Invion Limited (ASX:IVX)

Clinical-stage life sciences company targeting chronic inflammation

Investor Presentation
August | 2015

INVION

Targeting inflammation

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Assets in development

Respiratory

1. **INV102 (nadolol)**: is a beta blocker (beta adrenergic biased ligand) currently used to treat high blood pressure, coronary chest pain (angina) and migraine, being repurposed to treat chronic inflammatory airway diseases (e.g. asthma and COPD). Oral INV102 is being studied as an aid to smoking cessation in patients with COPD.

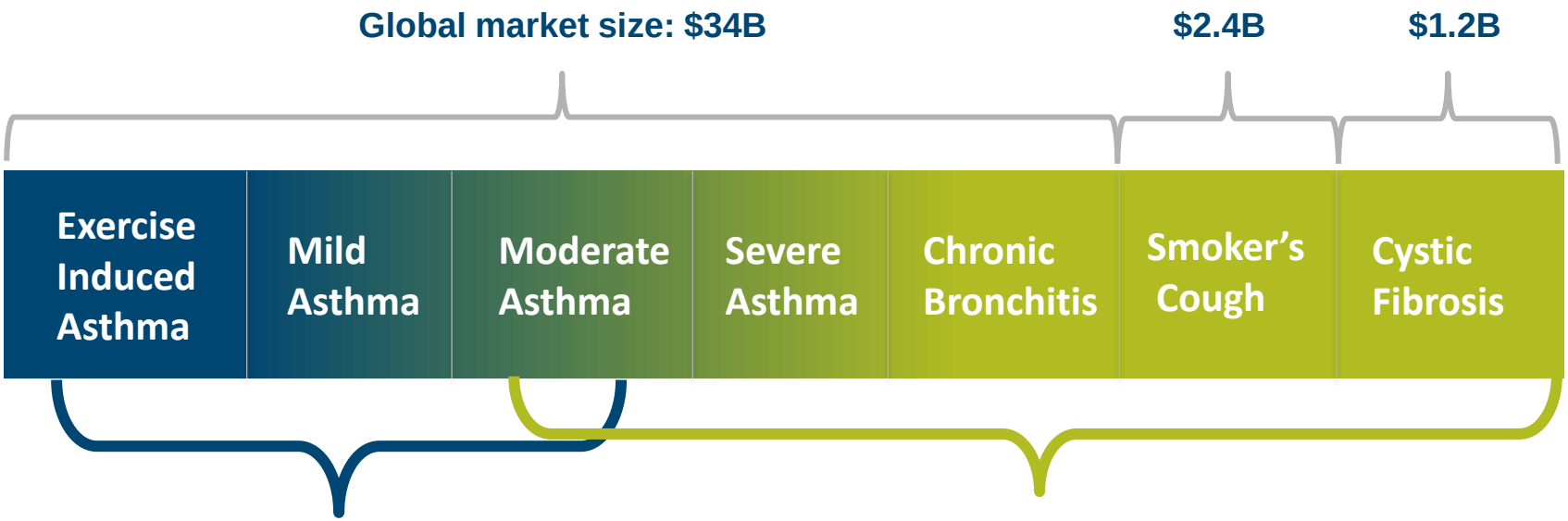
2. **INV104 (zafirlukast**): is a leukotriene receptor antagonist (LTRA) that reduces inflammation, constriction of the airways and the build-up of mucus in the lungs, that is being developed as an inhaled therapy to treat asthma in adults and children.

Autoimmune

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

    > Near-term partnering opportunity

Spectrum of airway disease and opportunities



INV104 (zafirlukast)
Monotherapy + combinations

INV102 (nadolol)
Monotherapy + combinations

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Targeting chronic inflammatory airway disease

Oral INV102 (nadolol)

Treating the airway: background and rationale

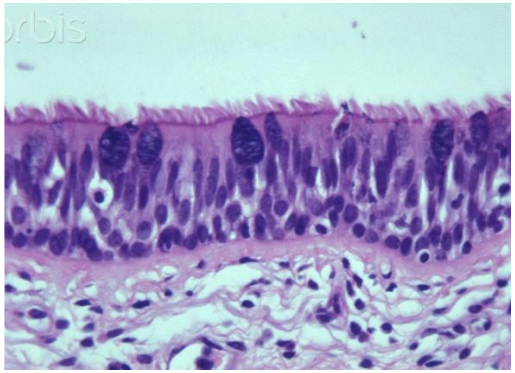
- Existing drugs do an excellent job in opening constricted airways:
  bronchodilators include β-adrenergic and anti-muscarinic drug classes

- Existing drugs do an excellent job in decreasing inflammatory cells in the airway:
  inhaled corticosteroid (ICS) and anti-IL5 monoclonal antibody drug classes

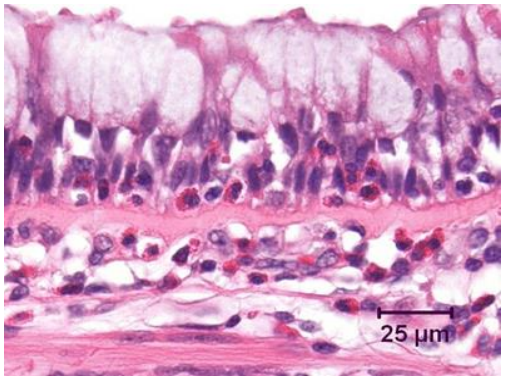
- Fixed combinations of beta agonists and ICS are the mainstay treatment of airway disease:
  e.g. Symbicort® and ADVAIR®

- **However: these drugs have had NO positive impact on death due to chronic airway disease; death is due to increased abnormal mucus and inflammation**

