Invion Limited (ASX:IVX)

Clinical-stage life sciences company targeting chronic inflammation

Corporate Presentation
March | 2014

INVION

Targeting inflammation

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Invion: targeting inflammation

- 3 drug candidates in development
  - Developing two new respiratory franchises
    - **INV102 (nadolol)**: *beta blocker* being repurposed to treat inflammatory airway diseases including COPD and cystic fibrosis
    - **INV104 (zafirlukast)**: *anti-leukotriene* being developed as inhaled product for treatment of asthma
  - An early partnering opportunity
    - **INV103 (ala-Cpn10)**: modified, *naturally occurring human protein* for the treatment of autoimmune diseases
- 3 FDA-regulated phase II clinical trials currently underway
- Collaborating with 3M on inhaled respiratory franchise

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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 pharmaceutical 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

- 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)
- Board certified pulmonary and critical care specialist
- 25 year veteran of Pharma (AZ, GSK) and Biotech (AGIX)

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Recent capital raise and development collaboration allow acceleration of clinical development

- Collaboration with 3M Drug Delivery systems
- Inhalation development expertise
- Proprietary formulation and device
- Works will assess the feasibility of inhaled INV102 (nadolol) and INV104 (zafirlukast) delivered using 3M's proprietary pressurised metered dose inhalation (pMDI) technology
- Collaboration encompasses manufacture for toxicology and phase I studies
- >50% of all MDIs worldwide use 3M technology
- Completion of $5M placement to institutional and professional investors, announcement of $2M Rights Issue

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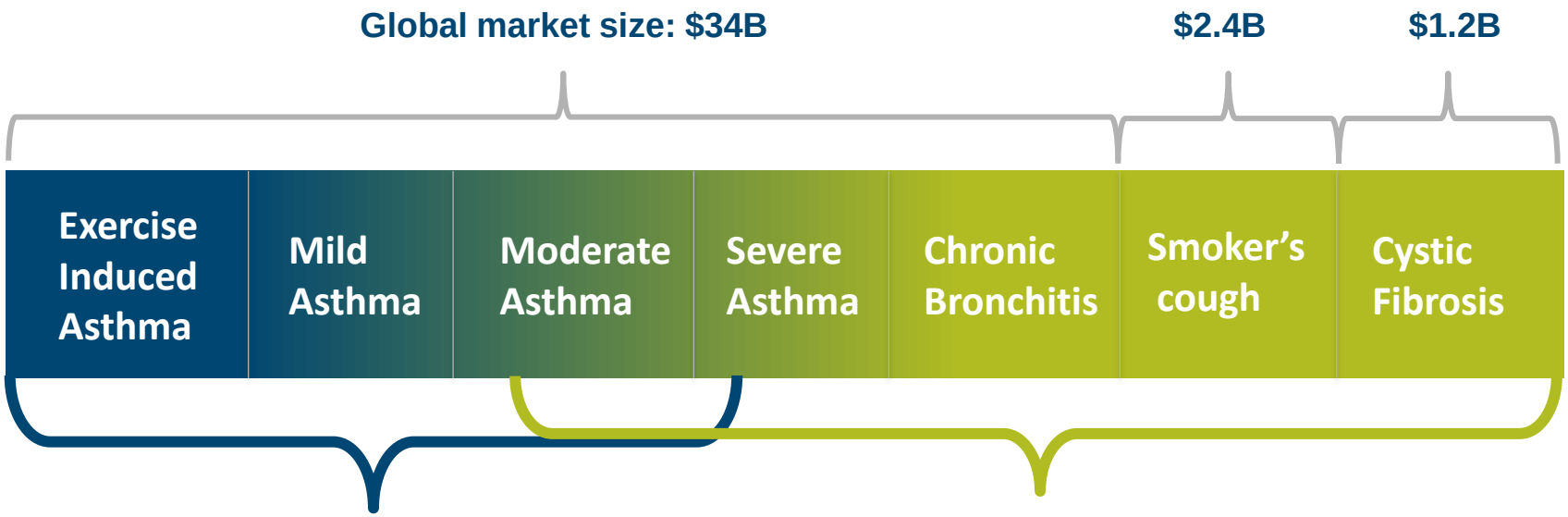
Targeting inflammation

