and Chief Executive Officer

- > 20 year career in pharma research, development and commercialisation
- > CEO ChemGenex Pharmaceuticals (sold to Cephalon \$230M)
- > 150 peer reviewed publications, 33 patents
- > Roche Award for Excellence

Mitchell Glass, M.D., Executive VP R&D and Chief Medical Officer

- > Board certified pulmonary and critical care specialist
- > 25 year veteran of Pharma (AZ, GSK) and Biotech (AGIX)
- > 5 FDA approved drugs
- > Managed more than 40 drug developments including “first in class”
 - > Led development of beta blocker carvedilol (Coreg)
 - > Led development phases I - III of oral zafirlukast (Accolate)



Targeting inflammation

Targeting respiratory disease

Asthma, COPD, chronic bronchitis, cystic fibrosis

Respiratory diseases: major and growing problem

Asthma

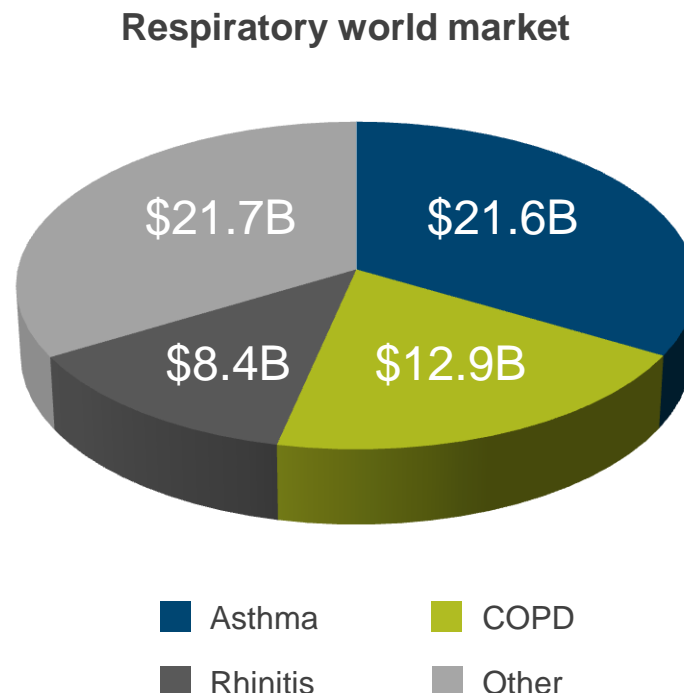
- > Up to 400M people worldwide will suffer from asthma by 2025
- > Prevalence increasing with rates of allergy
- > *Exercised induced* asthma is a specific diagnosis related to exercise or exposure to cold air
- > Economic cost \$56B (USA, 2007)

Chronic obstructive pulmonary disease (COPD)

- > 64M COPD patients worldwide, 3M deaths in 2005
- > WHO predicts 3rd leading cause of death by 2030
- > Smoking and air pollution primary risk factors
 - > up to 2M deaths per year related to air pollution
- > Economic cost \$49B (USA, 2010)

Large market opportunity, significant unmet need

- > Prescription respiratory world market \$64B
- > Asthma and COPD prescription drugs \$34B
 - > FDA Black box warning on all Long Acting Beta Agonists (LABAs) and LABA/Steroid combinations: increased risk of death
- > Smoking cessation drug market \$2.4B
 - > Nicotine replacement therapy (NRT) is bulk of existing market - does not address lung healing
 - > 10-15% of early failures due to cough associated with excess mucus*
 - > Opportunity to expand existing market
- > Cystic fibrosis drug market \$1.2B+
 - > Breakthrough therapy *Kalydeco* targets only 4% of CF population. Sales of \$360M.



Invion's respiratory strategy

Invion's respiratory portfolio is designed to treat a range of hereditary and acquired respiratory disorders, leveraging synergies and efficiencies in the development cycle

**Chronic inflammatory lung disease
– respiratory disease**

Hereditary

Asthma

Oral INV102



Inhaled INV102



Inhaled INV104



Inhaled INV104+LABA+ICS



Cystic Fibrosis

Inhaled INV102
+antibiotic



Acquired

Chronic obstructive pulmonary disease (COPD)