The “vicious cycle” of chronic inflammatory airway disease



Normal Histology



Mucous metaplasia found in COPD, asthma and CF

Inflammation from:
- cigarette smoke
- chronic infection (C.F.)
- allergen, O_3 (asthma)

Changes in basal cell populations

Increased IL-8 and beta-arrestin pathway activity

Increased goblet cell production/ loss of ciliated epithelial cells

↓ mucin clearance
↑ abnormal mucins
↑ total mucus

Increased recruitment of inflammatory cells (PMN/EOS)

Increased damage from inflammatory cells / infection

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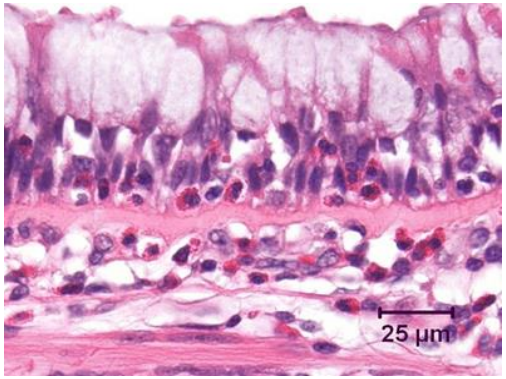
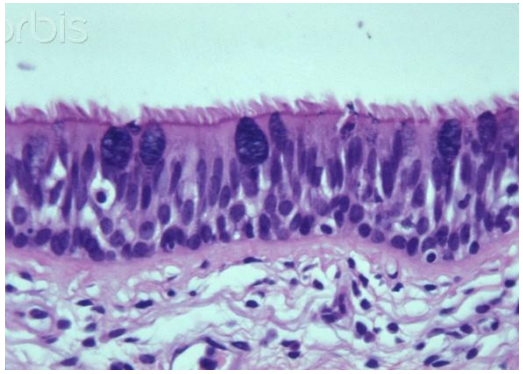
Nadolol has unique properties that could treat airway disease

- In cell experiments, INV102 (nadolol):
  - Blocks the β-arrestin pathway on airway epithelial cell β2 receptors (Lefkowitz)
- In animal experiments, nadolol:
  - Blocks (prevents) or reduces (treats) the increase in goblet cells caused by inflammation
  - Blocks the β-arrestin pathway in airway β2 receptors
  - Reduces markers of airway inflammation (IL-5) and abnormal mucus production (MUC5AC)
- In human studies, orally administered nadolol
  - Decreases biomarkers of inflammation (IL-8) and β-arrestin pathway activation (ERK2)
  - Decreases airway hyper-responsiveness, a hallmark of asthma
  - Can be safely administered by titration to minimize risk of cardiovascular side effects

Nadolol could reverse the “vicious cycle” of airway inflammation



Mucous metaplasia found in COPD, asthma and CF



Normal Histology

Nadolol

Shown in clinical trial

DECREASED IL-8 and beta-arrestin pathway activity

DECREASED goblet cell production/ loss of ciliated epithelial cells

↑ mucin clearance
↓ abnormal mucins
↓ total mucus

DECREASED recruitment of inflammatory cells (PMN/EOS)

DECREASED damage from inflammatory cells / infection

Restoration of ciliated epithelial cells

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Oral nadolol program: progress and active clinical trials and results

Clinical benefits

- ✓ the only drug targeted to address the unmet medical need of mucous metaplasia in the airway
- ✓ targeted as an add-on to existing therapies to make them safer and more effective by reducing mucous production
- ✓ targeted to assist lung healing and aid smoking cessation in patients trying to quit

Development strategy

- ✓ proof of concept
- ✓ identify speed to market commercial strategy (smoking cessation)
- ✓ identify wider use and IP opportunity (inhaled nadolol)
- ✓ phase II trials in mild asthma and smoking cessation
- > safety and biomarker data from phase II trials underpins inhaled drug program
- > endpoint in smoking cessation trial leads to EOPII / Phase III

Development program

- ✓ pharmacology is based on biased ligand and inverse agonist activity at beta receptor in airway
- ✓ chemistry and manufacturing, including titration dose development
- ✓ toxicology and metabolism profile
- ✓ IND status
- ✓ 2 x proof of concept studies in patients with mild asthma (Hanania)
- ✓ phase II in mild asthma (NIH sponsored, ongoing) & Phase II in smoking cessations (reports Q3 2015)
- ✓ interim data shows clinical relevant changes in biomarkers of inflammation
- > Final data to characterize airway epithelial response through biochemical markers; design next oral and inhaled studies; and create new intellectual property based on correlations of safety and efficacy with biochemical marker profiles.

Oral nadolol: 155 patient phase II smoking cessation study reporting Q315.

Leveraging the data: upcoming analysis and reporting

Third quarter planned analyses and reporting		Fourth Quarter
Biomarkers	**Smoking cessation**	**Combined data**

> Report on effects of nadolol vs placebo on key biomarkers
  > IL-8 (neutrophil attraction)
  > ERK2 (beta arrestin pathway)
  > MUC 5AC (abnormal mucus)
> Secondary analysis of responders and biomarker changes - identifying markers that are/are not useful in longer term studies
	> Report on smoking cessation rates in nadolol treatment versus placebo
	> Secondary analyis is on reduction versus cessation rates
	> Dose responses and responders as a function of dose, titration and history
		> Correlation of smoking cessation/ reduction data with baseline biomarkers
		> Correlation of smoking cessation/ reduction data with biomarker changes
		> New IP prosecution

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Oral nadolol: 155 patient phase II smoking cessation study reporting Q315.

Positive endpoint data

Safety

- Safety of titration doses
- No need for rescue medication
- Safely delivered to smokers trying to quit

+

Biomarkers

- Report on effects of nadolol vs placebo on key biomarkers IL8, ERK2, MUC5AC.

