

Invion Limited (ASX:IVX)

Clinical-stage life sciences company targeting chronic inflammation



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



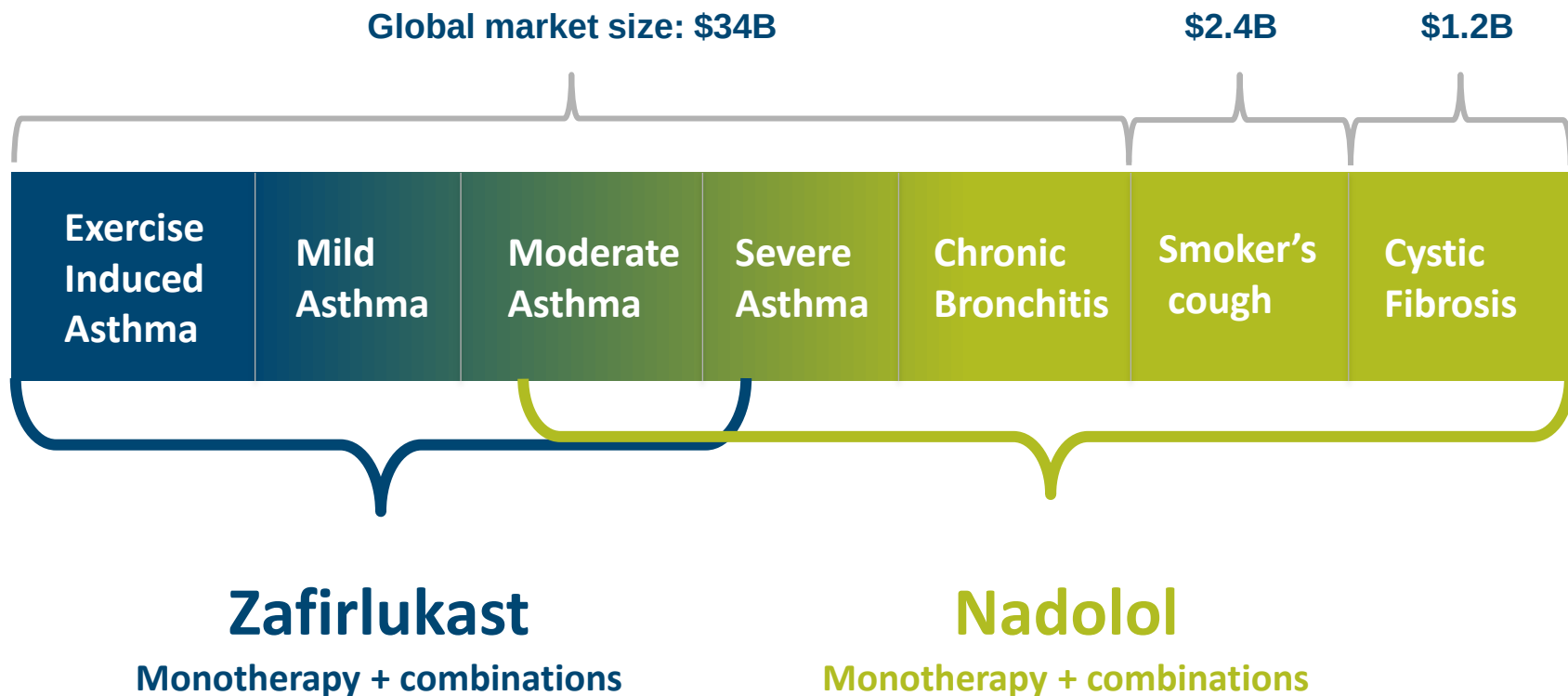
Targeting inflammation

Targeting respiratory disease

INV102 (nadolol) - *unique beta-blocker*

INV104 (zafirlukast) - *leukotriene receptor antagonist*

Spectrum of airway disease and opportunities



Professor Richard Bond, PhD, Professor of Pharmacology, University of Houston (USA)

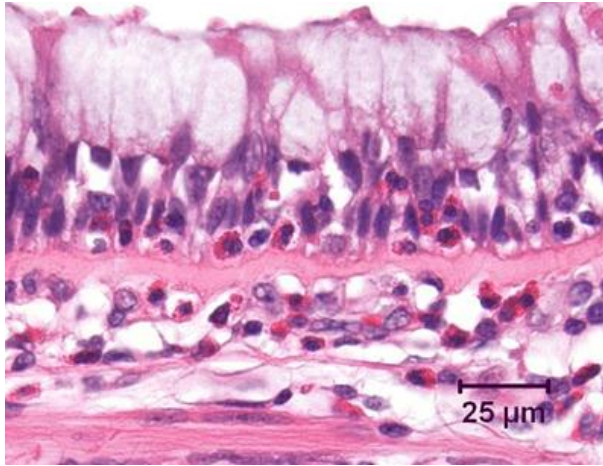
- > Early work provided functional evidence for a beta-adrenoceptor - eventually found to be the beta3-adrenoceptor
- > In collaboration with Nobel Prize winner R. J. Lefkowitz and others, undertook studies on the spontaneous activity of G-protein-coupled receptors and compounds
- > Research has focussed on paradigm shift that occurred with regard to the use of beta-blockers in the treatment of congestive heart failure, and whether a similar phenomenon could be applicable in asthma therapy
- > The work of Professor Bond and collaborators has been published in top scientific journals including Nature, Science, and the Proceedings of the National Academies of Science

“All beta-blockers are not created equally; the unique profile of INV102 (nadolol)”