Inhaled INV102



Smoking cessation

Oral INV102

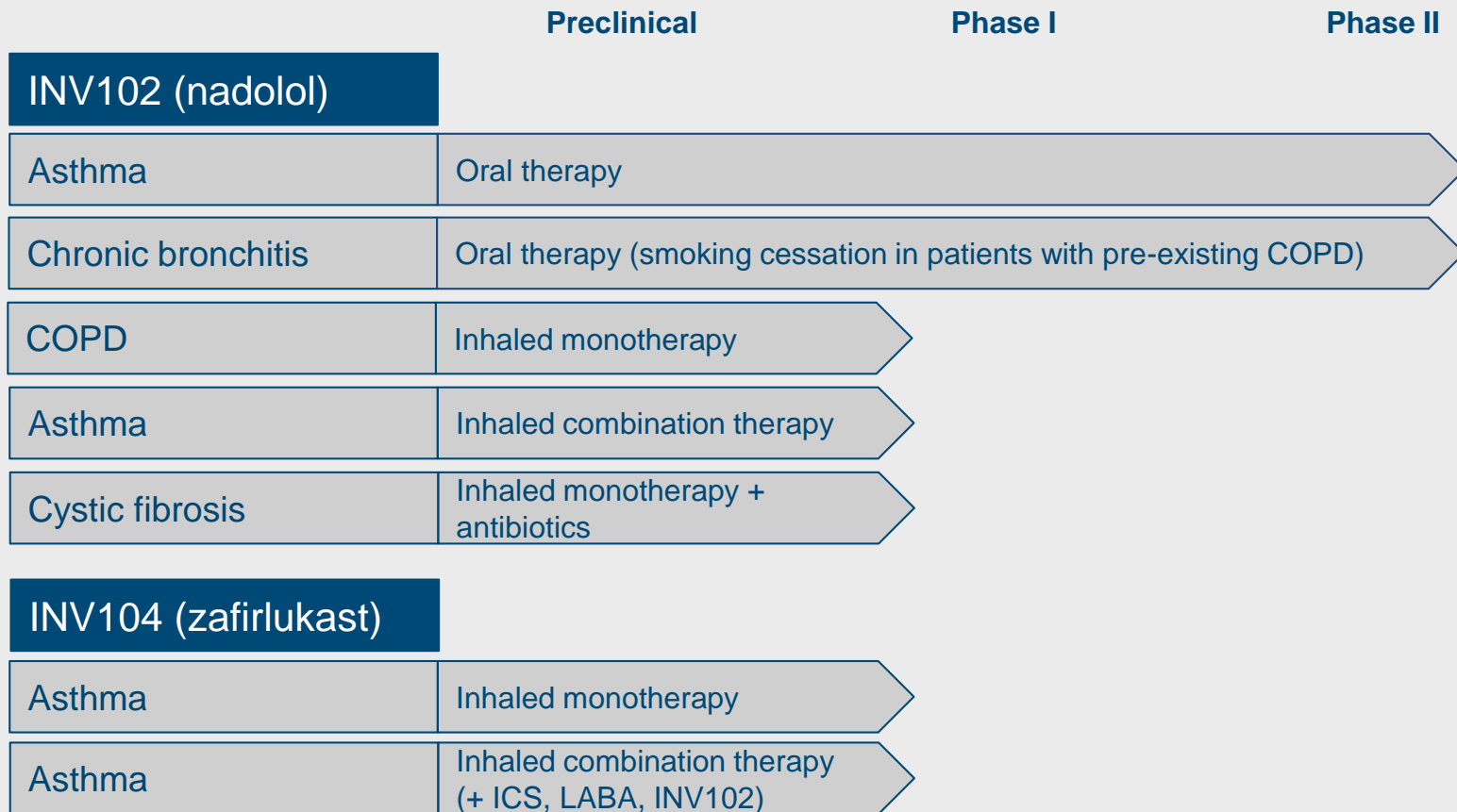


Chronic Bronchitis

Inhaled INV102
Inhaled INV104



Respiratory pipeline: clinical development stages





Targeting inflammation

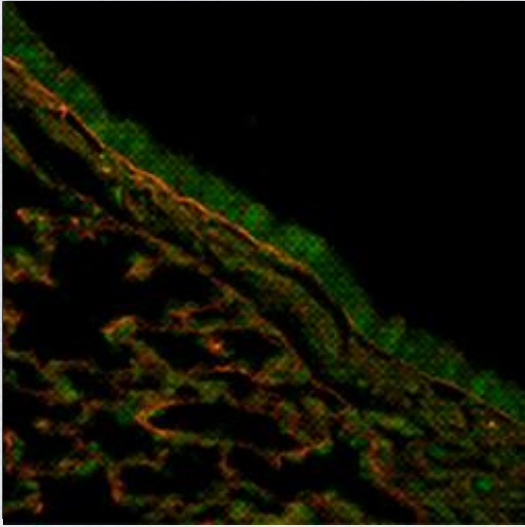
INV102 (nadolol)

Targeted to treat causes, symptoms and sequelae of inflammatory lung disease

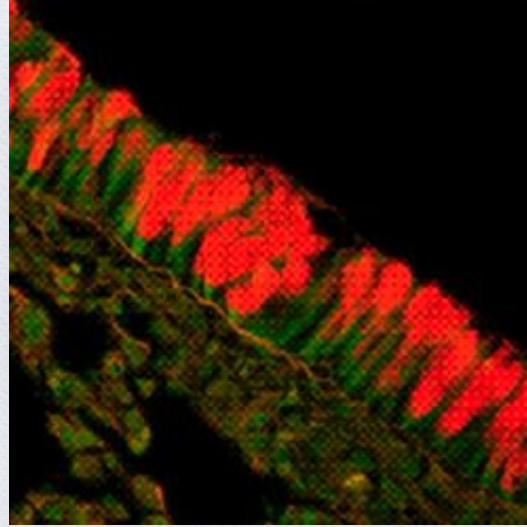
INV102 (nadolol)

