Investor Presentation
November | 2015

Invion Limited (ASX:IVX)

Clinical-stage life sciences company targeting chronic inflammation

Assets in development

Respiratory

1. **INV102 (nadolol)**: beta blocker being targeted to treat chronic inflammatory airway diseases (e.g. asthma and COPD). Oral INV102 is also being studied as an aid to smoking cessation.
    - Phase 2 completed:
        - proof of concept in biased ligand activity
        - clinically efficacious in Smoking reduction and cessation

2. **INV104 (zafirlukast**): leukotriene receptor antagonist (LTRA) that reduces inflammation, constriction of the airways and the build-up of mucus in the lungs
    - Risk mitigated program including prior clinical proof of concept
    - Development and manufacturing collaboration with Hovione

Autoimmune

3. **INV103 (ala-Cpn10)**: modified naturally occurring human hypothesised to maintain and restore immune homeostasis
    - Phase 2 data completed, partnering discussions underway

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5 OCT 2015 - 3:30PM

Invion eyes success with quit smoking drug

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Invion pushes to develop respiratory drug

AAP

2015-10-05

Drug developer Invion is stepping up efforts to pursue further development of its respiratory drug Nadolol, after completing Phase 2 clinincal trials in patients trying to quit smoking.

The company announced on Monday that data from its successful trials showed that smokers administered with the drug were more likely to stop smoking completely, or dramatically reduce the number of cigarettes smoked.

The results indicated the success rate was in the ballpark with that of two existing drugs in the market - from GlaxoSmithkline and Pfizer, but had lower side-effects, Invion chief executive

Market watch top he

Australian reports

- Aust markets: Share mar
- Aust dollar report: $A bo looks unlikely
- Aust credit close: Aust equities boost

World reports

- World commodities summary
- World markets:

Stocks to watch

Daily Telegraph

SYDNEY 18-33°C

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National

Anti-smoking drug Inv102 could help treat asthma, cystic fibrosis

October 5, 2015

HEALTH EDITOR Herald Sun

THE AUSTRALIAN

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HELP US RAISE MO for mental health research

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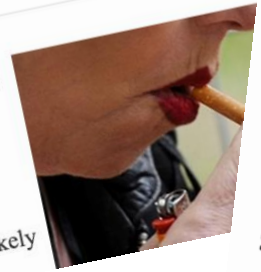
Invion eyes success with quit smok drug

BY PRASHANT MEHRA | AAP | OCTOBER 05, 2015 3:28PM

AUSTRALIAN drug developer Invion's migraine and blood pressure treatment drug Nadolol has found success as a new quit smoking agent.

RESULTS from its 155-patient, phase-two clinical trial indicate smokers administered with the drug are more likely to stop smoking completely, or



A New Australian drug shown to double smokers' chances of quitting in trials is being touted as a possible treatment for asthma, cystic fibrosis and other lethal respiratory conditions.

By directly targeting the damage being done to a smoker's lungs rather than their nicotine addiction, the experimental Inv102 drug is hoped to offer a whole new approach to quitting.

That process also opens the door to saving lives from airway conditions such as asthma by blocking the build up of mucus that can impact on breathing in the same way it creates "smokers cough".

Releasing results from its latest US trials on Monday, Australian developer Invion revealed one-in-five chronic smokers were able to completely quit cigarettes after using Inv102 for two months, compared to one-in-10 participants who quit while using a placebo.

Invion chief executive officer Dr Greg Collier said he hoped to use the results to push for a final trial and approval from the US Food and Drug Administration as a smoking cessation medication, which would fast-track Inv102's "bigger picture" approval for other diseases.

"We are right in that sweet spot in terms of approval for smoking cessation," Dr Collier said.

"The beauty of this is drug is that it does not have the neurological effects — it is a totally different mechanism and goes straight to the lungs whereas both the (existing nonsmoking) drugs have

thepharmaletter

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Invion says Phase II trial of airway disea successful, pushes for further study

05-10-2015 | COMMENTS (0)

Australia | Drug Trial

BUSINESS REVIEW

Drug trials show new 'quit' strategy

Life sciences minnow Invion is claiming early success i its quest to improve smoking cessation rates among candidates with chronic bronchitis and other airway ailments. On the back of its results from a 155-patient, phase-two clinical study

STOP PRESS: Invion successfully completes Phase 2 study of INV102 (nadolol) to aid smoking cessation

Data announced 5 October 2015:

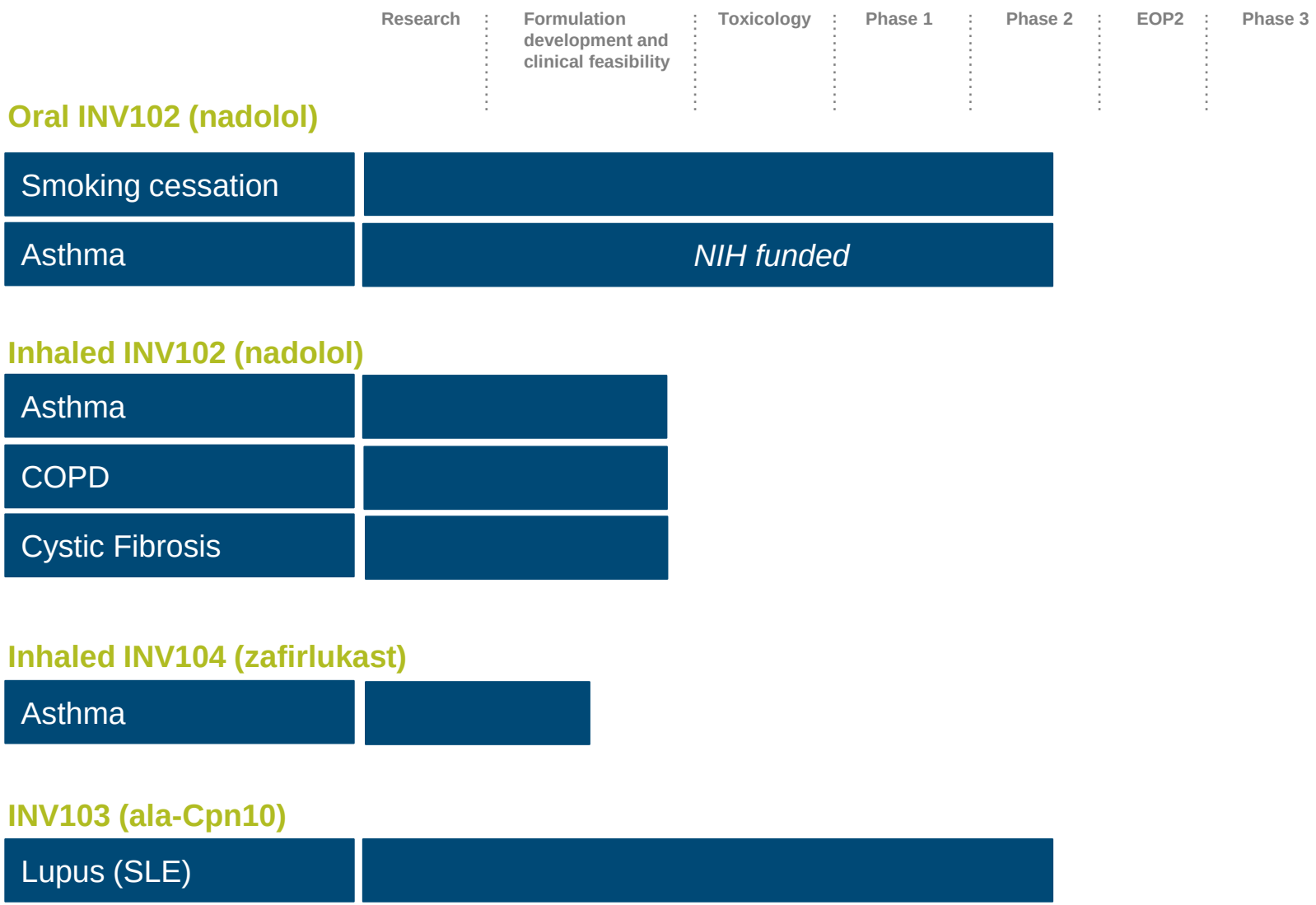
- Completed Phase 2 trial data demonstrates INV102 treated smokers were more likely to stop smoking completely or dramatically reduce the number of cigarettes smoked
- Data demonstrates that INV102 is a safe and effective treatment for patients with chronic bronchitis who are enrolled in smoking cessation programs
- Invion is preparing an End of Phase 2 Meeting request to submit to the FDA during Q4 2015
- New data paves the way for INV102 to be developed as a novel inhaled treatment for chronic airway diseases including asthma, COPD and cystic fibrosis

Milestone update: achievements in 2015

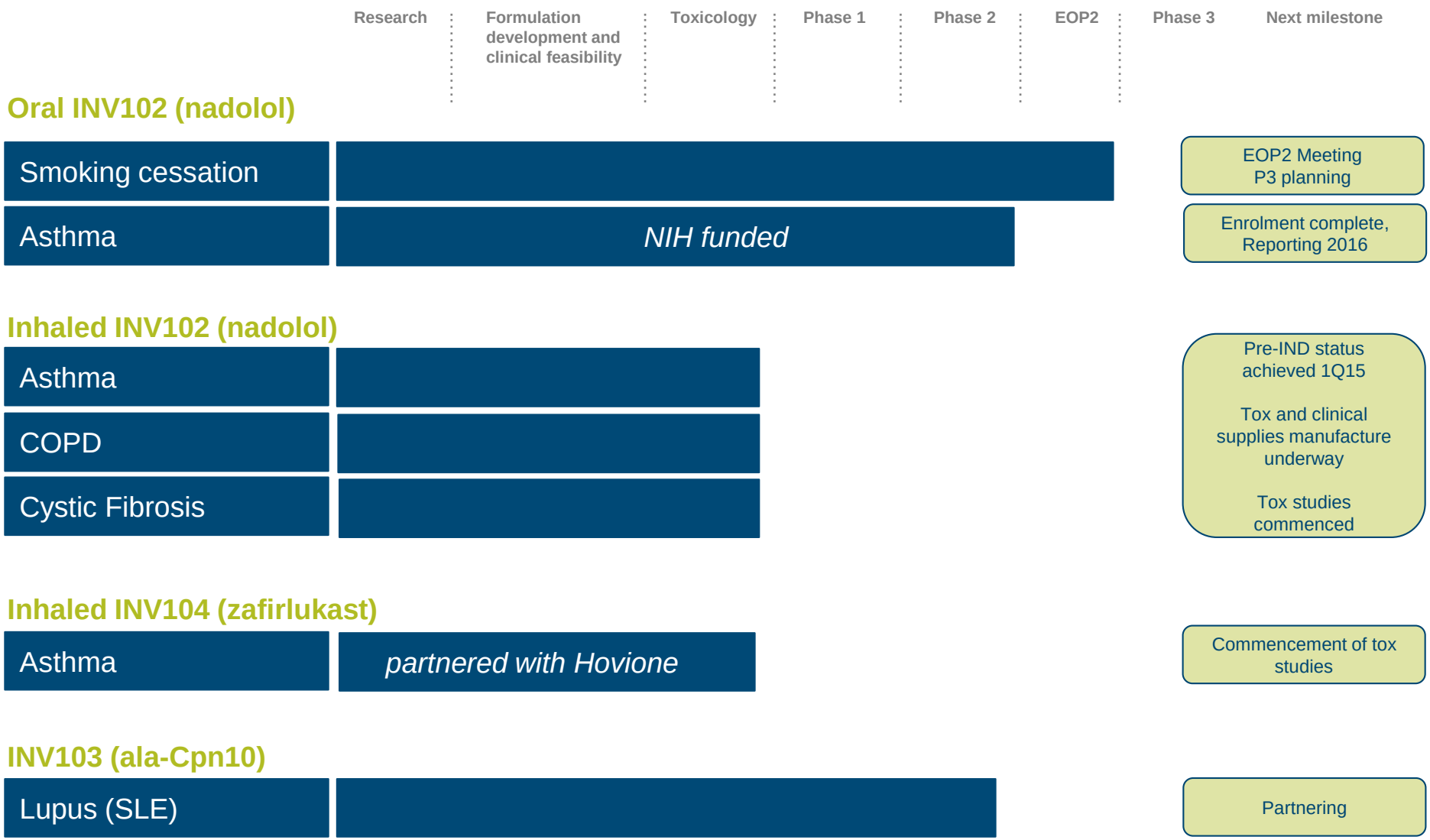
3 drug assets in 3 phase 2 clinical trials across 4 development programs