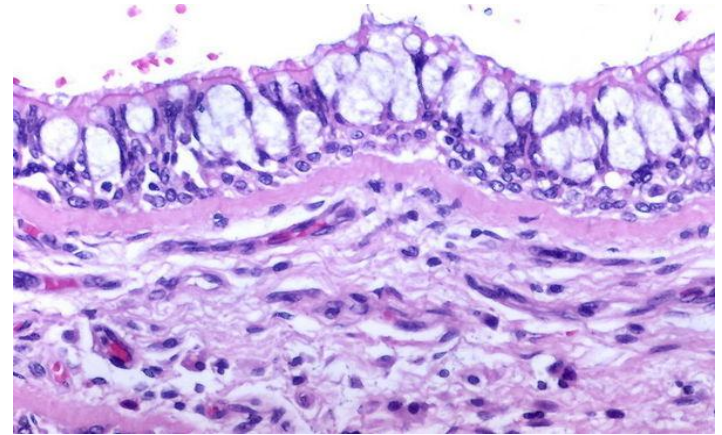
Background

- > Beta-Agonists are approved for the treatment of asthma
- > Acutely, Beta-Agonists are potent bronchodilators, but chronic use can cause loss of asthma control and an increase asthma related mortality
- > Beta-Blockers are contraindicated for the treatment of asthma

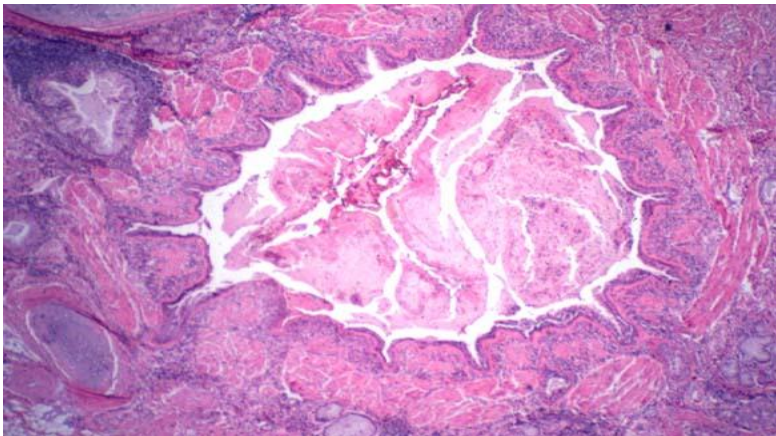
The critical role of the epithelium in the phenotype of severe airway disease