Targeting respiratory disease

INV102 (nadolol) - *beta adrenergic inverse agonist*

INV104 (zafirlukast) - *leukotriene receptor antagonist*

Spectrum of airway disease and opportunities



Zafirlukast

Monotherapy + combinations

Nadolol

Monotherapy + combinations

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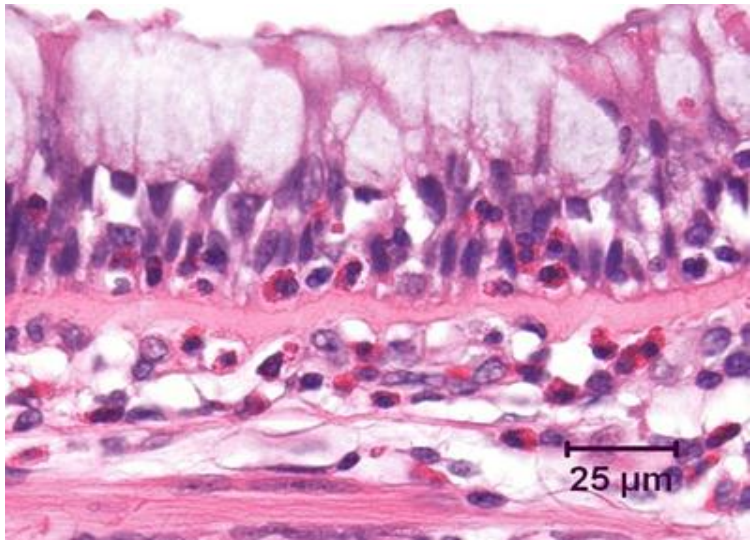
INV102 (nadolol)

- Nadolol is uniquely an inverse β-agonist in the airway
  - inactivates intracellular inflammatory events that are stimulated spontaneously or by β agonists
  - Hypothesized to utilize the beta-arrestin pathway

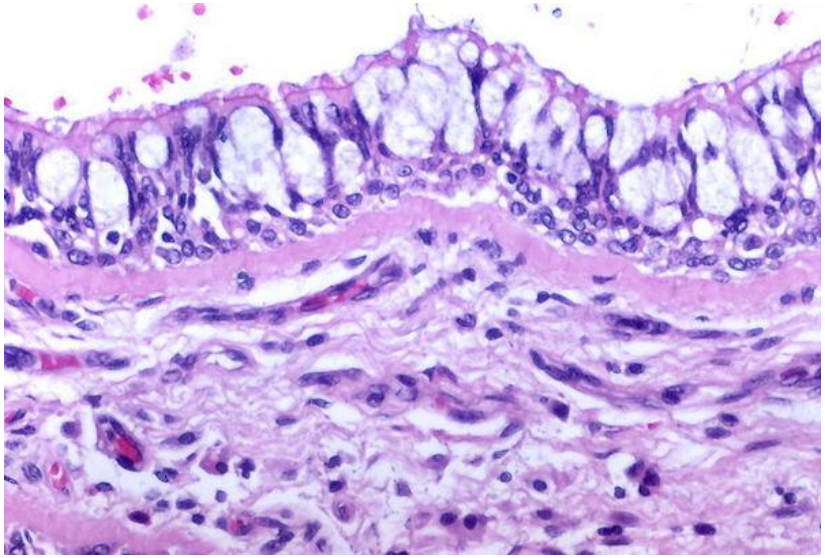
- Clinical data to date
  - Two phase II clinical trials completed
    - Safety profile enhanced by titration starting at very low doses
    - Dose-related reduction of airway hyper-responsiveness

- Goals of oral INV102 (nadolol) program
  - Asthma program (phase II) is NIH funded; follow-on study could target severe asthma
  - Smoking cessation program is a 'speed to market' opportunity; proprietary titration strategy and dose strengths
  - Invion / 3M collaboration accelerates inhaled program
  - Inhaled INV102 targeted to treat COPD and cystic fibrosis