+

Smoking cessation

- Report on smoking cessation rates in nadolol treatment versus placebo

=

Leads to

Oral nadolol program:

end of Phase II meeting with FDA / Phase III

PLUS

Inhaled nadolol program:

development to proof of concept / Phase II

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Oral nadolol: 155 patient phase II smoking cessation study reporting Q315.

Positive endpoint data

Leads to

Safety

- Safety of titration doses
- No need for rescue medication
- Safely delivered to smokers trying to quit

+

Biomarkers

- Report on effects of nadolol vs placebo on key biomarkers IL8, ERK2, MUC5AC.

Smoking cessation

- Report on smoking cessation rates in nadolol treatment versus placebo

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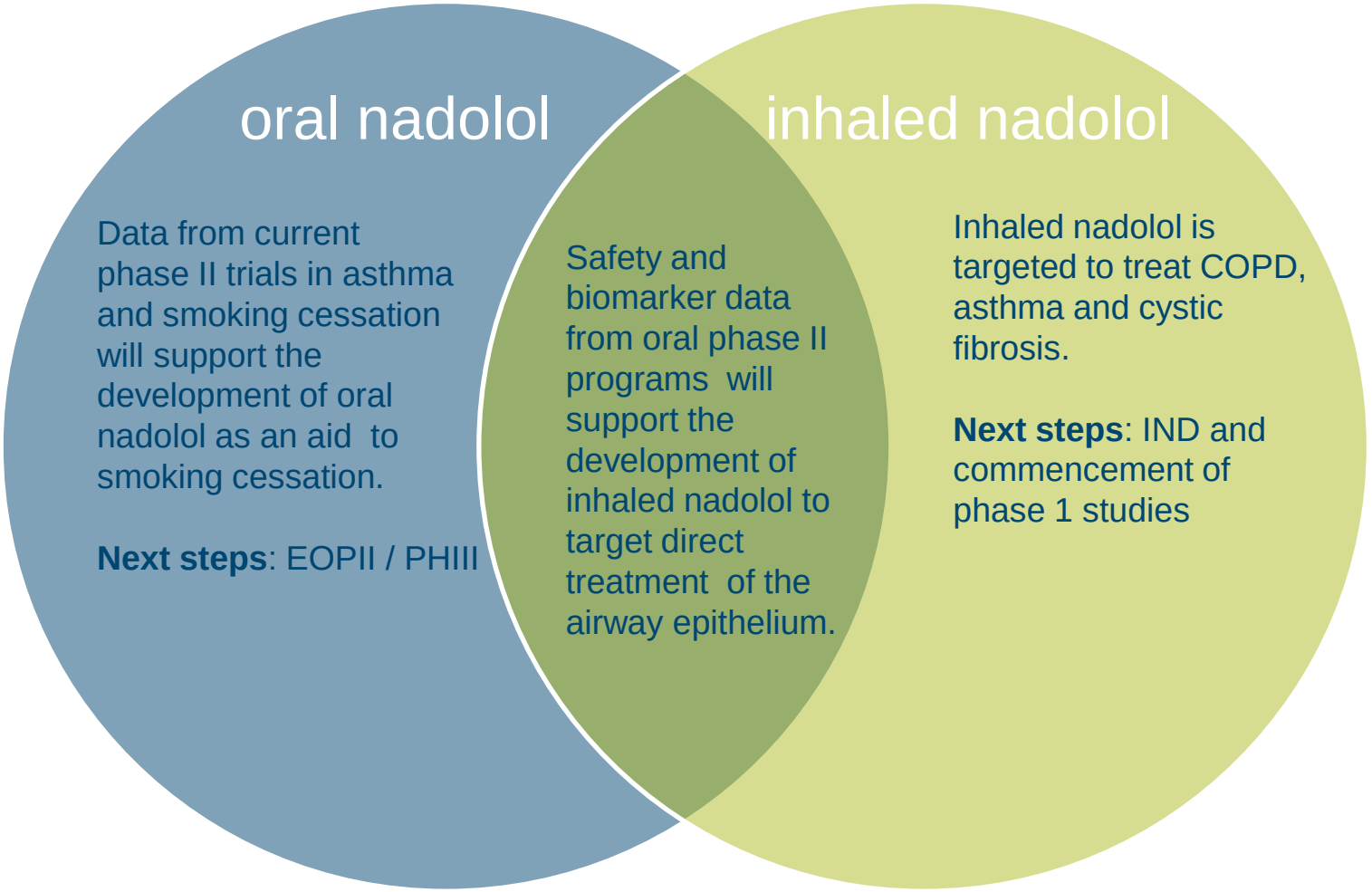
Inhaled nadolol program: development to proof of concept / Phase II in asthma, COPD and cystic fibrosis

Nadolol franchise: progressively de-risked



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Respiratory therapeutics: inhaled program

INV102 (nadolol) in asthma, COPD & cystic fibrosis

Inhaled nadolol program: progress and clinical development strategy

Clinical benefits

- ✓ once daily dosing directly to the site of injury at 1/100 of the oral dose to mitigate systemic side effects
- ✓ targeted for long term use in COPD, severe asthma and cystic fibrosis as an add-on to existing therapies to make them safer and more effective by reducing mucous production an enabling lung healing
- > Medium-term development: combination therapies
  - > inhaled nadolol + ICS (Asthma)
  - > inhaled nadolol + LAMA or LABA (COPD)
  - > inhaled nadolol + antibiotics (CF)

Status of collaboration with 3M Drug Delivery systems for proprietary formulation and device using 3M's pressurised metered dose inhalation (pMDI) technology

- ✓ Formulation and device selected
- ✓ Toxicology supplies manufactured
- ✓ Clinical supplies manufactured
- ✓ Toxicology supplies provided to CRL (Montreal QUE); toxicology studies have commenced

Development program

- ✓ Pre-IND status with FDA
- ✓ Commencement of toxicology studies
- > IND submission (2016)
- > Phase I and Phase II clinical studies in asthma, COPD and cystic fibrosis (2016-7)

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
- Formulation and device selected
- Toxicology supplies manufactured
- Clinical supplies manufactured
- Toxicology supplies provided to CRL (Montreal QUE); short-term toxicology ongoing in rats and dogs

Nadolol franchise: market size, relevance and interconnectedness

Chronic Obstructive Pulmonary Disease (COPD) is an umbrella term used to describe chronic lung diseases that cause limitations in lung airflow.