- ✓ Blind-broken interim data from phase 2 smoking cessation trial of INV102 (nadolol)
- ✓ Pre-IND status for inhaled INV102 (nadolol) as a potential therapy for asthma, COPD & cystic fibrosis
- ✓ Manufacture of toxicology and clinical supplies and commencement of toxicology studies for inhaled INV102 (nadolol)
- ✓ Completion of phase 2 clinical trial of INV103 (ala-Cpn10) in lupus patients
- ✓ Data from phase 2 clinical trial of INV013 (ala-Cpn10) in lupus patients
- ✓ Selection of formulation and device for inhaled INV104 (zafirlukast)
- ✓ Commencement of manufacture of toxicology and clinical supplies for INV104 (zafirlukast)
- ✓ Completion of dosing in phase 2 smoking cessation trial of INV102 (nadolol)
- ✓ Positive safety and efficacy data from phase 2 oral INV102 (nadolol) study in patients undergoing smoking cessation
- ✓ Completion of enrolment of NIH-funded phase 2 study of INV102 (nadolol) in asthma patients

Pipeline: 4Q 2014



Pipeline: 4Q 2015



INVION

Targeting inflammation

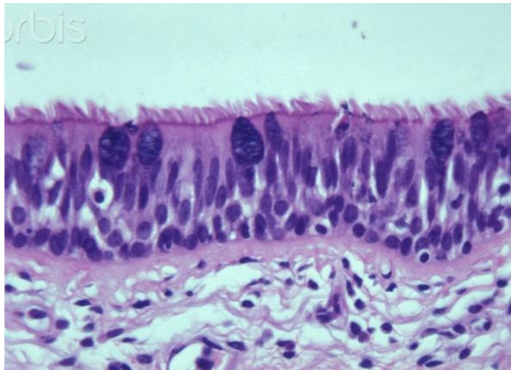
Targeting chronic inflammatory airway disease

INV102 (nadolol)

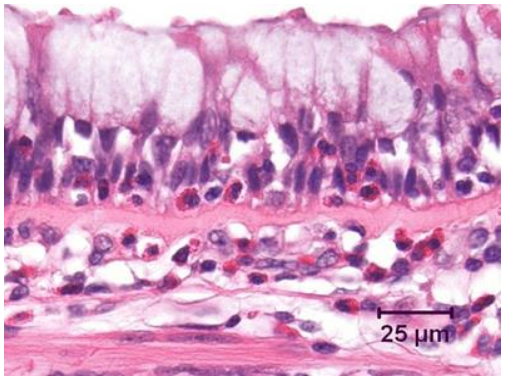
Treating the airway: background and rationale

- 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 β agonists and ICS are the mainstay treatment of airway disease: e.g. SYMBICORT® and ADVAIR® and DULERA®
- **However: these drugs have had NO positive impact on death due to chronic airway disease; death is due to increased and abnormal mucus**