- > Generic drug being repurposed for a new target
- > Suite of patents granted and in prosecution
- > Aim to develop an inhaled drug for the treatment of respiratory diseases including asthma and COPD
- > Short term path to commercialisation with oral treatment
- > Nadolol is uniquely an inverse β -agonist in the airway
 - > inactivates intracellular inflammatory events that are stimulated
 - > spontaneously or
 - > by β agonists
- > Clinical data to date
 - > Two phase II clinical trials completed
 - > Safety profile enhanced by titration starting at very low doses
 - > Dose-related reduction of airway hyper-responsiveness

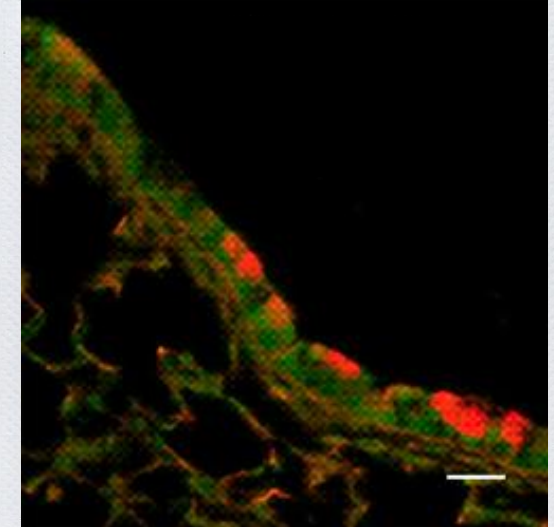
Preclinical studies demonstrate airway healing



Control lung tissue



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

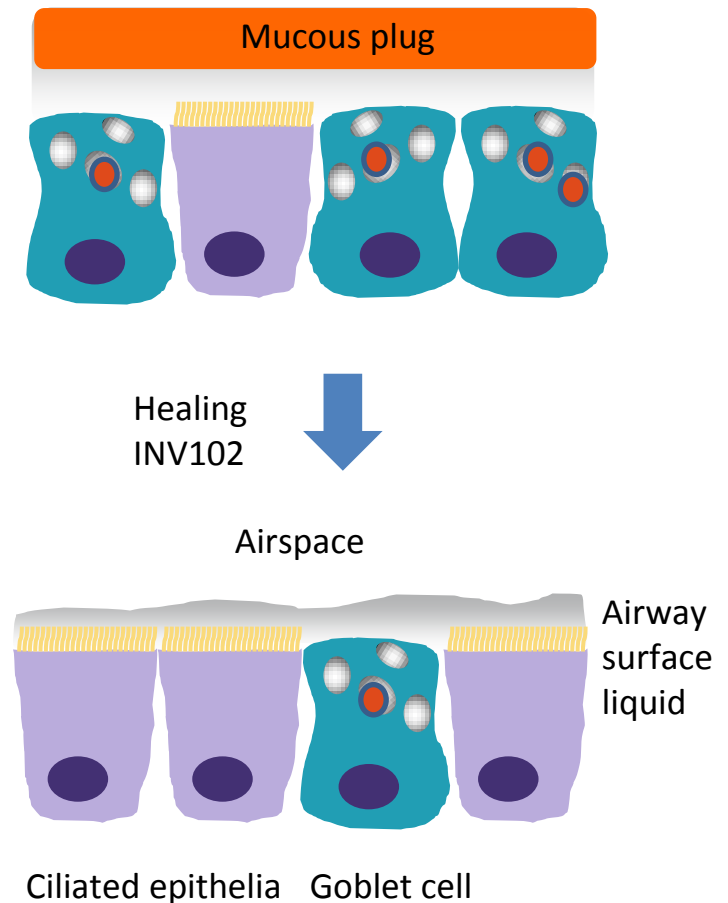


Lung tissue of 'asthmatic' mice **treated with INV102 (nadolol)** for 28 days: **restored epithelium**

Proof of concept has been achieved in pre-clinical studies
with inhaled INV102

Mechanism of action targets multiple pathways

- > Reduction of goblet cell metaplasia
 - > Reduced mucous hypersecretion
 - > Restoration of ciliated epithelium
- > Reduced levels of pro-inflammatory cytokines: IL-5, IL-10, IL-13
- > 50% reduction in eosinophils
- > Restoration of lung function
- > Effects are potentially beneficial (relevant) to exacerbations of chronic inflammatory lung diseases



Medical, regulatory and commercial precedent

Precedent: Chronic Heart Failure (CHF)

FROM

CONTRAINDICATED

Warning against use of beta blockers in CHF for > 25 years.
Carvedilol annual sales (1998) \$40m



TO

STANDARD OF CARE

After careful titration, beta blocker **Carvedilol** reduced mortality in all classes of CHF
First in class: Carvedilol peak annual sales \$1.5 BILLION (2010)

Invion target: Chronic Obstructive Pulmonary Disease (COPD)

FROM

CONTRAINDICATED

Warning against use of beta blockers in COPD for > 25 years.
Nadolol current sales: \$ nominal (generic)