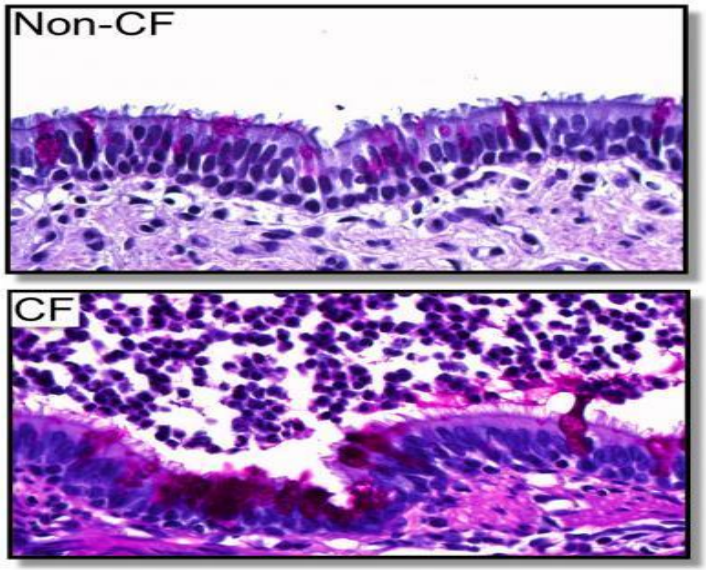
Severe airway diseases share the phenotype



Severe asthma



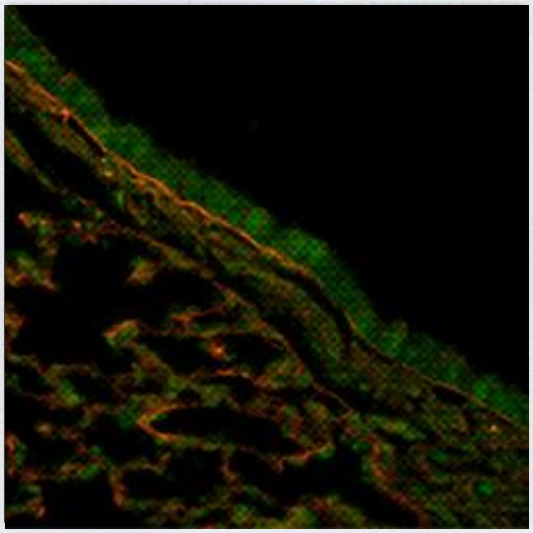
COPD



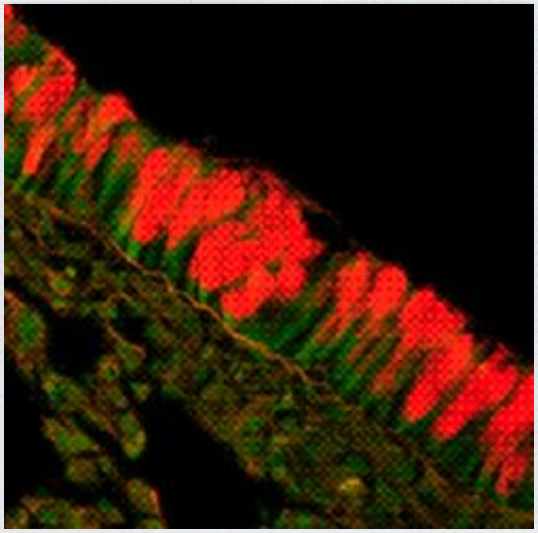
Cystic fibrosis

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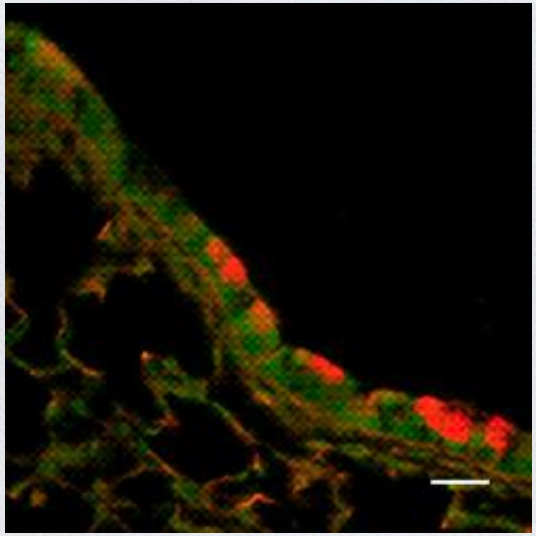
Preclinical studies demonstrate airway healing



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

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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. β1 success in the heart (CHF) mitigates the risk of β2 success in the lung (COPD)