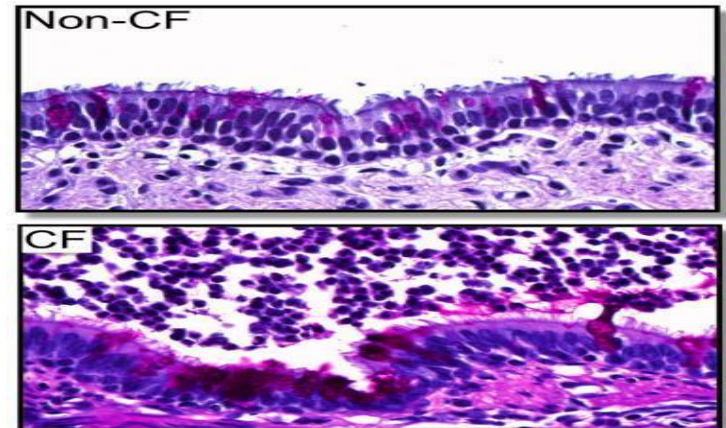
Asthma



COPD

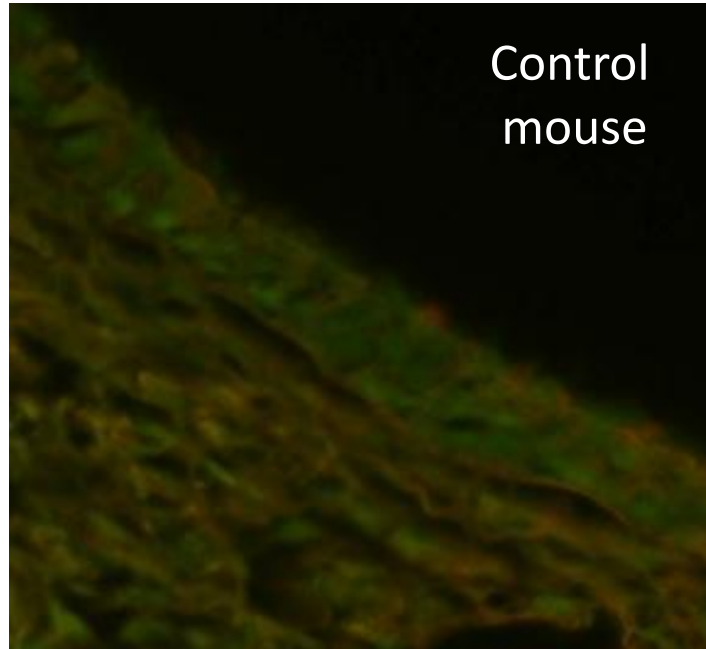


8 y.o. girl treated at Texas Medical Centre

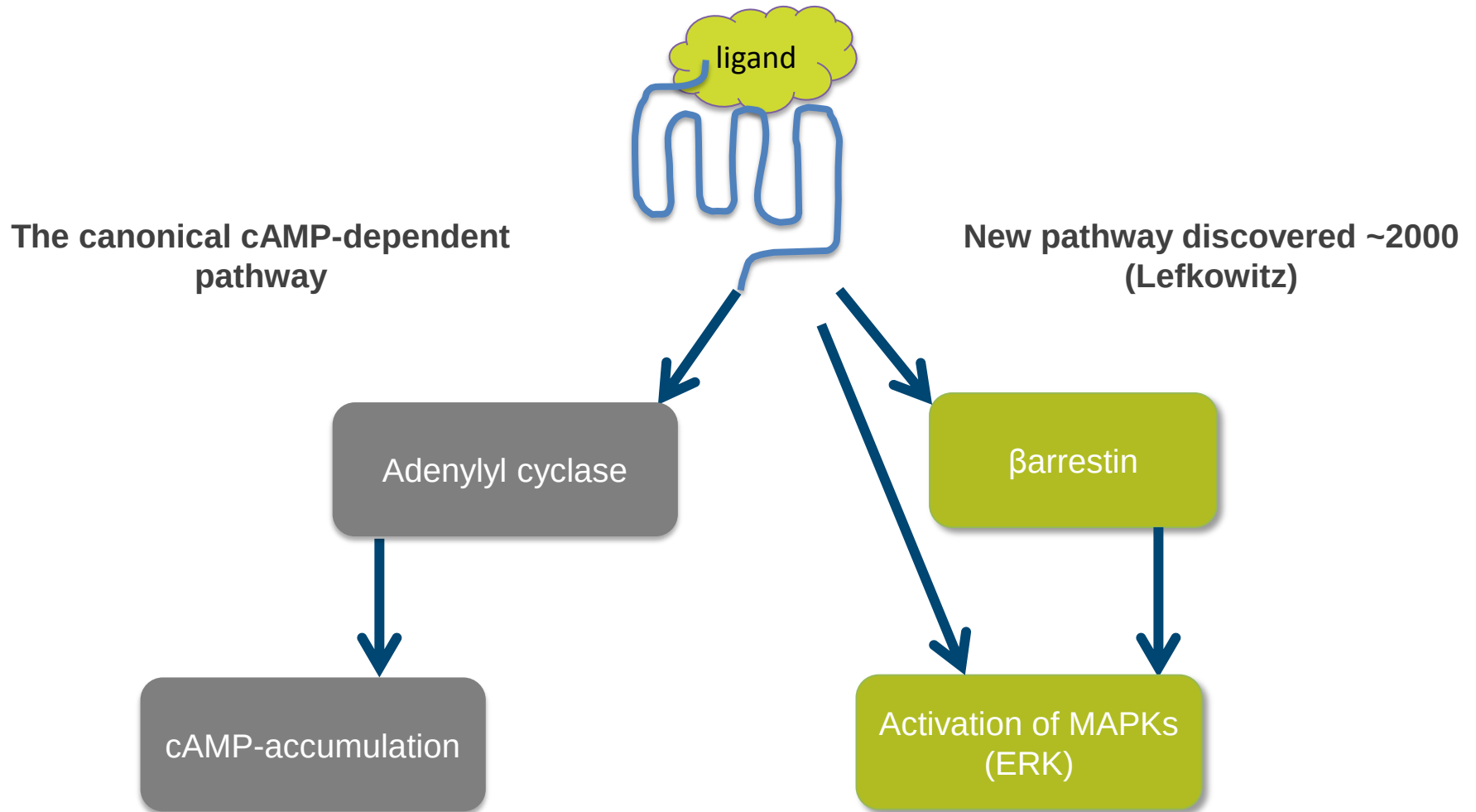


Cystic Fibrosis

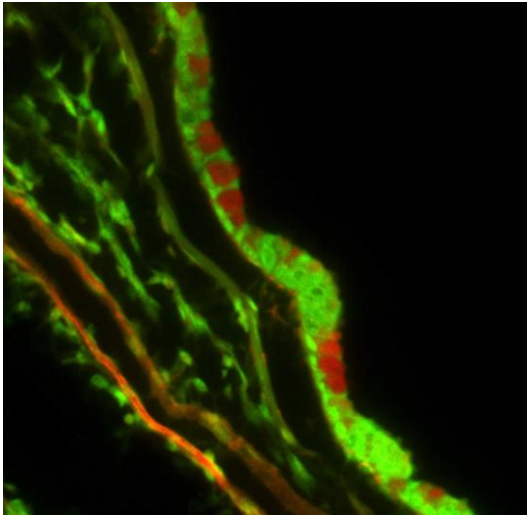
Validity of the preclinical murine model



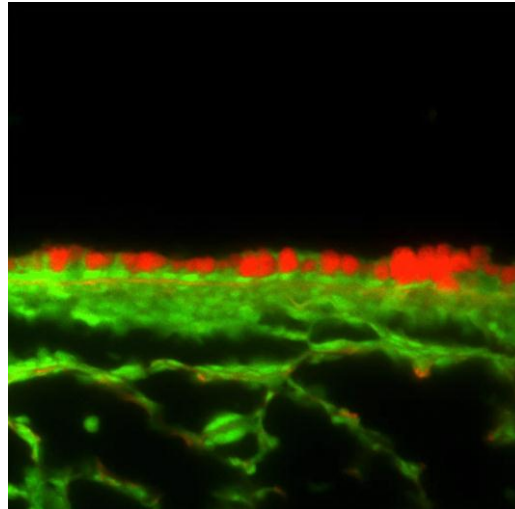
β_2 -adrenoceptor signaling pathways



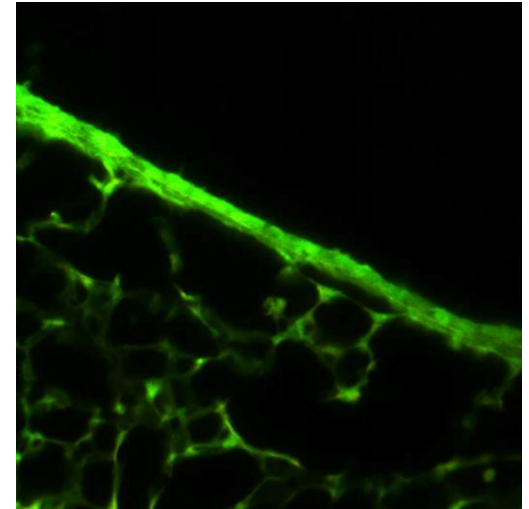
Effects of different beta-blockers on mucous in mouse asthma model