TO

STANDARD OF CARE

After careful titration, beta blocker **INV102 (nadolol)** targeted to reduce airflow obstruction due to damaged airways.
Target: First in class

NOTE: The effect of INV102 (nadolol) on airways cells is unique among β blockers. β 1 success in the heart (CHF) mitigates the risk of β 2 success in the lung (COPD)

Completed two phase II clinical trials: POC

Objective: Proof-of-concept to evaluate safety and effects on airway with escalating doses administered to 19 subjects with mild asthma

Primary endpoint: Objective measure of airway hyper-responsiveness (PC20 MeChFEV1), the diagnostic hallmark of asthma

Key Findings:

- > Safety: well tolerated in doses up to 40mg
- > Efficacy: airway hyper-responsiveness:
 - > dose response with ineffective dose at 10mg/day
 - > 9 -10 weeks of treatment produced a dose-dependent decrease in airway hyper-responsiveness that achieved clinically significant improvement
- > Lung function:
 - > attenuation of first dose decrease in FEV1 by titration
 - > same benefit and commercial strategy as Coreg in CHF
- > Findings led US NIH to fund larger phase II study in asthma patients

INV102: phase II trial design – mild asthma

Trial name	INV102 (nadolol) in mild asthma (NIMA)
Trial design	Double-blinded, randomised, placebo-controlled, multi-centre
Patients	60 subjects (30 subjects in each of two treatment arms)
Timing	Commenced Q1 2013 Expected completion 2015
Inclusion criteria	Mild asthma: only β agonists as needed
Principal Investigator	Nicola A. Hanania, M.D., M.S., Baylor College of Medicine
Sites	Baylor, Washington University, Duke University
Doses	1.25mg, 2.5mg, 5mg, 10mg, 25mg, 50mg (dose titration)
Primary endpoints	Improved airway hyper-responsiveness via change in methacholine PC20 (based on FEV1)
Safety endpoints	Safety of titration and 6 months' dosing
Exploratory endpoints	Reduced airway inflammation and mucous metaplasia; increased β 2AR density, affinity and signaling in airway epithelial cells; change in exhaled (eNO)
Comment	Clinical program under US IND (submitted Feb '07)
Regulatory Status	www.clinicaltrials.gov ID: NCT01804218

INV102: phase II trial design – chronic bronchitis

Trial name	INV102 (nadolol) in smoking cessation of patients with pre-existing COPD	
Trial design	Double-blinded, randomised, placebo-controlled	
Patients	130 (65 per arm: 54 needed for analysis)	
Timing	Commenced Q3 2013	Initial data Q4 2013
Inclusion criteria	Previously failed to quit, have COPD and chronic cough	
Principal Investigator	Prof Mario Castro	
Sites	Washington University (St Louis)	
Doses	2.5mg, 5mg, 10mg, 25mg, 50mg (dose titration)	
Primary endpoints	Abstinence from smoking in last 2 weeks of trial	
Secondary endpoints	Number of cigarette-free days; clinical COPD questionnaire; MMRC Dyspnea Scale; markers of COPD; sputum markers of COPD	
Safety endpoints	Change in FEV1; requirement for rescue medication; COPD exacerbation rate	
Comment	Data will support broader oral and inhaled development program	
Regulatory Status	www.clinicaltrials.gov ID: NCT01825122	



Targeting inflammation

INV104 (zafirlukast)

Inhaled reformulation of a successful oral therapeutic for asthma

INV104 (zafirlukast)