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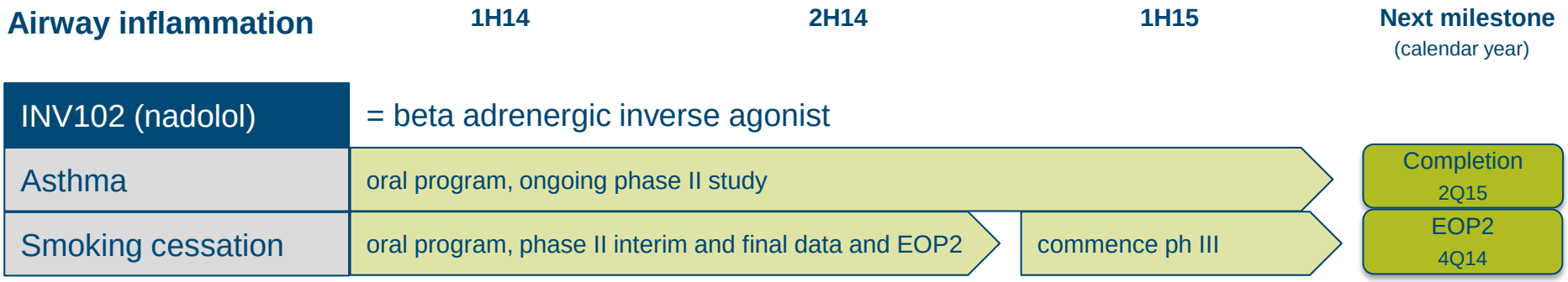
INV102: phase II trial design – mild asthma

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 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 β2AR 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 – smoking cessation

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 2013 Expected Completion H2 2014
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	Change from baseline in number of cigarettes smoked per day for the last 28 days on study medication
Secondary endpoints	Number of cigarette-free days; Saint George's Respiratory Questionnaire; markers of COPD including sputum
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

INV102 (nadolol): oral program



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Respiratory therapeutics: inhaled program