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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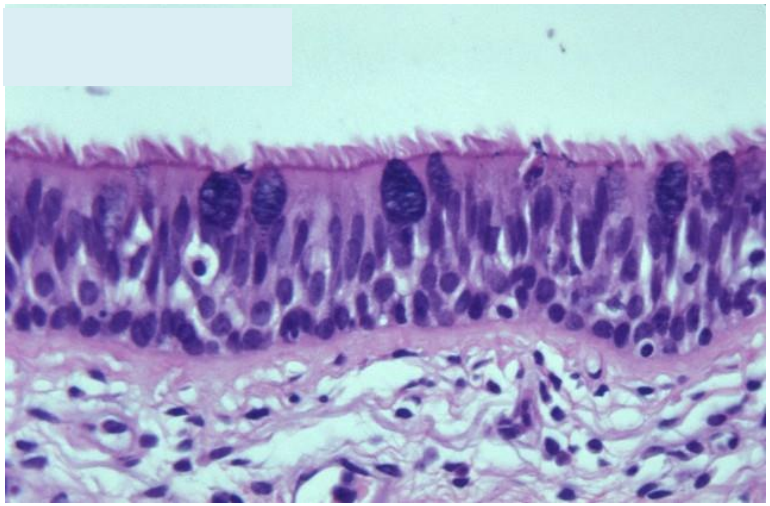
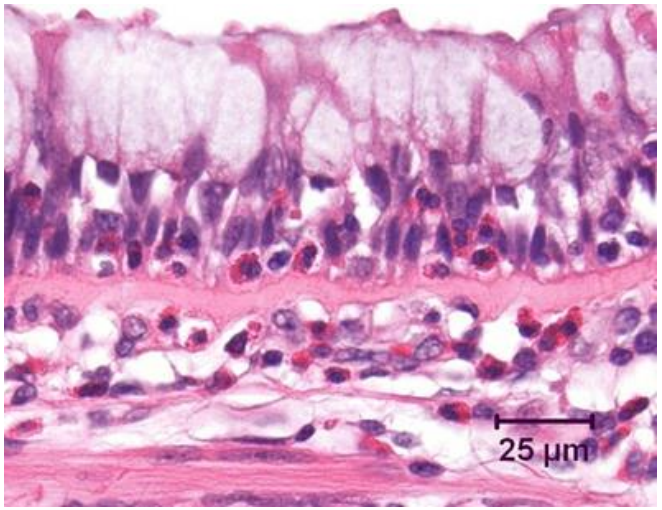
Targeting inflammation