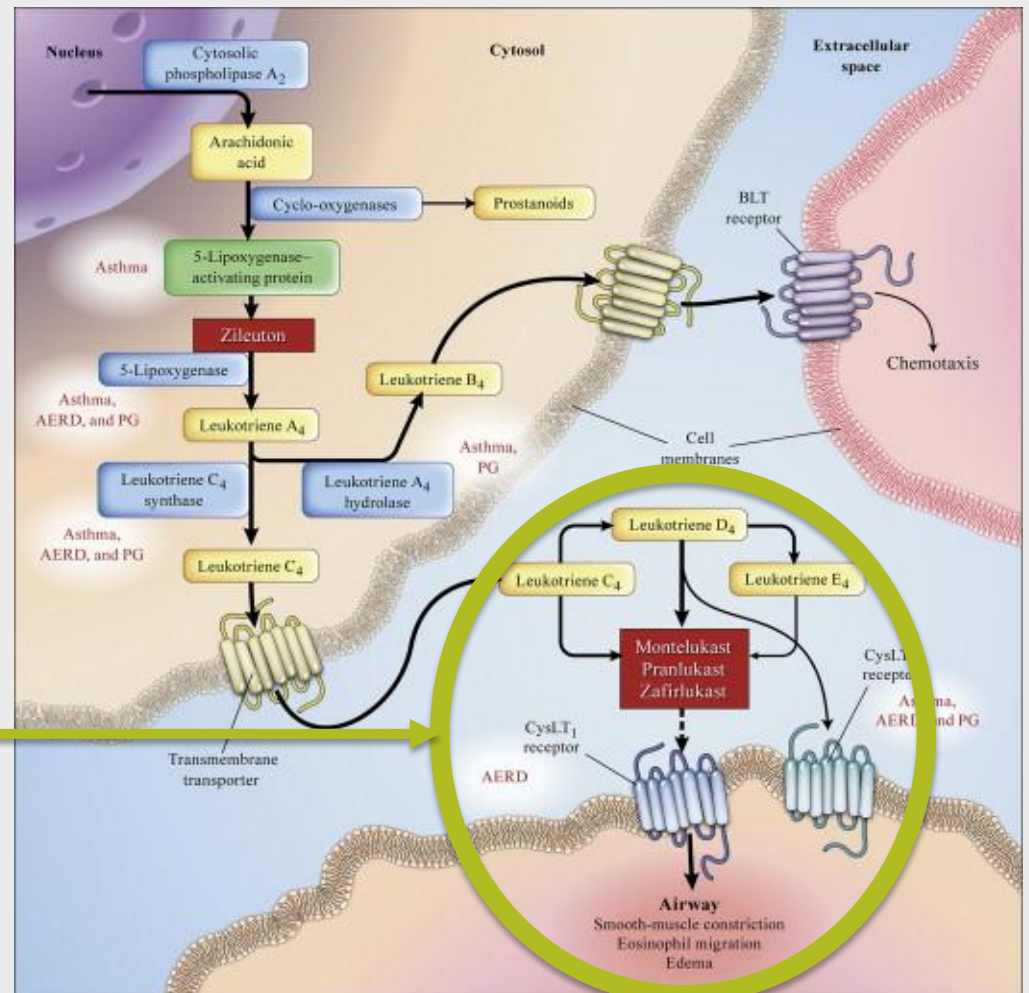
- > *Leukotriene Receptor Antagonist (LTRA) or anti-leukotriene*
- > Targeted as first inhaled non-steroidal anti-inflammatory treatment for asthma
- > Established activity by inhalation route with excellent flow and deposition (MDI and DPI)
- > Large market potential with mitigated risk of a reformulated drug
- > Data to date
 - > 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
 - > FDA response to pre-IND meeting requires limited toxicology package
 - > 2 species x 28 days + 6 months, 1 species
- > Intellectual Property position
 - > Expired zafirlukast patents (public domain)
 - > New patent protection from combination, delivery, and linked diagnostic filings

Mechanism of action

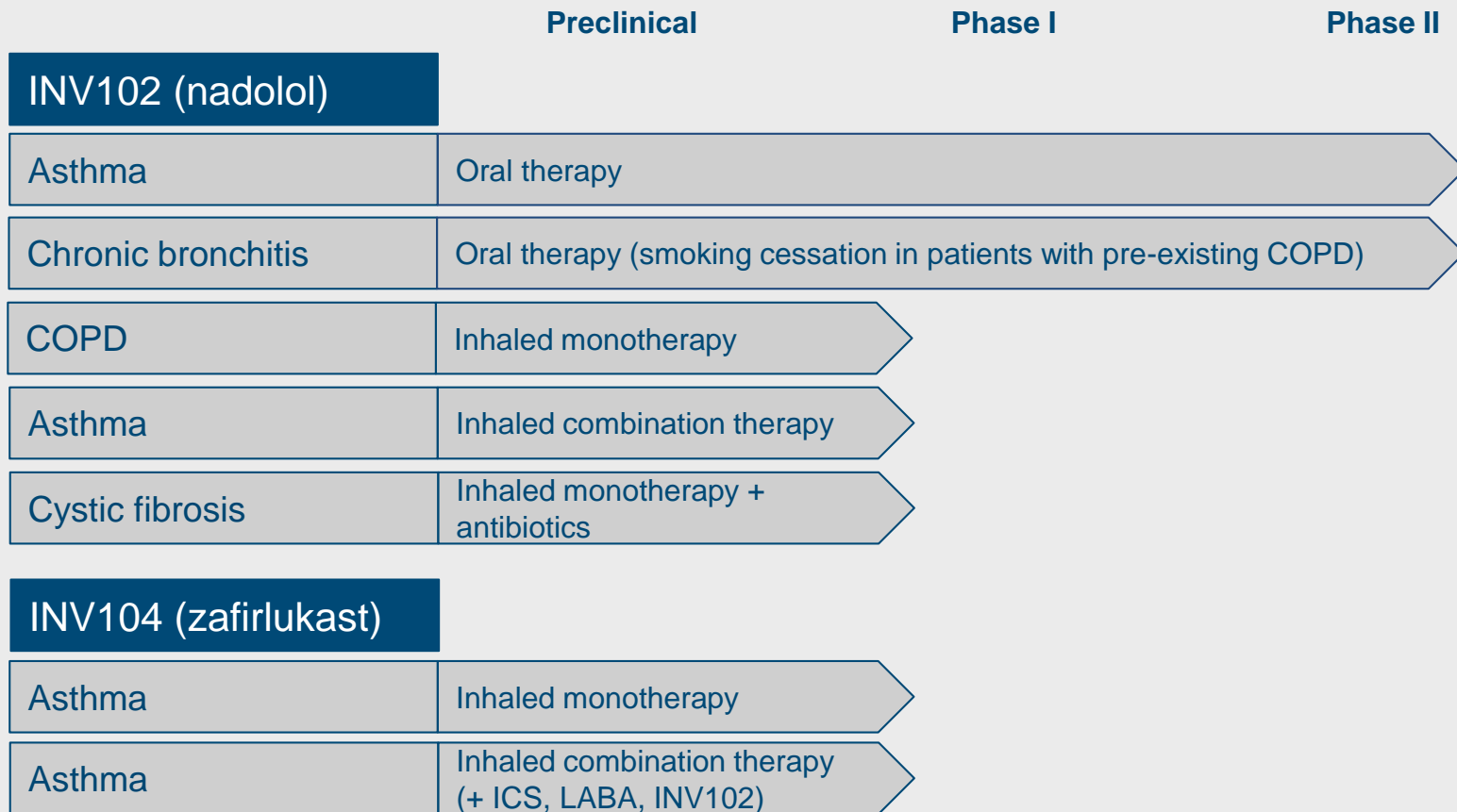
Zafirlukast is a leukotriene receptor antagonist (LTRA) that blocks the action of the cysteinyl leukotrienes on the CysLT₁ receptors to reduce:

- >inflammation
- >airway constriction
- >mucus

Genetics and pharmacogenetics of the leukotriene pathway *Journal of Allergy and Clinical Immunology*, Volume 124, Issue 3, September 2009, Pages 422-427 Kelan G. Tantisira, Jeffrey M. Drazen



Respiratory pipeline: clinical development stages



Respiratory: milestones to watch

Asthma

- > INV102: Oral phase II study NIH funded (\$4M+ non-dilutive) commenced Q1 2013
 - > Initial data on airway histology and sputum biomarkers anticipated Q1 2014
 - > Complete phase II data anticipated 2015
 - > Target outcomes: improve airway hyper-responsiveness, reduce airway inflammation and mucus metaplasia
- > INV104: Inhaled formulation and delivery device to commence Q4 2013
 - > Preclinical studies to commence Q3 2014, IND submission Q1 2015
 - > Phase II study to commence Q2 2015

Chronic bronchitis (smoking cessation)

- > INV102: Oral phase II trial commenced Q3 2013, initial data anticipated Q4 2013
 - > Target outcomes: increase smoking cessation, reduce airway inflammation, decrease peri-operative complications

Respiratory: milestones to watch

Asthma & COPD

- > INV102: Inhaled formulation and delivery to commence Q1 2014
 - > Preclinical studies due to complete Q3 2014
 - > Phase II study to commence Q2 2015

Cystic fibrosis

- > INV102: Inhaled formulation and delivery to commence Q1 2014
 - > Preclinical studies due to complete Q3 2014
 - > Phase II study to commence Q2 2015



Targeting inflammation

Targeting autoimmune disease

Inflammation caused by an over-active immune system

Autoimmune disease

- > Chronic disabling disorders in which underlying defects in the immune response lead the body to attack its own organs and tissues
- > More than 80 autoimmune diseases have been identified, most common include:
 - > systemic lupus erythematosus (SLE or Lupus)
 - > multiple sclerosis
 - > psoriasis
 - > rheumatoid arthritis
- > Global market for autoimmune treatments reached \$34 billion in 2010
 - > Expected to reach \$55 billion by 2016
 - > US is largest market for autoimmune treatments, holding 43% share
- > Current leading therapies including steroids, antibody therapies and 'blocking agents', have long term safety & efficacy concerns
 - > Global pipeline remains strong due to large unmet needs of patients



Targeting inflammation

INV103 (ala-Cpn10)

Modified natural human protein targeting inflammatory disease

INV103 (ala-Cpn10)

- > Modified natural human protein targeting inflammatory disease
- > Demonstrated anti-inflammatory and immunoregulatory activity in multiple indications
- > Activity ideally suited to the treatment of inflammation associated with autoimmune disease
- > Data to date
 - > Dose response reduction in biomarkers of inflammation including serum IL-6, MCP1
 - > Strong safety profile >250 patients, including RA, psoriasis
 - > Subcutaneous and intravenous dosing data
- > Intellectual Property position
 - > Composition of matter protection in all major markets
 - > US protection to 2026
- > Strong pre-clinical data in lupus animal model (3 studies)
 - > significantly reduced kidney pathology, improved survival, prevented cutaneous lupus, reduced renal and circulating levels of key pro-inflammatory mediators (TNF- α , 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)