INV102 (nadolol) in COPD & cystic fibrosis

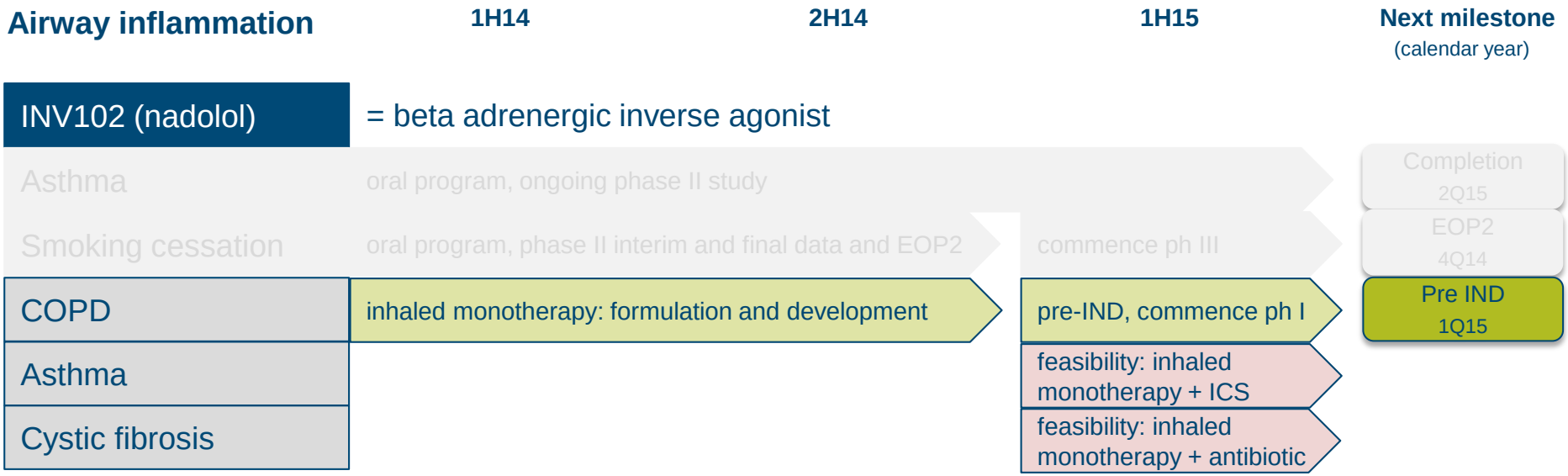
INV104 (zafirlukast) in asthma

INV102 (nadolol): comparison oral vs inhaled

Target Product Profile	
Oral	**Inhaled**
> IP protection: titration and method of use (USA)	> IP protection based on 3M formulation and device
> Once daily dosing including titration to avoid systemic side effects	> Once daily dosing with no need for titration and no systemic side effects
> Invion phase II and III data limited to 13 weeks for smoking cessation	> Target long term regular use for chronic airway diseases
> New indication limited to smoking cessation	> Approved for long term use in COPD, severe asthma and cystic fibrosis
> No efficacy data on concomitant use of inhaled corticosteroids (severe asthma) or antibiotics (CF)	> Safety and efficacy data in combination with LABA + ICS (Asthma), antibiotics (CF), and LAMA + ICS (COPD)
> Limited data on reducing cough, sputum production, “smoker’s cough”, avoiding use of steroids or preventing/ameliorating exacerbations	> Indicated for reducing cough, sputum production, “smokers’ cough”, decreasing use of steroids or preventing/ameliorating exacerbations

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INV102 (nadolol): inhaled program



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INV104 (zafirlukast)

- Nanomolar potent *Leukotriene Receptor Antagonist* (LTRA) or *anti-leukotriene*
- Targeted as first inhaled non-steroidal anti-inflammatory treatment for asthma
- Large market potential with mitigated risk of a reformulated drug

- Accolate® (zafirlukast)
  - Developed by ICI / AstraZeneca, program headed by Dr. Glass
  - First LTRA to be approved by FDA, used worldwide as oral tablet for asthma
  - Well established clinical & safety profile
  - Non-oral uses never actively pursued by AZ, despite well established activity by inhalation route
  - Invion / 3M collaboration accelerates inhaled drug franchise, target = asthma

- 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

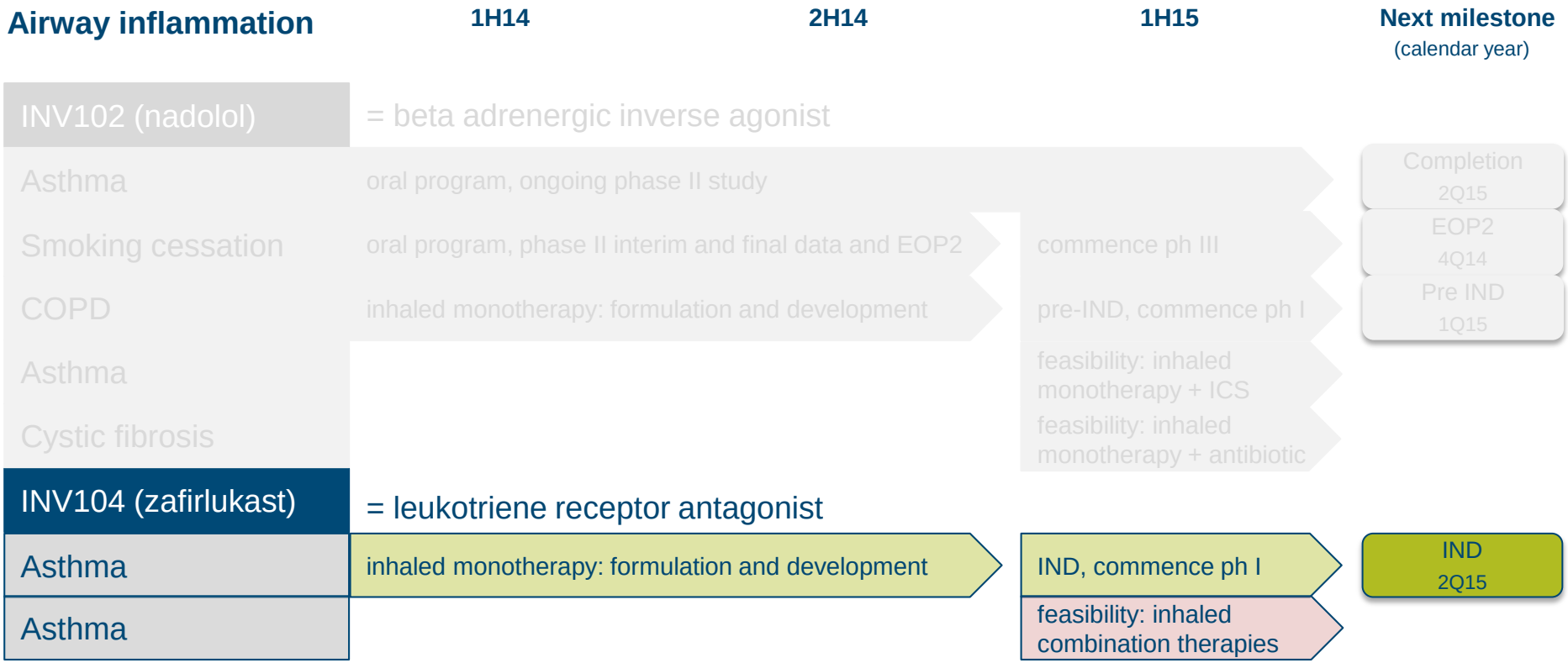
- Intellectual Property position
  - Expired zafirlukast patents (public domain)
  - New patent protection from combination, delivery, and linked diagnostic filings