$47.1 billion by 2017

The global market for respiratory drugs is estimated to be **$47.1 billion by 2017**.

Nadolol is targeted to be used in conjunction with existing therapies to make them safer and more effective representing a niche in an existing large and growing market.

$3.8 billion by 2017

The smoking cessation drug market is predicted to be **$3.8 billion by 2016.**

Nicotine-focussed therapies comprise the bulk of the existing market, but they do not address lung healing. **Nadolol** represents an opportunity to add-on and expand an existing market.

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INV104 (zafirlukast)

Target: a novel inhaled non-steroidal anti-inflammatory treatment for asthma

Target: an inhaled reformulation of a successful oral therapeutic for asthma

INV104 (zafirlukast):

- Leukotriene-receptor antagonist (LTRA) or “anti-leukotriene” that reduces inflammation, constriction of the airways, and the build-up of mucus in the lungs
- Approved worldwide as an oral tablet for asthma (AstraZeneca)
- Well established clinical efficacy & safety profile
- Inhaled proof of concept using propellants that are now banned (CFCs)
- Inhaled formulation indicated as monotherapy for mild persistent asthma and exercise-induced asthma
- Indicated to reduce inhaled corticosteroid (ICS) dependency in adults and children
  - as an alternative as first controller medication in mild persistent and moderate asthma
  - by addition of low dose ICS treatment rather than doubling ICS
  - by enabling reduced ICS dose “steroid sparing” in steroid-dependent asthma

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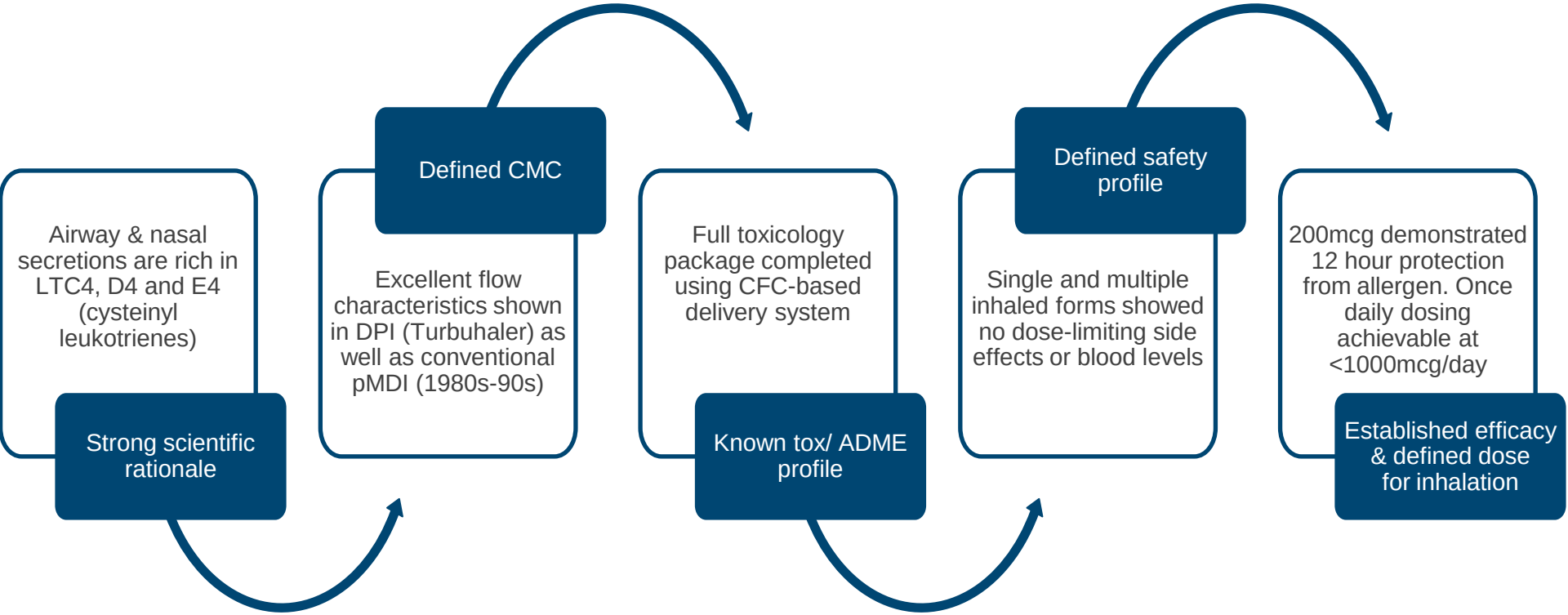
Inhaled zafirlukast an anti-leukotriene: background and rationale



- Zeneca (now A/Z) stopped inhaled development in mid 1990s.
- Zafirlukast and montelukast have resisted formulation in non-cfc propellant systems.