INV103 completed clinical trials

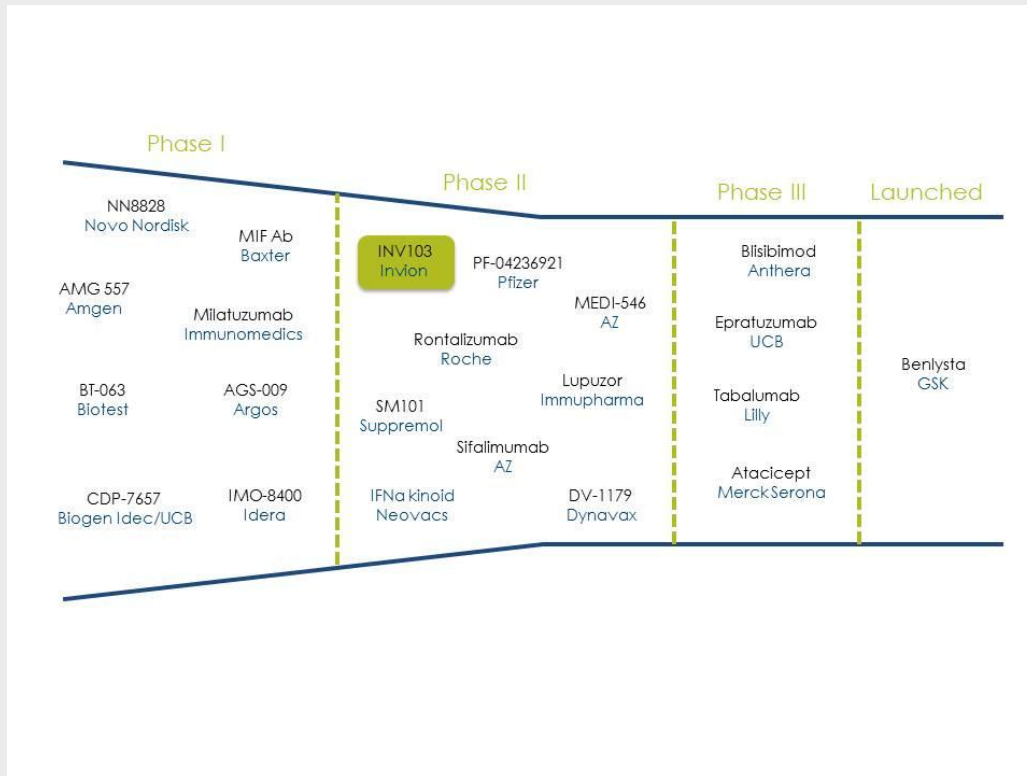
Phase	Indication	Route	Total patients	INV103 patients	Doses
1a	Healthy volunteers	IV/SC	19	14	1.2, 5.5, 10mg IV 5mg SC
1b	Multiple Sclerosis	IV	12	9	2.5 or 5mg, 5 doses
2a	Multiple Sclerosis	IV	50	39	Placebo, 5mg
2	Ulcerative Colitis	IV	8	8	5mg 2x weekly
2a	Plaque Psoriasis	IV	24	24	5, 7.5 or 10mg 2x weekly
2a	Rheumatoid Arthritis	IV	23	23	5, 7.5 or 10mg 2x weekly
1a	Healthy volunteers	SC	24	16	10,30,60,100mg sc
1a	Healthy volunteers	SC	22	17	30, 30x2, 60, 60x2, 80mg/weekly
2a	Rheumatoid Arthritis	SC	155	105	Placebo, 25mg, 75mg 2x weekly

INV103: phase II clinical strategy

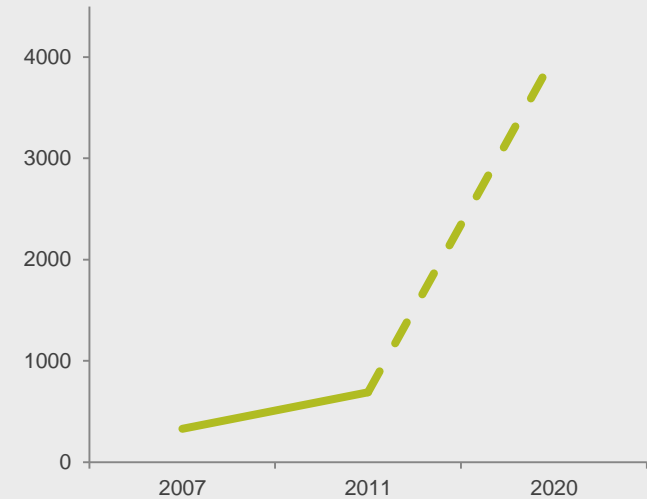
Systemic lupus erythematosus (SLE or lupus)

- > Lupus is a vascular inflammatory disease
 - > IL-6 is a marker of vascular inflammation
 - > INV103 has a significant effect on IL-6
- > Pre-IND meeting with US FDA Q4 2012
 - > FDA confirmed lupus as important unmet clinical need
 - > Also confirmed IL-6 as useful marker for dose-ranging
- > IND submission Q2 2013
- > Phase II trial commenced Q3 2013
- > Target outcomes: safety in lupus patients, reduction of IL-6 in lupus patients, PK to support future increased dosing
 - > Dose selection for future clinical outcomes study

Lupus: market size, global pipeline, continued unmet need



Lupus market size (\$millions)



Lupus market growth drivers

- Major unmet clinical need
- FDA approval of Belimumab (Benlysta) in 2011 – first lupus drug approval in 50 years
- Will increase patient awareness with positive effect on incidence and prevalence