Alprenolol



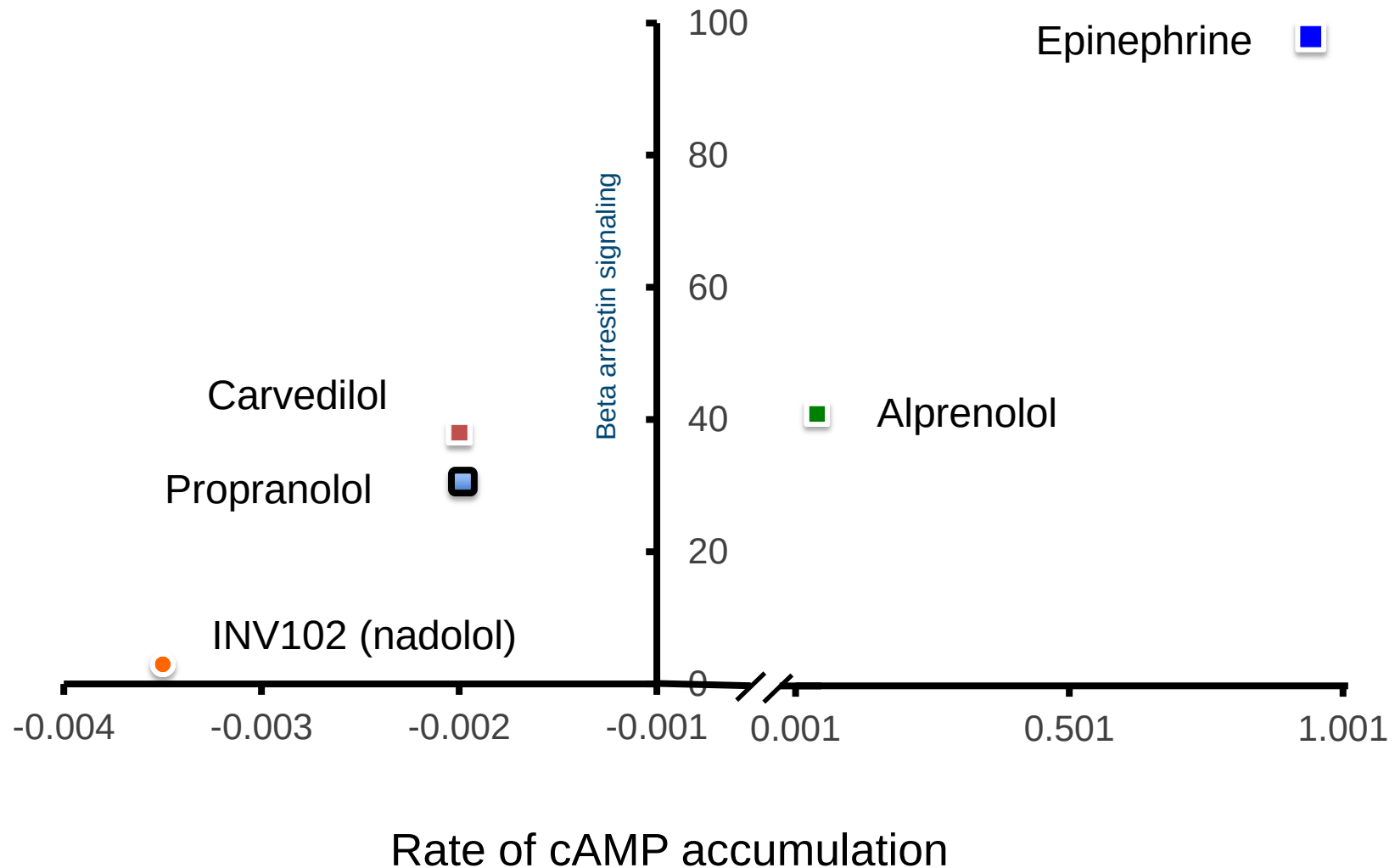
Carvedilol



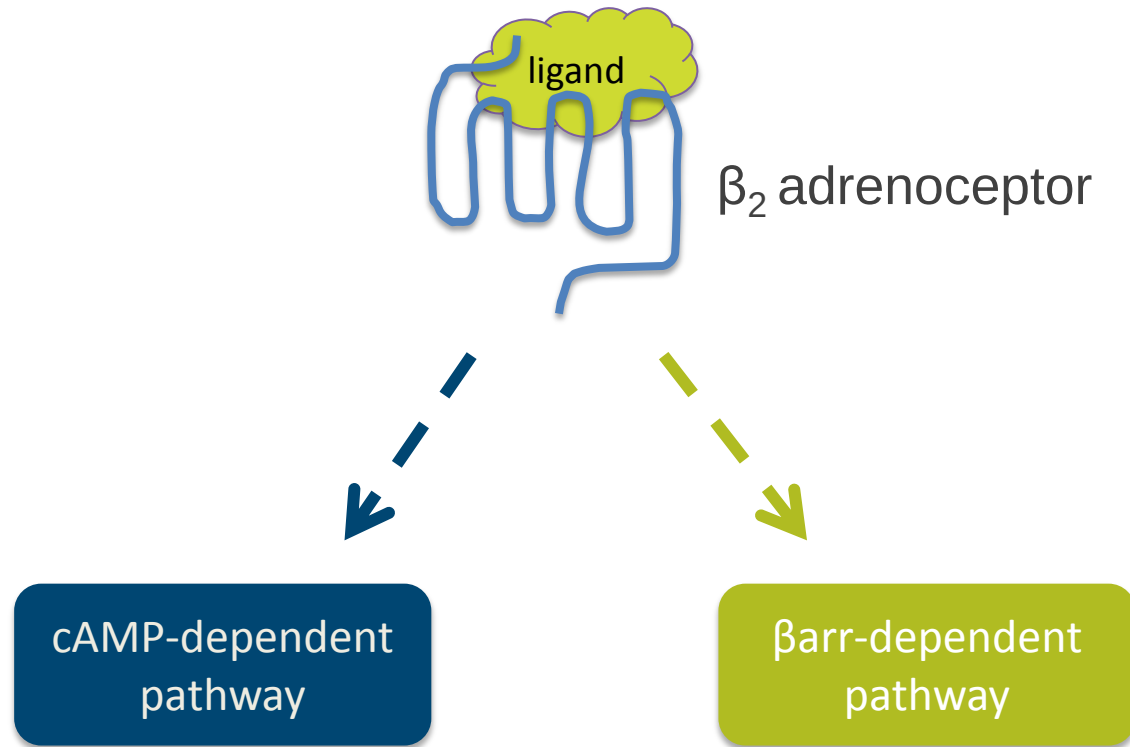
INV102 (nadolol)