The critical role of the epithelium in severe airway disease

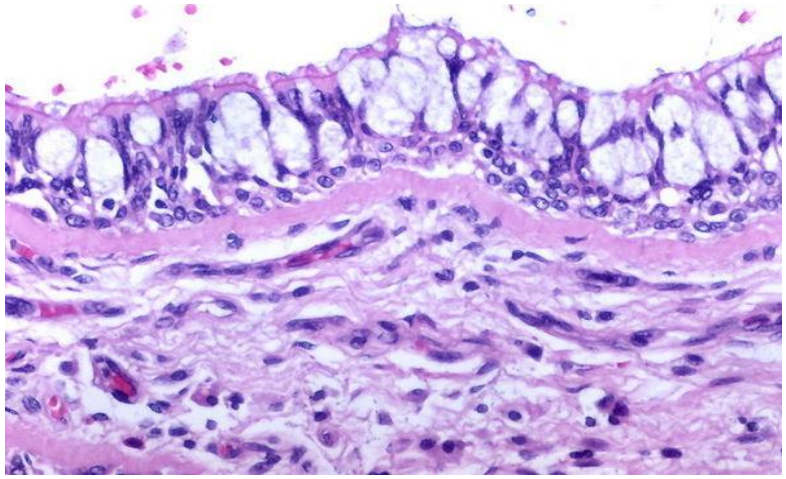
Normal respiratory epithelium



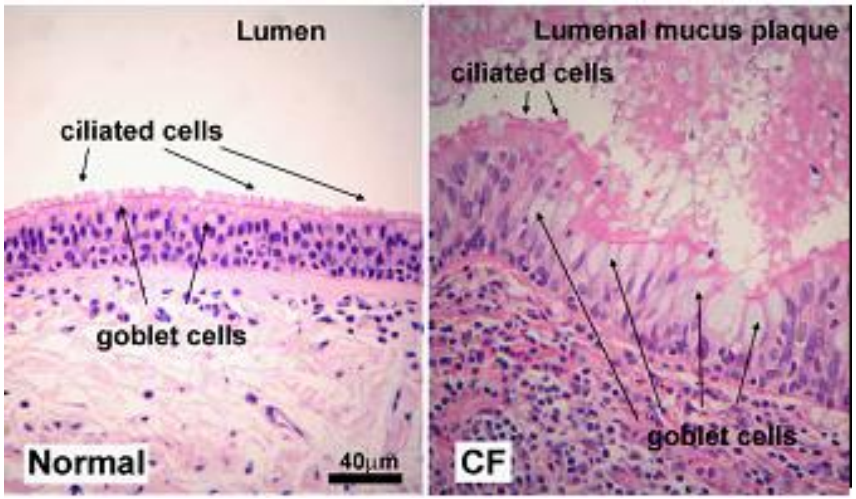
Severe asthma



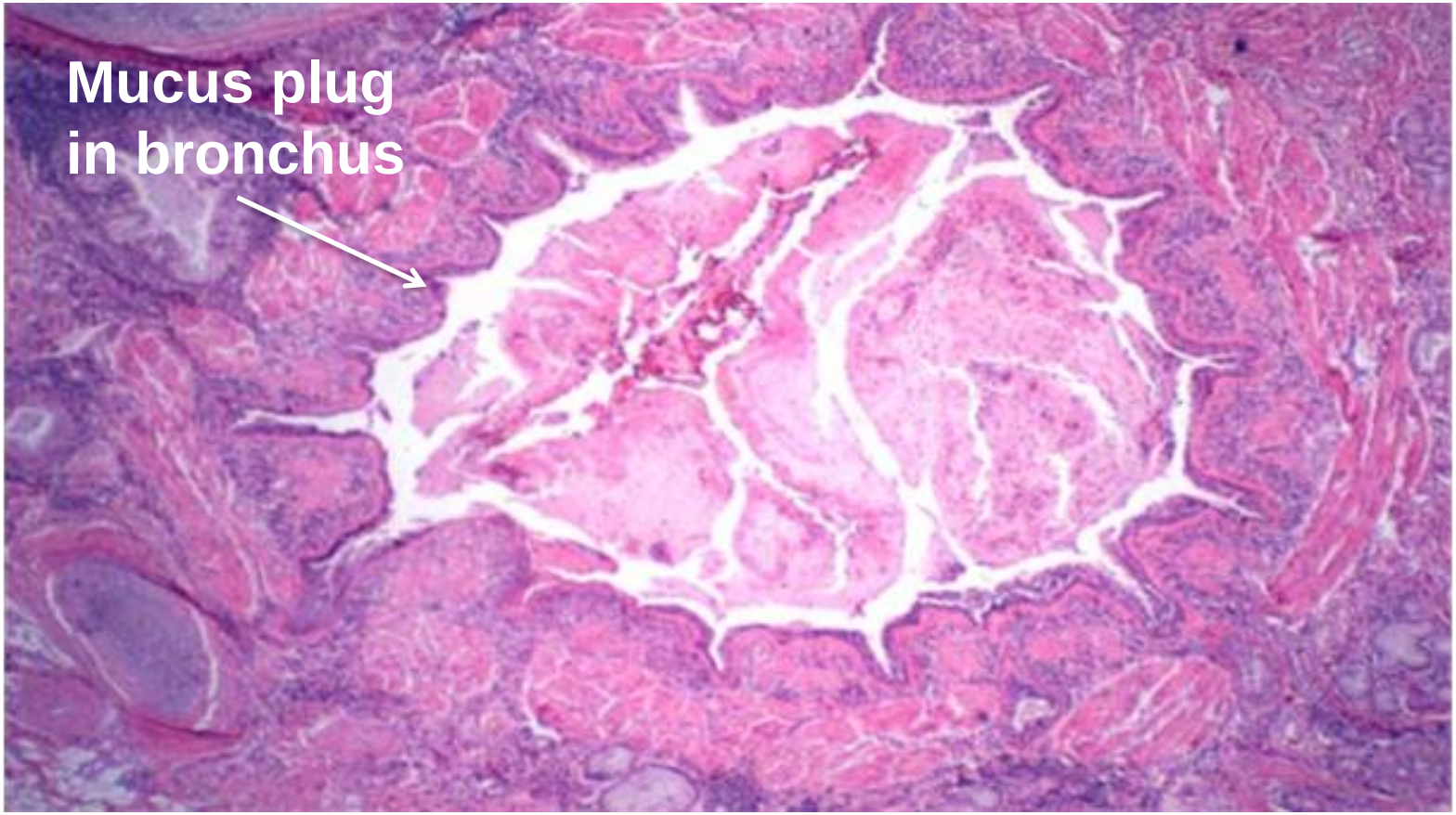
Chronic bronchitis



Cystic Fibrosis



Mucus causes death due to asthma, COPD and cystic fibrosis



Autopsy slide from 8 year old girl with fatal asthma. Mucus is increased **AND** abnormal.

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Smoking cessation, COPD and chronic airway disease: market size and interconnectedness

$47.1 billion by 2017

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

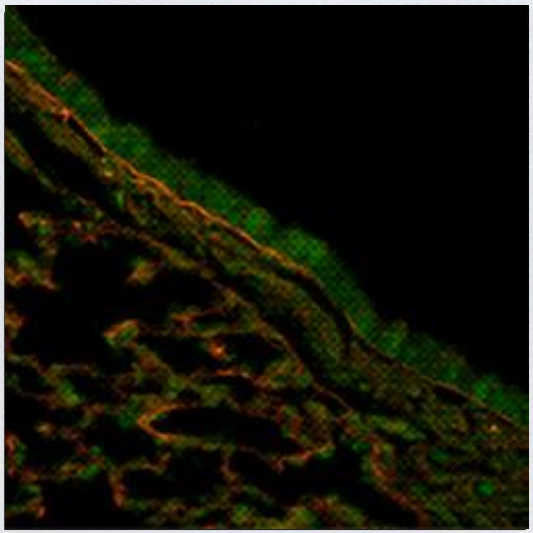
Nadolol is targeted to be used in conjunction with existing therapies to make them safer and more effective representing a niche in an existing large and growing market.

$3.8 billion by 2017

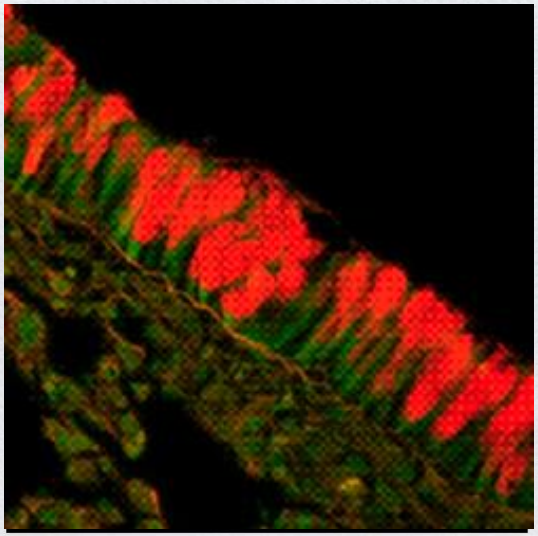
The smoking cessation drug market is predicted to be **$3.8 billion by 2017.**

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.