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FDA pre-IND established framework for reformulation of zafirlukast

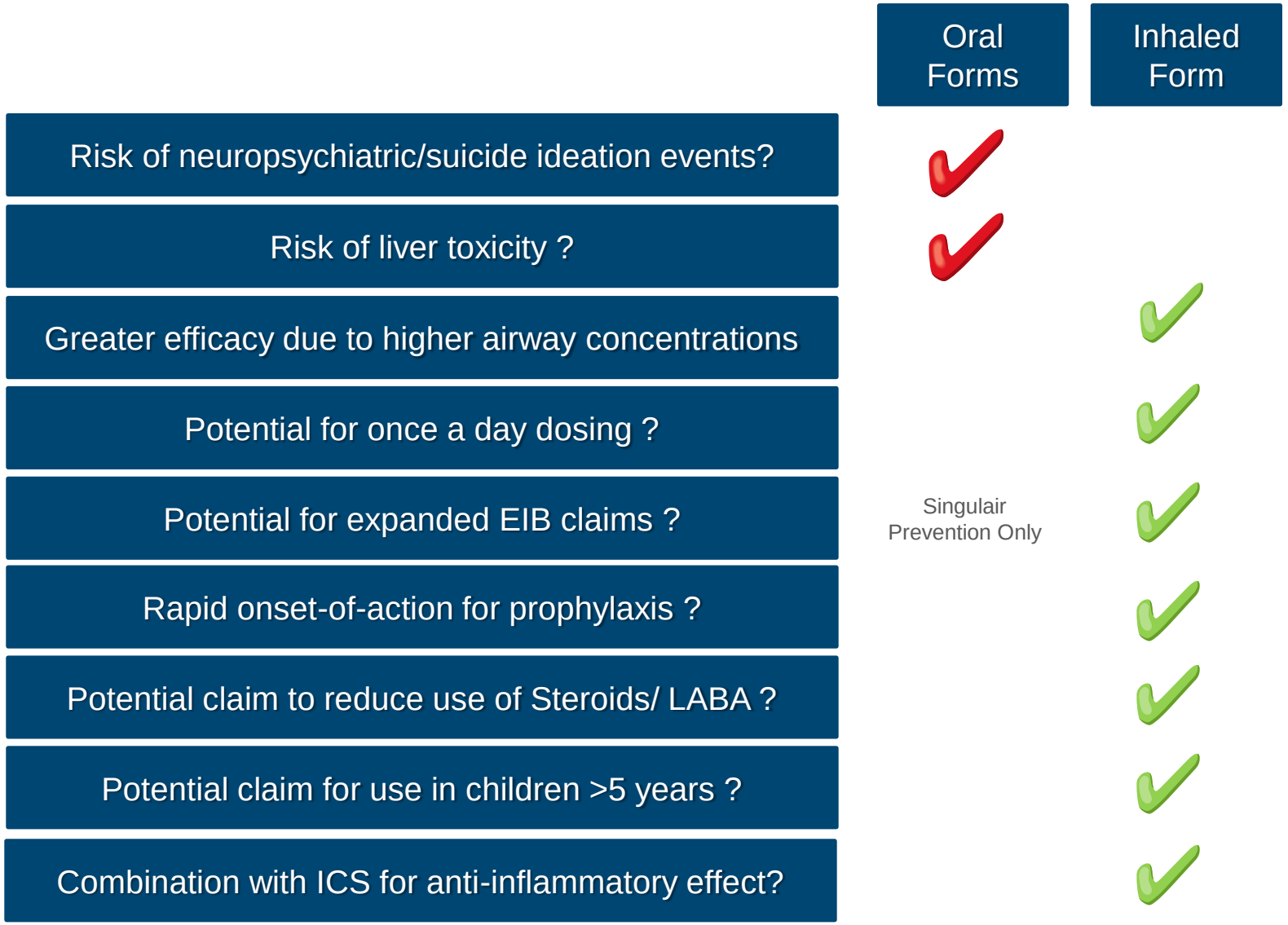
Agreement reached with FDA on:

- chemistry manufacturing and controls (GMP)
  - active pharmaceutical ingredient (API) with drug master file (DMF)
  - formulation: dry powder inhaler (DPI) approved for development

- toxicology and bioanalytical assay (GLP) to support 4 weeks' dosing
  - 2 species for 28 days: naso-pulmonary exposure
  - 1 species for 6 months

- IND submission and clinical program
  - phase I: single rising dose study for safety (paradoxical bronchoconstriction) and pharmacokinetics
  - phase I: multiple dose safety study for safety (paradoxical bronchoconstriction) and pharmacokinetics
  - phase II: challenges to reprise previous studies: cold air, exercise and allergen [cat and ragweed]; steady state dosing for signs and symptoms of asthma [diary card] and attenuation of response to exercise and/or allergen

Inhaled Product Rationale



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Hovione CMC collaboration mitigates major risk of inhaled zafirlukast development

Formulation & device partner, Hovione

- Invion will collaborate with Hovione to develop the proprietary novel technology – a dry powder formulation of zafirlukast and the accompanying inhalational delivery device
- under the terms of the agreement, Hovione will provide chemistry and manufacturing services to develop and optimise the dry powder inhalation formulation which will be delivered using its proprietary device technology known as the XCaps inhaler system
- Hovione device is ideally suited for fixed combination with ICS, bronchodilators, or INV102 (nadolol).
- IP protection provided under licence via Hovione formulation and device, Invion retains commercialisation rights

CMC solution complements existing and planned toxicology and clinical packages

- previously completed using CFC-based device
- Clinical proof of concept based on inhalational challenge studies; previously completed using CFC-based device

About Hovione and the XCaps inhaler

- International company with over 50 years' experience in the development and compliant manufacture of active pharmaceutical ingredients and drug product intermediates
- With four FDA inspected sites in the U.S., China, Ireland, and Portugal, the company focuses on the most demanding customers, in the most regulated markets
- In the inhalation area, Hovione is the only independent company offering such a broad range of services.