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

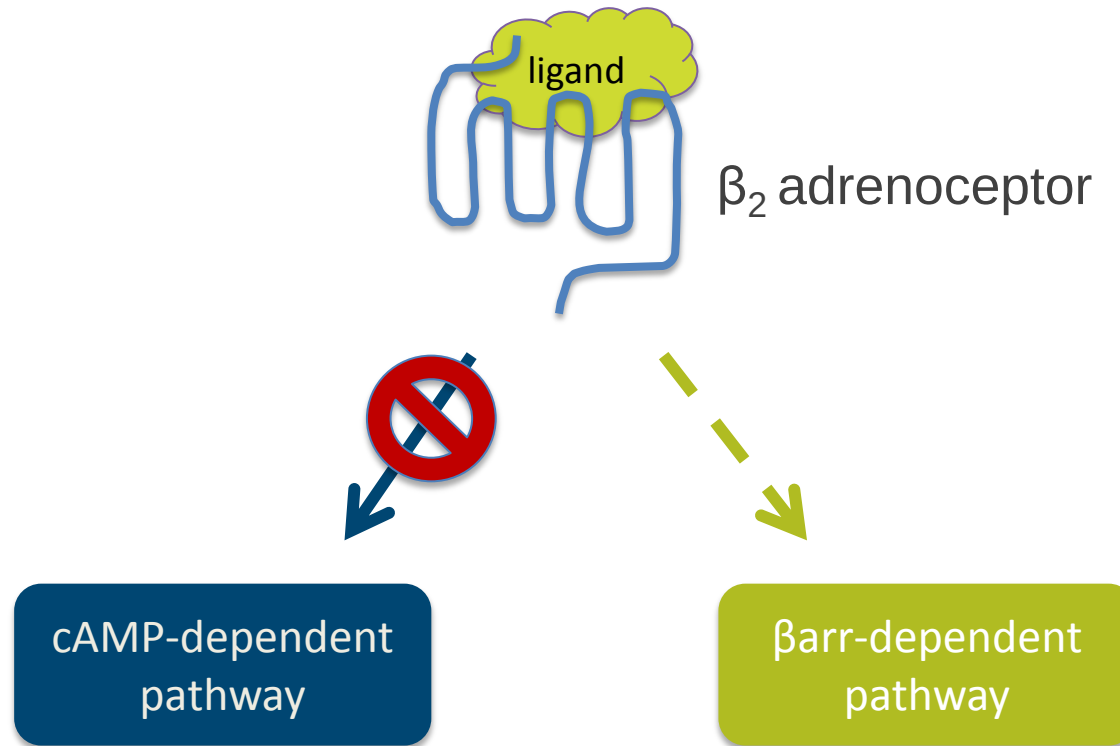
Nadolol is different from other beta-blockers