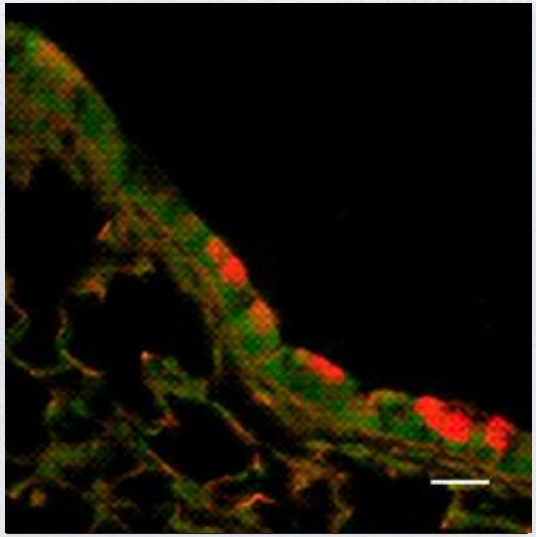
Oral or inhaled nadolol reverses epithelial changes and decreases inflammatory cytokines



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**

References: Nguyen LP., et.al., 2011. Complementary anti-inflammatory effects of a β-blocker and a corticosteroid in an asthma model. Arch Pharmacol. 2011: Oct 2; Nguyen, LP, et al. (2008). Am J Respir Cell Mol Biol 38:256-262

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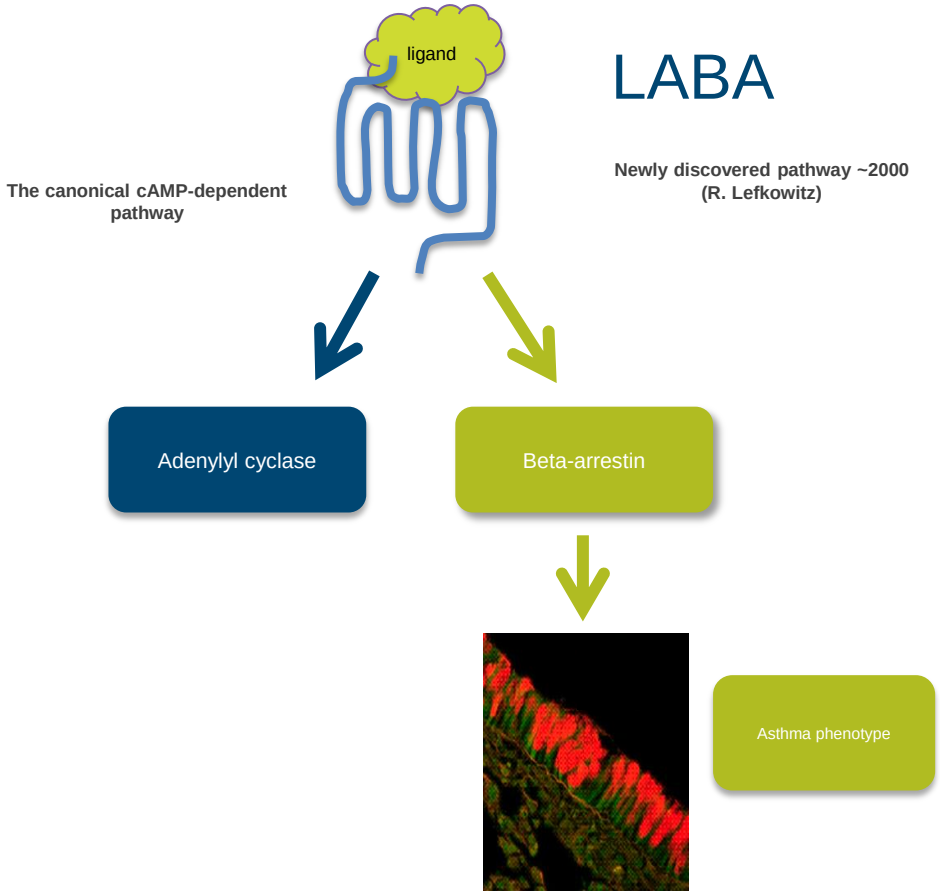
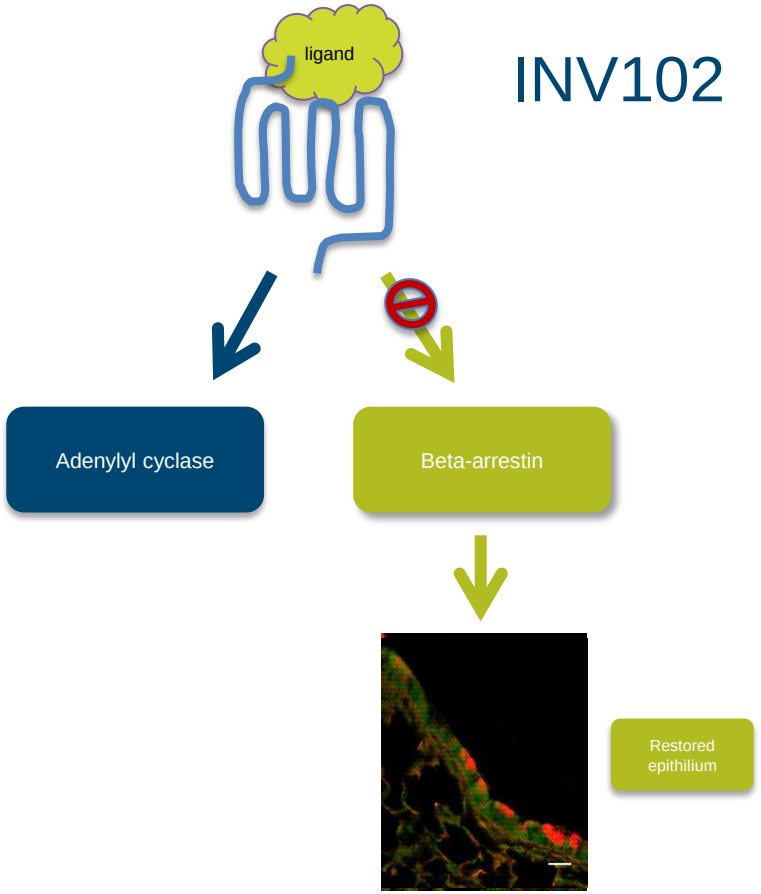
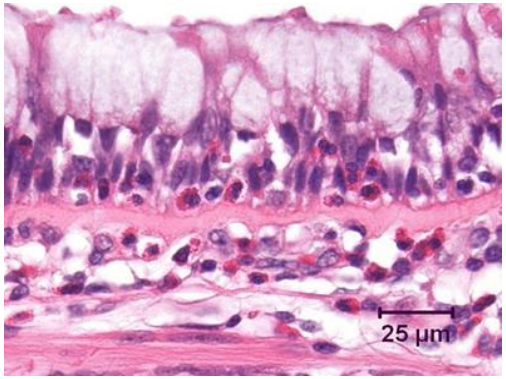
Mechanism of action of INV102 is unique among drugs:

INV102 reverses epithelial changes via inhibition of the beta-arrestin pathway in β2 airway receptors

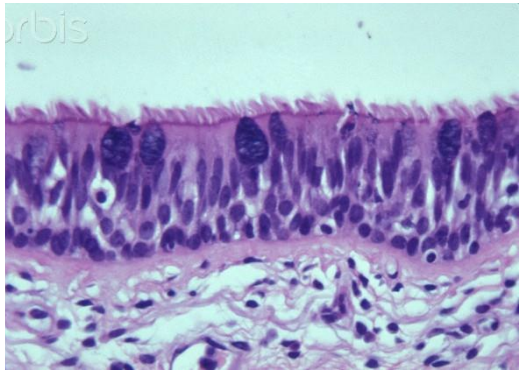




INV102: reversing the vicious cycle of airway inflammation



Mucous metaplasia found in COPD, asthma and CF



Normal Histology

INV102 (nadolol)

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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INV102: Phase 2 smoking cessation trial design

INCLUSION

Randomised (IWRS) Controlled Clinical Trial

N=155

Failed to quit and chronic cough

ORAL DOSING 11-15wks

Nadolol Treatment (n=78)
3-7wks titration &
8wks maintenance

Placebo Control (n=77)
titration & maintenance

WASHOUT 2wks

ENDPOINTS

Primary
% Decrease in # of cigarettes per day during last 14 days

Safety
Change in FEV1, exacerbations, adverse events

Trial conducted under Invion-sponsored IND with the the FDA Division of Anesthesia, Analgesia and Addiction Products (DAAAP).
Principal Investigator: Mario Castro, MD (Washington University)

Washington University in St. Louis

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Phase 2 data strong confirmation of Invion's strategy

Invion hypothesis	Demonstrated in Phase 2 trial
Proprietary titration scheme safe and enables subjects to reach efficacious doses of drug - no need for rescue medication	✔ Trial subjects treated with INV102 were more likely to achieve abstinence at the conclusion of dosing (12/62, 19.3%) compared to those administered placebo (7/59, 11%)
INV102 therapy will lead to reduction in cigarettes smoked	✔ More patients treated with INV102 achieved a >70% reduction in cigarettes smoked compared with placebo treated patients (38/62, 61% on INV102 and 21/59, 36% on placebo)
INV102 therapy will lead to complete abstinence in some subjects	✔
INV102 (nadolol) inhibits the beta arrestin pathway – a cellular pathway necessary for the activation of mucous metaplasia in the airway	✔ MUC5AC levels were reduced by 82% in INV102 treated patients, compared to 54% in placebo subjects. ERK1 levels were reduced by 47% for INV102 compared with 27% for placebo

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Leveraging the data: upcoming analysis and reporting

Data reported 5 October 2015

- Report on effects of nadolol vs placebo on key biomarkers
  - ERK1/2 (beta arrestin pathway)
  - MUC 5AC (abnormal mucus)
- Report on smoking cessation rates in nadolol treatment versus placebo
- Secondary analyis is on reduction versus cessation rates

Ongoing analysis 4Q 2015

- Correlation of smoking cessation/ reduction data with baseline biomarkers
- Correlation of smoking cessation/ reduction data with biomarker changes
- New IP prosecution
- Secondary analysis of responders and biomarker changes - identifying markers that are/are not useful in longer term studies
- Dose responses and responders as a function of dose, titration and history

Forward strategy: progress on 3 routes to a new class of airway-specific therapy

Phase 2 data validates Invion approach for directly treating the airway epithelium even in the face of ongoing insult, such as cigarette smoking

1. Oral INV102 in smoking cessation is Invion's "short path to market strategy".
   - > Invion proposing End of Phase 2 meeting to be convened early in 2016
   - > Phase 3 Program design ready for H2 2016

2. Inhaled INV102
   - > Data validates development plan and pathway for inhaled INV102 for asthma, COPD and cystic fibrosis where there is a substantial unmet medical need and commercial opportunity.

3. Finalizing collaboration to design new chemical entity (NCE) that is a biased ligand and inverse agonist at the β2 receptor in the epithelium

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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 1 and Phase 2 clinical studies in asthma, COPD and cystic fibrosis (2016-7*)

*The information above (and where reflected elsewhere in this presentation) sets out indicative timeframes and assumes: Invion will continue to obtain the full benefit of the available R&D tax incentive for its eligible R&D activities and clinical trials; the studies will proceed based on budgeted costs, assuming normal patient recruitment and clinical trial timelines, and with no material regulatory hurdles; and ordinary R&D expenditure will continue broadly at the same levels as for past financial years