XCaps is a patent protected device filed and granted in over 40 countries, including US (US 8677992) and EU (EP 2546460). XCaps device is simple, reusable and low-cost. This DPI is indicated for applications where a chronic or a medium term acute capsule based delivery of an API is needed.

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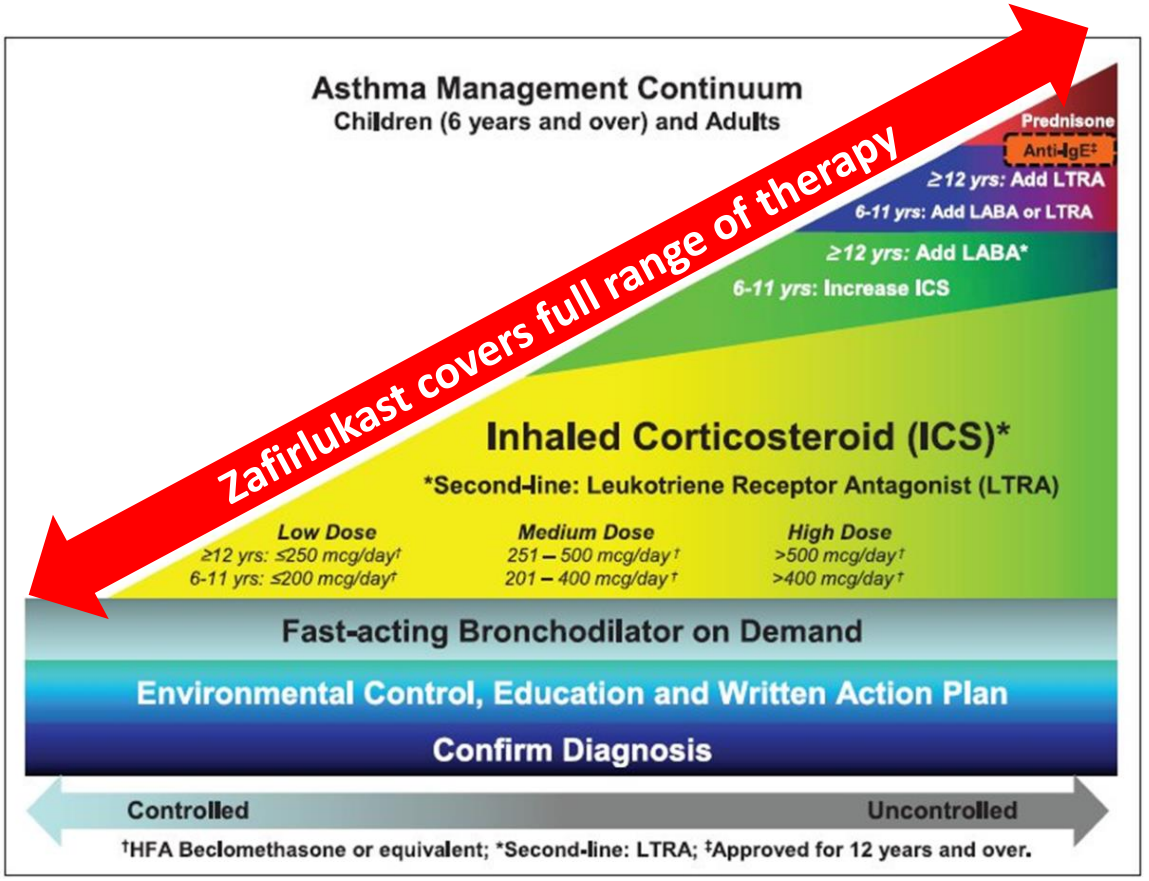
Expected placement of inhaled zafirlukast in treatment regimes

- As many as 334 million people have asthma which occurs in people of all ages. Wheeze is the most common symptom and the burden of disability is high.
- In 2007 the U.S. spent over $56 billion on asthma care, of which nearly $27 billion was spent on pediatric asthma.

Inhaled zafirlukast

- targeted for use as a controller/ preventer with few or no side effects for the full range of asthma therapy
- especially useful in LTD4-driven asthma including aspirin sensitivity and in children
- indicated as steroid sparing
- inhaler will facilitate substitution for inhaled corticosteroids (ICS)
- for many patients, inhaled product alone (monotherapy) will be effective



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Inhaled zafirlukast program: progress and clinical development strategy

Clinical benefits

- ✓ FDA approved as an oral asthma therapy
- ✓ Proof of concept previously conducted using inhaled drug
- ✓ Non-steroidal
- ✓ Higher local concentrations without systemic exposure (decreased risk of generic duplication)

Status of collaboration with Hovione for proprietary formulation and device using Hovione's patented XCaps inhaler system

- ✓ Formulation and device selected
- ✓ Program of works for manufacture of toxicology and clinical supplies
- > Formulation complete for toxicology (non GMP) (3Q2015)
- > Toxicology supplies manufactured (3Q2015)
- > Clinical supplies manufactured to support IND and Phase 1 (4Q2015-1Q2016)

Development program

- ✓ Pre-IND status with FDA
- ✓ Formulation and device collaboration
- > Commencement of toxicology studies (4Q2015)
- > IND submission (1Q2016)
- > Phase I and Phase II clinical studies in (Q1-4 2016)

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Targeting chronic inflammation caused by autoimmune disease

INV103 (ala-Cpn10)