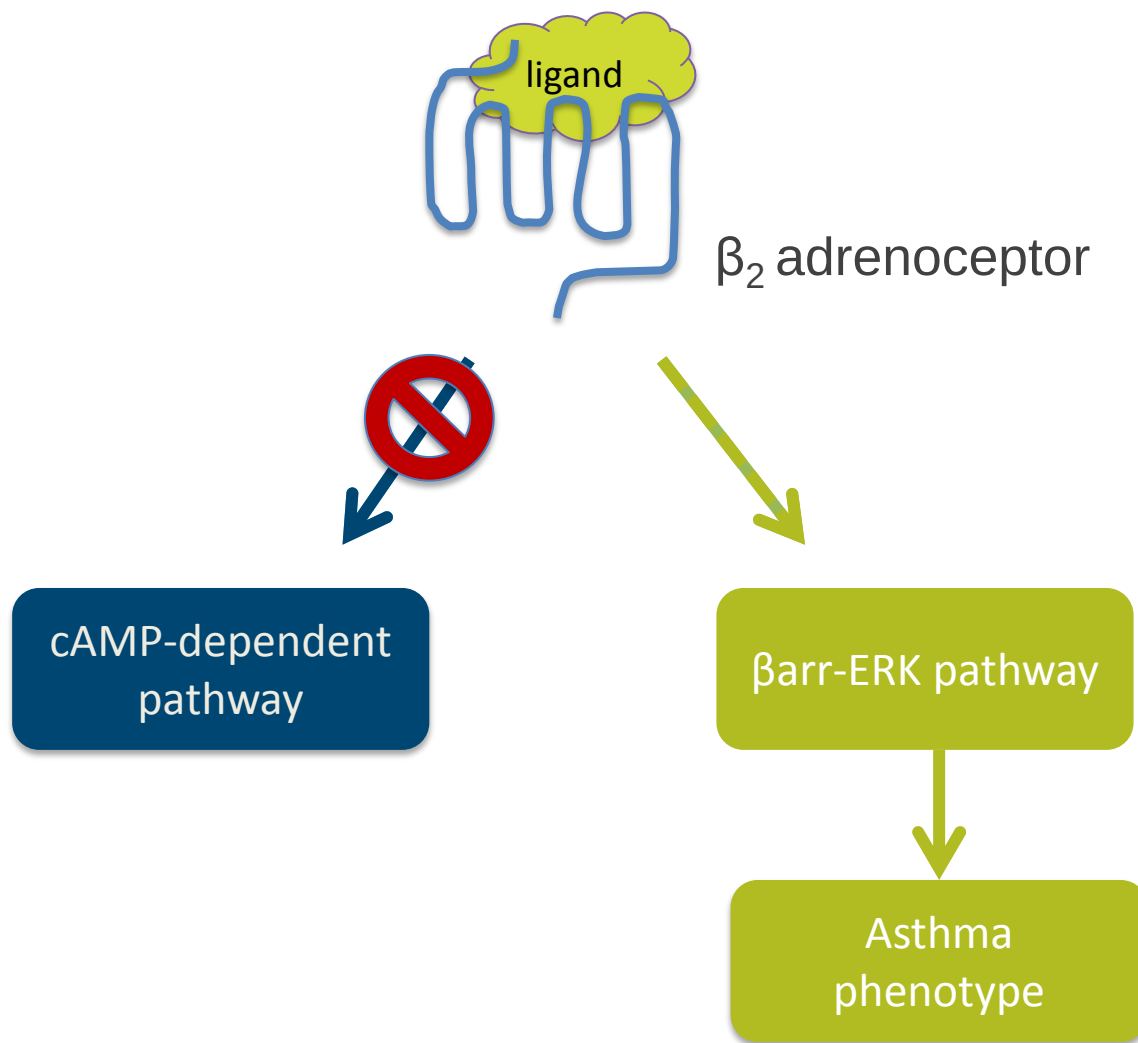
Alprenolol



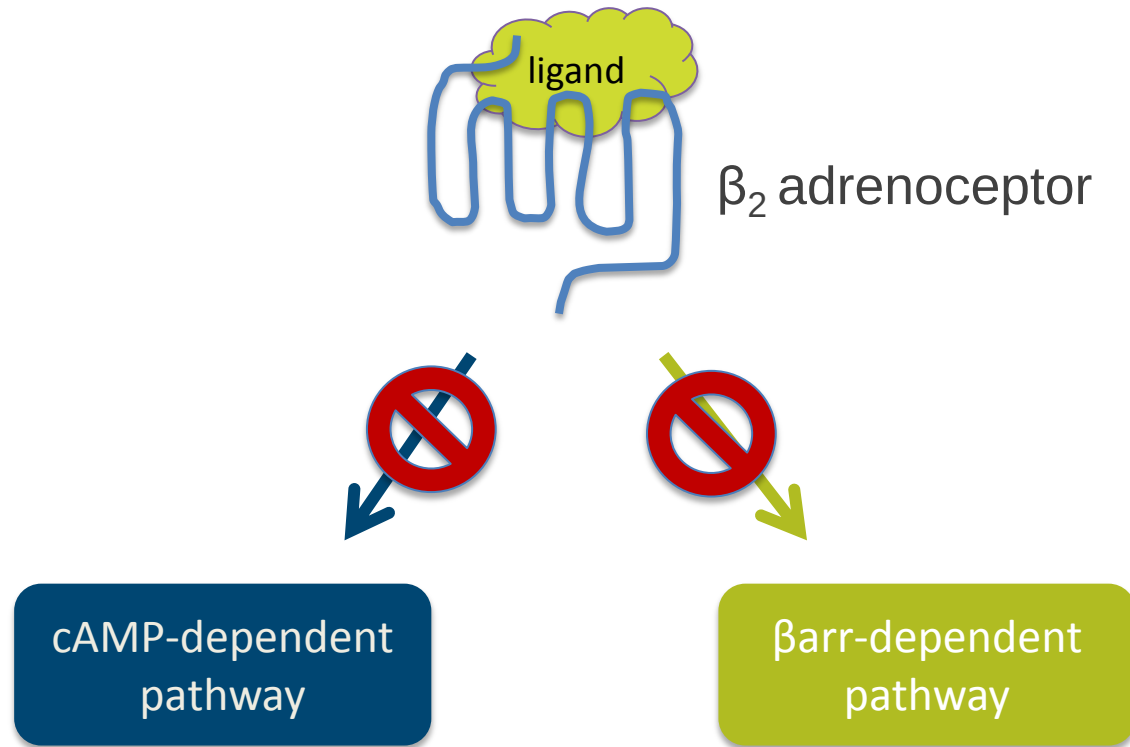
Carvedilol