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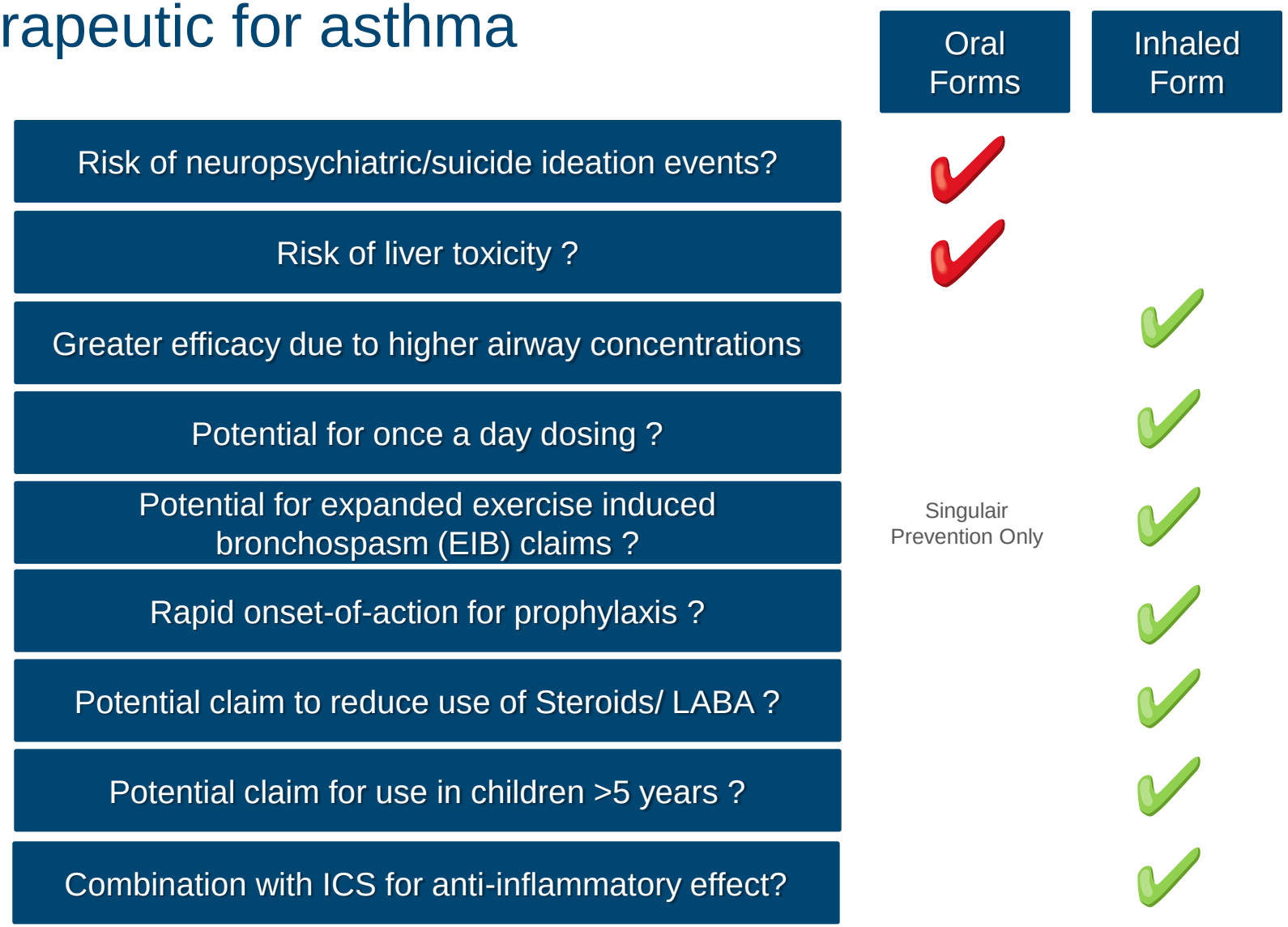
INV104 (zafirlukast)

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

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



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 1: single rising dose study for safety (paradoxical bronchoconstriction) and pharmacokinetics
  - phase 1: multiple dose safety study for safety (paradoxical bronchoconstriction) and pharmacokinetics
  - phase 2: 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

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.

POWDAIR® is a patent protected device filed and granted in over 40 countries, including US (US 8677992) and EU (EP 2546460). POWDAIR® 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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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)

INV103 (ala-Cpn10): phase 2 lupus data

- Three sets of data were reviewed from subjects who received twice-weekly doses of 10, 30 or 100mg of ala-Cpn10, or placebo
- INV103 (ala-Cpn10) well tolerated at 3 and 10 times previous highest dose
- 10mg iv twice weekly showed no effect on stimulated peripheral blood mononuclear cells (PBMC) production of 3 key cytokines (IL-1Beta, IL-6 and TNF-alpha) at 1 month of dosing
- In contrast, 30mg and 100mg iv twice weekly showed reduced response to stimulation by LPS after 1 month of dosing
- These data reflect relevant activity at the target cell type in patients with a target (autoimmune) disease
- Extending these findings will require a partner. Data is now being provided to pharma groups with a view to partnering the program

Milestone update: achievements in 2015

3 drug assets in 3 phase 2 clinical trials across 4 development programs

- ✓ Blind-broken interim data from phase 2 smoking cessation trial of INV102 (nadolol)
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- ✓ Positive safety and efficacy data from phase 2 oral INV102 (nadolol) study in patients undergoing smoking cessation
- ✓ Completion of enrolment of NIH-funded phase 2 study of INV102 (nadolol) in asthma patients

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 (2-Nov-15)	$0.012
Shares on issue	~894 M
Options on issue	~115M
Market cap (2-Nov-15)	$10.7M
Cash at bank (30-Sep-15)	$0.5M
R&D tax rebate received (9-Oct-15)	$2.4M

INVION

Targeting inflammation

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