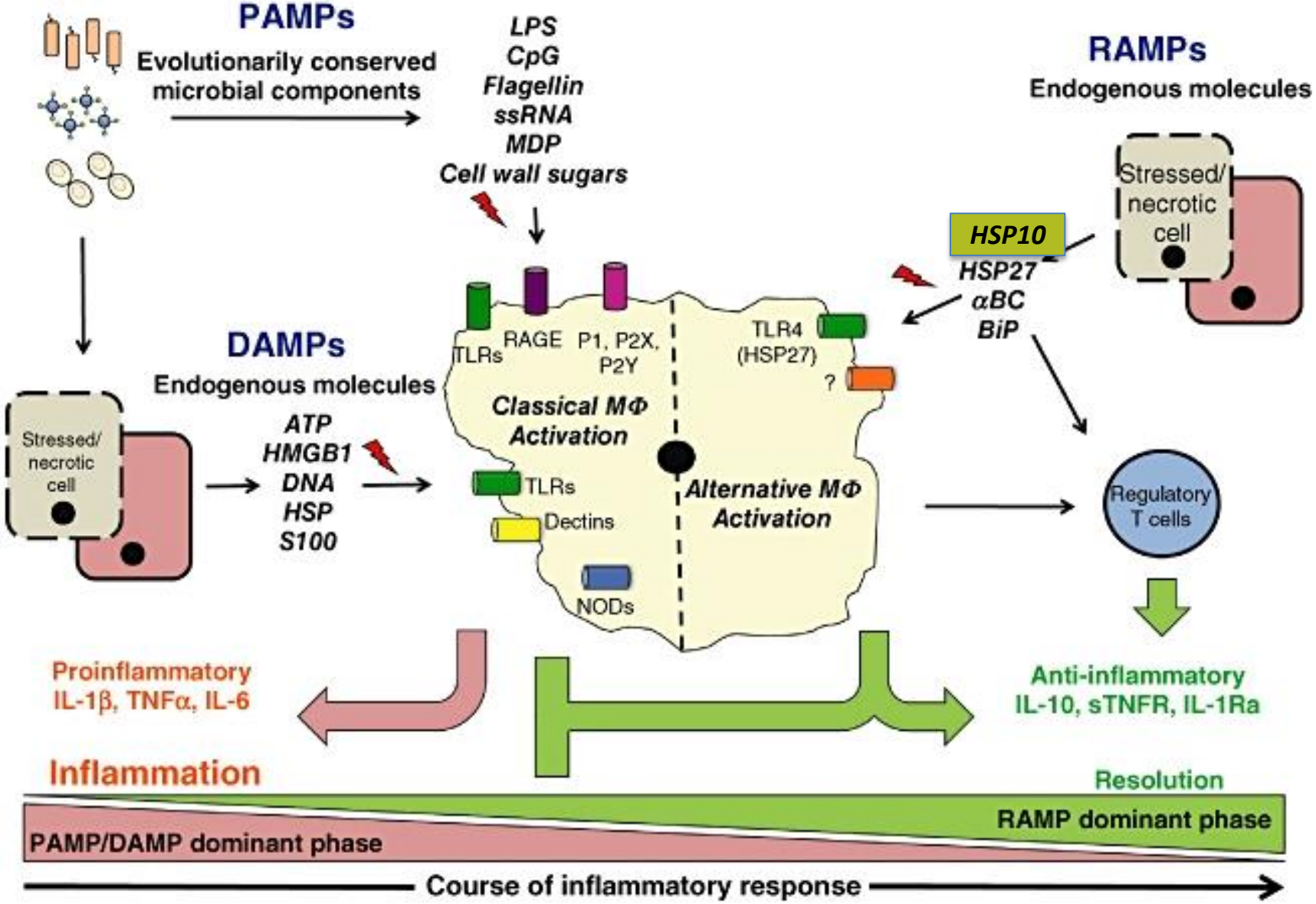
INV103 (ala-Cpn10): background and rationale

- Minimally modified form of naturally occurring protein
- Maintains heptameric structure and function
- Intracellular function: prevent protein misfolding
- Extracellular function: Cpn10 proposed as a founding member of the Resolution Associated Molecular Pattern (RAMPs) family (Shields et al, Clin Exp Immunol, 2011, 165: 292-300) 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 (3 studies)
  - 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)

- Toxicology support through 3 months' dosing
- Intellectual Property position: composition of matter protection in all major markets (US 2026)



References: 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)