INV103: phase II trial design – lupus

Trial name	INV103 (ala-Cpn10) in mildly active Systemic Lupus Erythematosus (lupus)
Trial design	Double-blinded, randomized, placebo-controlled, intravenous dosing
Patients	32 subjects (8 subjects per dose cohort, 4 cohorts)
Timing	Commenced Q3 2013 Initial data Q4 2013
Inclusion criteria	Mild lupus without clinical kidney disease
Principal Investigator	Alan Kivitz, M.D., Altoona Center for Clinical Research
Sites	Altoona, Pennsylvania; Dallas, Texas
Doses	10 mg - 300mg twice weekly
Primary endpoint	Reduction from baseline serum IL-6 levels
Safety endpoints	Safety and toxicity; pharmacokinetics; assessment of anti-drug antibodies
Exploratory endpoints	SELENA-SLEDAI score (disease activity index); pharmacodynamics; markers of systemic inflammation and vascular damage
Comment	Clinical program under US IND
Regulatory Status	www.clinicaltrials.gov ID: NCT01838694

INV103: phase II milestones

Lupus

- > Q4 2013 completion of 1 or 2 cohorts
 - > biochemical evidence of efficacy; safety of increased doses
 - > driver for scale manufacture of INV103
 - > driver for clinically outcome-based dose-ranging in lupus



Targeting inflammation

Summary

- ✓ 3 drug assets with multiple paths to market
- ✓ 3 FDA-regulated phase II clinical trials
- ✓ experienced management team
- ✓ significant valuation drivers: 12-36 months

Milestones to watch

2013

- Q1 ✓ Asthma - phase II study in asthma initiated, enrollments and patient dosing underway
- Q2 ✓ Lupus - IND filed with FDA
- Q3 ✓ Lupus - commencement of phase II study
✓ Chronic bronchitis (smoking cessation) – commencement of phase II study
- Q4 ✓ Licence agreement for new asset INV104 (zafirlukast)
> Chronic bronchitis - early signal of activity expected with secondary endpoints from sputum samples and inflammatory markers

2014

- Q1 > Lupus - completion of 1 or 2 cohorts, biochemical evidence of efficacy; safety of increased doses
> Asthma - initial data on airway histology and sputum biomarkers
- Q2 > Inhaled program - non-clinical development of inhaled INV102 (nadolol)

Corporate snapshot

Sector	Life Sciences (Biotechnology)
Principal activities	Clinical-stage pharmaceutical drug development
Pipeline	3 drug candidates
Operations	Australia & USA
ASX code	IVX
Share price (24-Oct-13)	\$0.095 (9.5 cents)
Shares on issue	~463M
Options on issue	~31M
Market cap (24-Oct-13)	\$44M
Cash at bank (30-Jun-13)	\$3.03M
Anticipated R&D tax credit inflow	\$1.46M
Cash burn (12 months to 30-June-13)	~\$6M



Targeting inflammation

Dr Greg Collier
Managing Director and CEO
Invion Limited

GPO Box 1557
Brisbane, QLD, 4001
Australia

P: +61 7 3295 0500
E: greg.collier@inviongroup.com
W: www.inviongroup.com

Corporate Presentation
October | 2013

References

Respiratory Market

World Health Organization Report: Global surveillance, prevention and control of chronic respiratory diseases (2007); DataMonitor: R&D Trends: COPD (2012); Respiratory and Inflammation, AstraZeneca Annual Report (2012); Smoking Cessation Drugs: World Market Prospects 2012-2022; U.S. Department of Health and Human Services. National Institutes of Health. National Heart Lung and Blood Institute. Morbidity and Mortality: 2009 Chartbook on Cardiovascular, Lung and Blood Diseases (as taken from the American Lung Association 2013); Visiongain Reports (2012) ; Healthcare Finance, Bloomberg Brief, 13 August 2012; Full-Year and Fourth-Quarter Financial Results, Merck & Co (2011). Sandler Research: Cystic Fibrosis (CF) Therapeutics Market – Opportunity Analysis and Forecasts to 2017 (2013); FDA news release '*FDA approves Kalydeco*' (2012); Cystic Fibrosis Foundation; *Company estimates.

INV102 (nadolol)

Chronic Exposure to Beta-Blockers Attenuates Inflammation and Mucin Content in a Murine Asthma Model. Nguyen et al. Am J Respir Cell Mol Biol. 2008 Mar;38(3):256-62; β -Adrenoceptor signaling is required for the development of an asthma phenotype in a murine model. Nguyen et al. Proc Natl Acad Sci USA. 2009 Feb 17;106(7):2435-40. Bond et al. 'Complementary anti-inflammatory effects of a -blocker and a corticosteroid in asthma' Arch Pharmacol 2011.

INV103 (ala-Cpn10)

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. (Shields A.M., et. al., 2011, Clin and Exp. Immunology, 165, 292-300).

Lupus Market

Decision Resources: Treatment Trends Systemic Lupus Erythematosus (2013); Lupus Foundation of America "How is Lupus treated?" (2013); Datamonitor: Systemic Lupus Erythematosus Market Forecast (2011); BCC Research: Drugs & Treatments for Autoimmune Diseases: Global Markets (2011); Decision Resources: Systemic Lupus Erythematosus (2012).