INV104 (zafirlukast): comparison oral vs inhaled

Oral (Accolate®) Label	Target Product Profile Inhaled INV104 (zafirlukast)
> Astra Zeneca patent for zafirlukast expired	> IP protection based on 3M formulation and device
> Twice per day dosing with food effect, suicidal ideation warning, and liver toxicity reported	> Once (or twice) daily dosing with no systemic side effects
> Limited commercial uptake as a generic drug	> Novel monotherapy with opportunities for combinations
> Not indicated for PRN (as needed) use	> Approved for single dose prophylaxis of Exercise-Induced Bronchospasm (EIB)
> Not indicated for reducing Long Acting Beta Agonist (LABA)	> Indicated to reduce use of LABA in adults and children
> Not indicated for reducing use of corticosteroids	> Indicated for reducing use of corticosteroids
> No indication or clinical experience in children under 12 years of age	> Indicated for use in children 5 years of age or above with mild asthma or EIB

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INV104 (zafirlukast): inhaled program



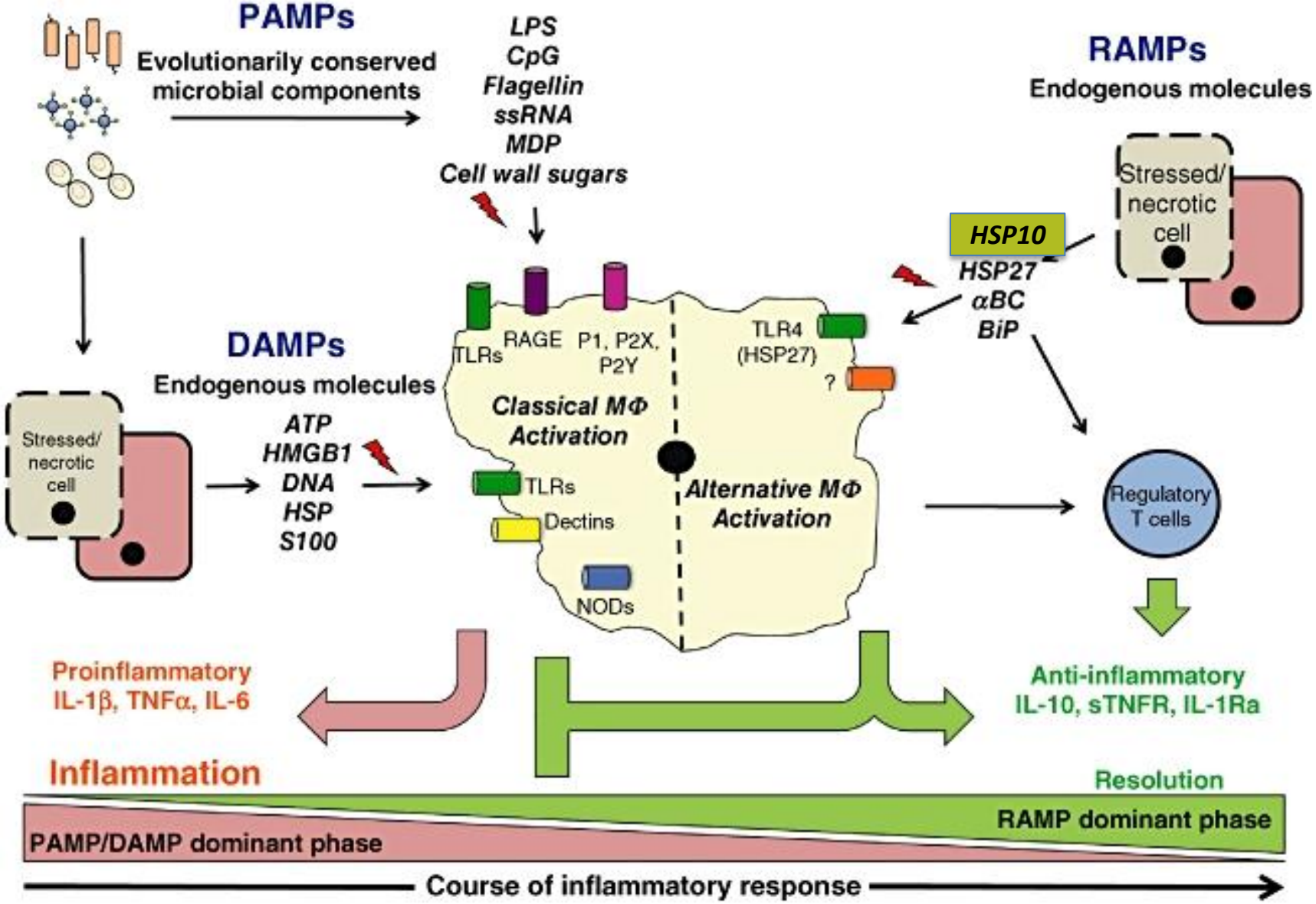
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Targeting inflammatory disease