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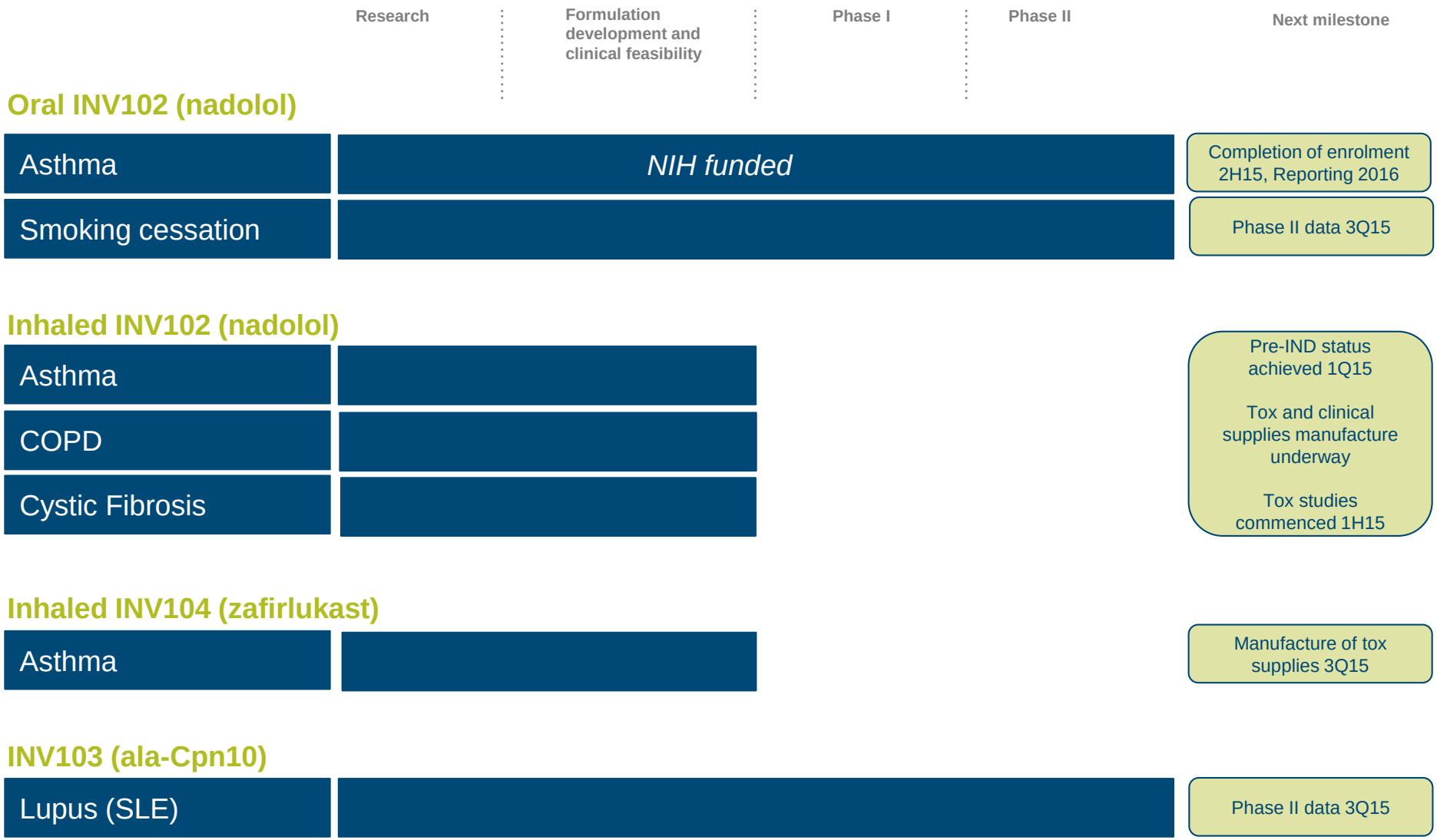
Ala-Cpn10 deliverables

- Completion of dosing of all 4 cohorts
- Safety, pharmacokinetics and anti-drug antibodies
- Biomarkers of SLE activity including:
  - Serum IL-6, TNFα, ICAM-1, MCP-1, VCAM-1,
  - Urinary protein and MCP-1
- Focus on Peripheral Blood Monocytic Cells (PBMC) stimulated by LPS to measure immunosuppressive effect of ala-CPN10.
- We will be looking at PMBC to support further development with partners of ala-Cpn10 in autoimmune diseases, such as progressive MS and orphan diseases.
- The data generated above will be shared with potential pharmaceutical partners in the coming months.

Pipeline


Research
Formulation development and clinical feasibility
Phase I
Phase II
Next milestone
Oral INV102 (nadolol)
Asthma
NIH funded
Completion of enrolment 2H15, Reporting 2016
Smoking cessation
Phase II data 3Q15
Inhaled INV102 (nadolol)
Asthma
COPD
Cystic Fibrosis
Pre-IND status achieved 1Q15
Tox and clinical supplies manufacture underway
Tox studies commenced 1H15
Inhaled INV104 (zafirlukast)
Asthma
Manufacture of tox supplies 3Q15
INV103 (ala-Cpn10)
Lupus (SLE)
Phase II data 3Q15

Program targets: 12-18 months

- Oral nadolol:
  - advanced into Phase III as an adjunct to smoking cessation in patients with chronic cough and/or chronic bronchitis
  - IP based on combination of nadolol safety and efficacy with diagnostics from smoking cessation study
- Inhaled nadolol:
  - Proprietary formulation in PMDI (CMC)
  - Completion of toxicology program in 2 species to support POC (Tox)
  - Completion of robust Phase I program to support phase II in 3 indications
- Inhaled zafirlukast:
  - Proprietary formulation and device
  - Completion of toxicology 28 days, 2 species with Charles River Labs
  - Phase I studies showing safety of inhaled zafirlukast
  - Plans for repeat of Phase II studies which had previously provided POC (1994)
- Ala-Cpn10: collaboration/partnership deal

Board and Management with proven track record

- **Chairman of Board of Directors, Mr Brett Heading**
  - Senior partner of law firm McCullough Robertson, 27 years as a company director. Former Chairman, ChemGenex Pharmaceuticals (sold to Cephalon $230M); former Director, Peplin Biotech Limited.
- **Managing Director & CEO, Dr Greg Collier**
  - 20 year career in pharmaceutical research, development and commercialisation, former CEO ChemGenex Pharmaceuticals, 150 peer reviewed publications, 33 patents, Roche Award for Excellence
- **Executive VP R&D and CMO, Dr Mitchell Glass**
  - 25 year veteran of the pharmaceutical industry, Graduated from the University of Chicago, board certified in internal medicine, pulmonary and critical care medicine. Senior executive roles at AZ & GSK. 5 FDA-approved drugs, including “first in class” and for the beta blocker carvedilol (Coreg®).
- **James Campbell, PhD MBA, Non- executive Director**
  - Senior biotechnology director and executive with 20+ years experience in research, research management, advisory. Formerly COO and CFO, ChemGenex Pharmaceuticals.
- **Warren Brown, B Eng, Non-executive Director**
  - Experienced in corporate strategy and project management. Background in consulting engineering and contract negotiation.

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 (5-Aug-15)	$0.023 (2.3 cents)
Shares on issue	~822 M
Options on issue	~60M
Market cap (5-Aug-15)	~$19M
Cash at bank (31-July-15)	$2.285M

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Investor Presentation

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