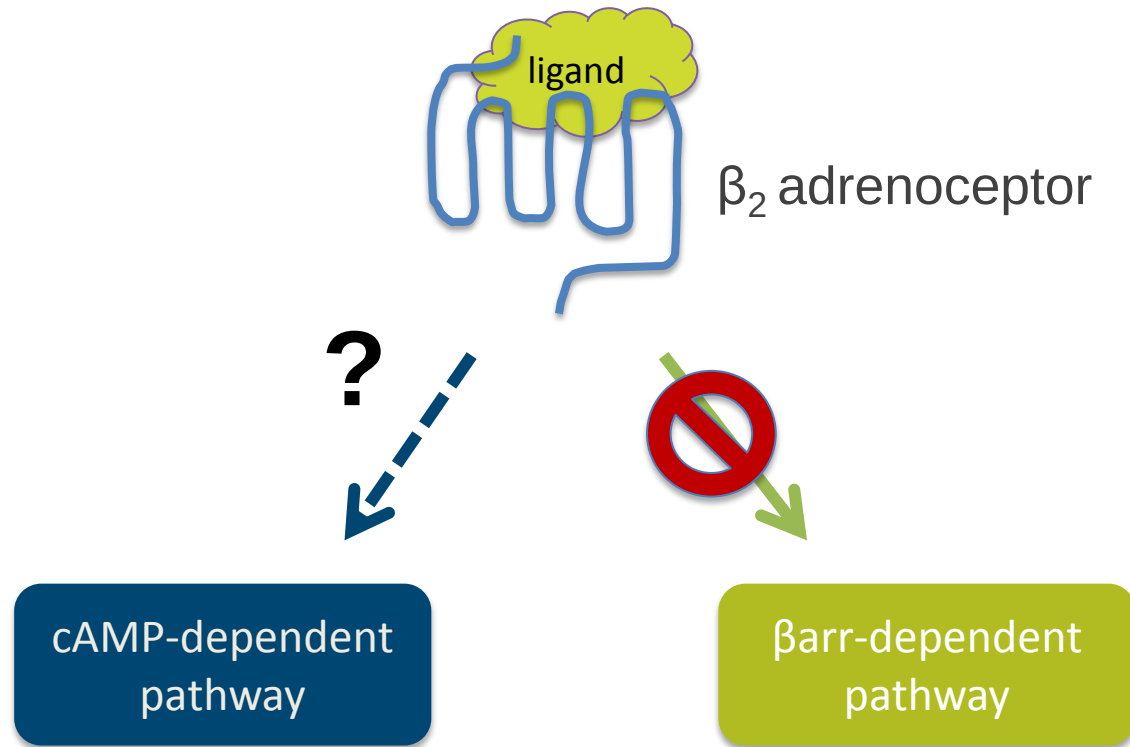
Carvedilol and alprenolol did not work



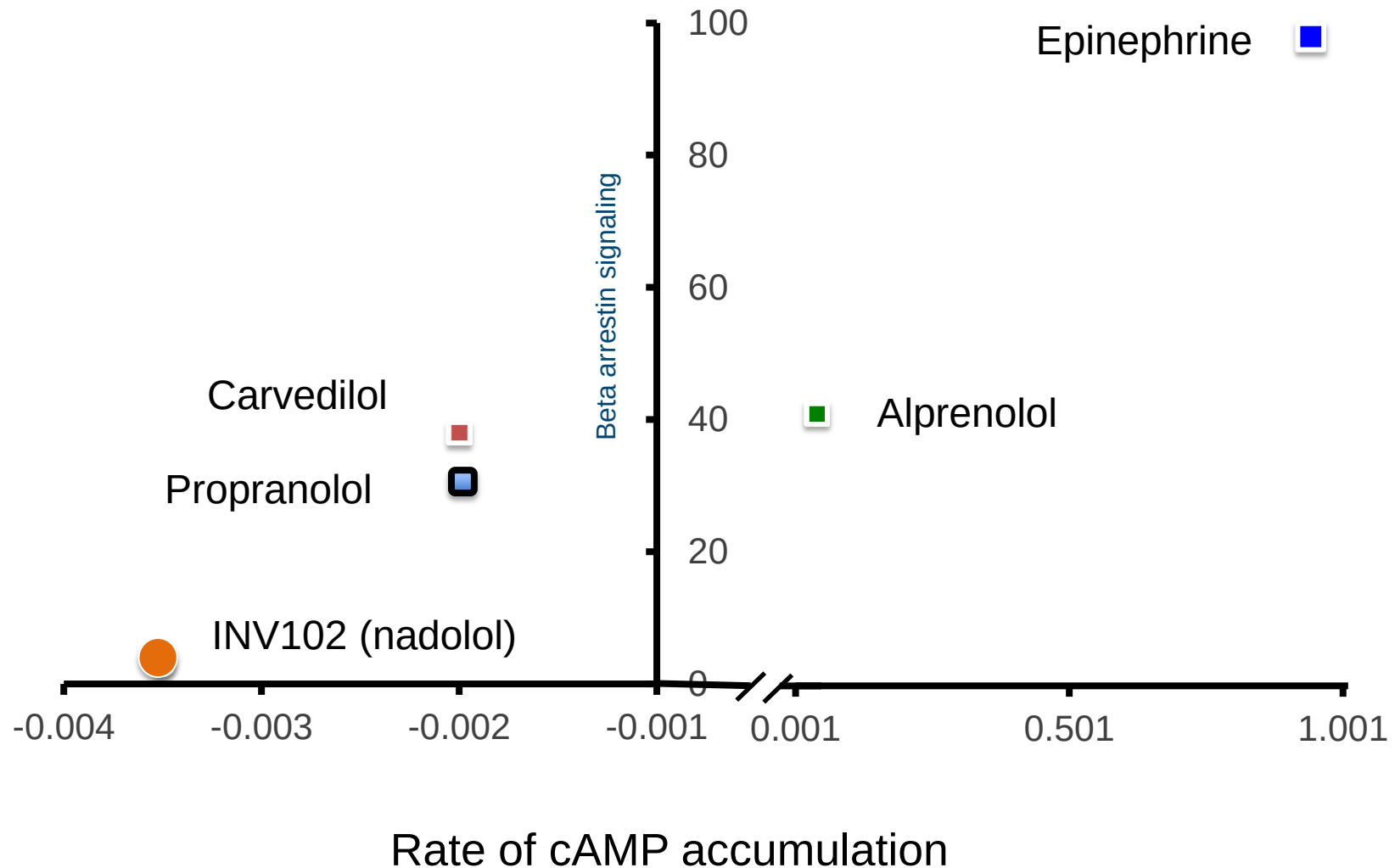
Nadalol (acute)