INV103 (ala-Cpn10): modified natural human protein



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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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: 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 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 Completion 2014
Inclusion criteria	Mild lupus without clinical kidney disease
Principal Investigator	Alan Kivitz, M.D., Stanley Cohen, M.D.
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 (ala-Cpn10): autoimmune program

Airway inflammation	1H14	2H14	1H15	Next milestone (calendar year)
INV102 (nadolol)	= beta adrenergic inverse agonist			
Asthma	oral program, ongoing phase II study			Completion 2Q15
Smoking cessation	oral program, phase II interim and final data and EOP2		commence ph III	EOP2 4Q14
COPD	inhaled monotherapy: formulation and development		pre-IND, commence ph I	Pre IND 1Q15
Asthma			feasibility: inhaled monotherapy + ICS	
Cystic fibrosis			feasibility: inhaled monotherapy + antibiotic	
INV104 (zafirlukast)	= leukotriene receptor antagonist			
Asthma	inhaled monotherapy: formulation and development		IND, commence ph I	IND 2Q15
Asthma			feasibility: inhaled combination therapies	

Autoimmune disease

INV103 (ala-Cpn10)	= modified natural human protein	
Lupus (SLE)	completion ph II study, IV/SC bridging study	Partner

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Pipeline: 12-18 month outlook

Airway inflammation

INV102 (nadolol)	= beta adrenergic inverse agonist		
Asthma	oral program, ongoing phase II study	phase II trial complete	Completion 2Q15
Smoking cessation	oral program, phase II interim and final data and EOP2	phase III commenced	EOP2 4Q14
COPD	inhaled monotherapy: formulation and development	phase I commenced	Pre IND 1Q15
Asthma		feasibility: inhaled monotherapy	
Cystic fibrosis		feasibility: inhaled monotherapy	
INV104 (zafirlukast)	= leukotriene receptor antagonist		
Asthma	inhaled monotherapy: formulation and development	IND, phase I commenced	IND 2Q15
Asthma		feasibility: inhaled combination therapy	

Autoimmune disease

INV103 (ala-Cpn10)	= modified natural human protein		
Lupus (SLE)	completion ph II study, IV/SC bridging study	Partner	Partner

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Summary

- ✓ 3 drug assets with multiple paths to market
- ✓ early partnering opportunity for INV103 (ala-Cpn10)
- ✓ 3 FDA-regulated phase II clinical trials
- ✓ two de-risked novel and proprietary inhaled respiratory assets
- ✓ collaboration with global partner on inhaled franchise
- ✓ experienced management 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 (21-Feb-14)	$0.089 (8.9 cents)
Shares on issue	~530M
Options on issue	~30M
Market cap (21-Feb-14)	$47M
Cash at bank (31-Dec-13)	$1.864M
Placement completed (21-Feb-14)	$5M
Rights Issue announced (26-Feb-14)	$2M

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