Nadolol (chronic)



Nadolol is different from other beta-blockers



Conclusions

- > The β_2 adrenoceptor has two signaling pathways
- > Beta-blockers can act at the two pathways in different ways
- > Their signaling determines their efficacy in asthma
- > INV102 (nadolol) is beneficial in mouse asthma models
 - > other beta-blockers are not

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)
- > Leads Invion’s experienced clinical development team

INV102 (nadolol)

- > 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

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)



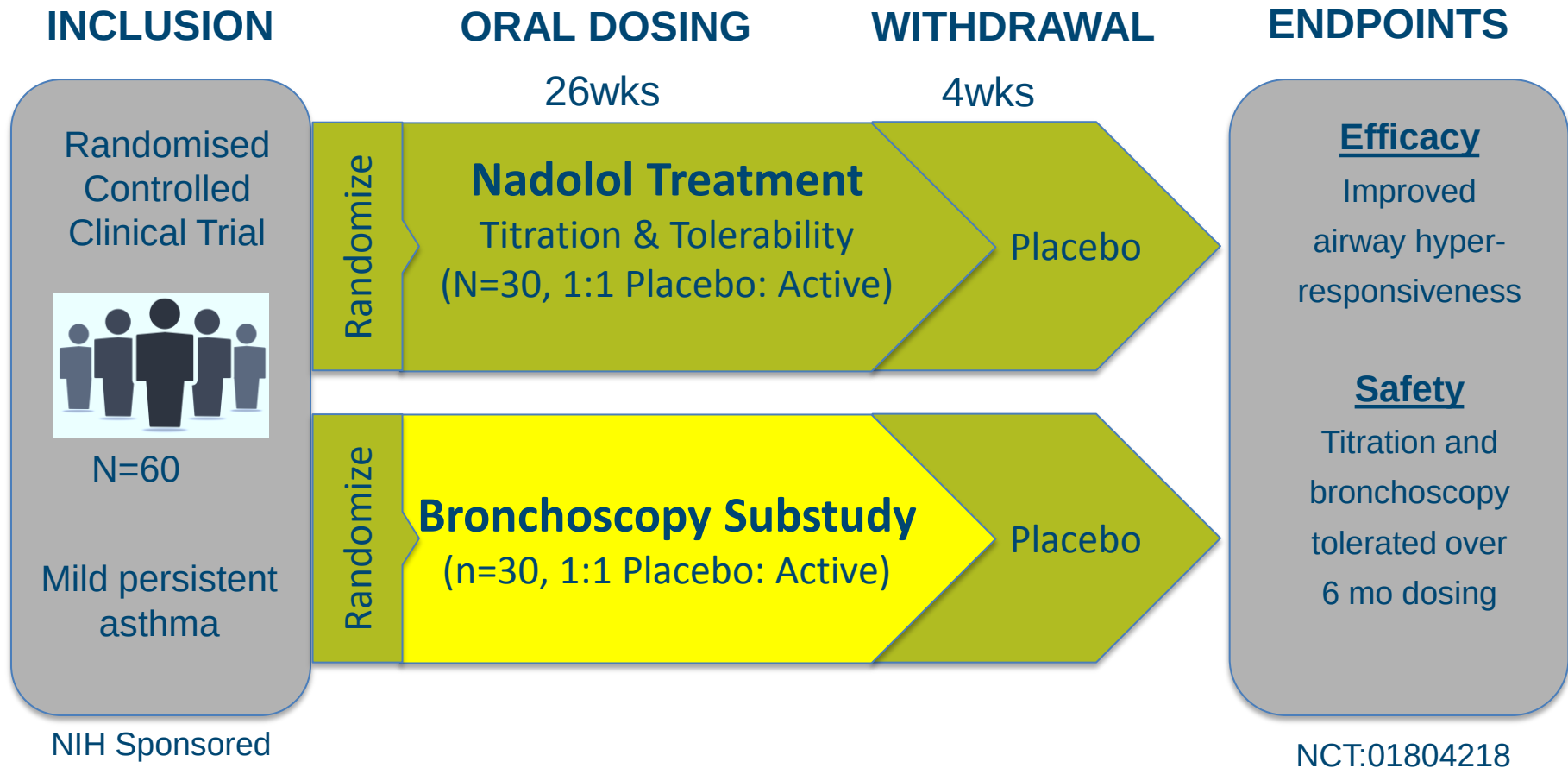
TO

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)

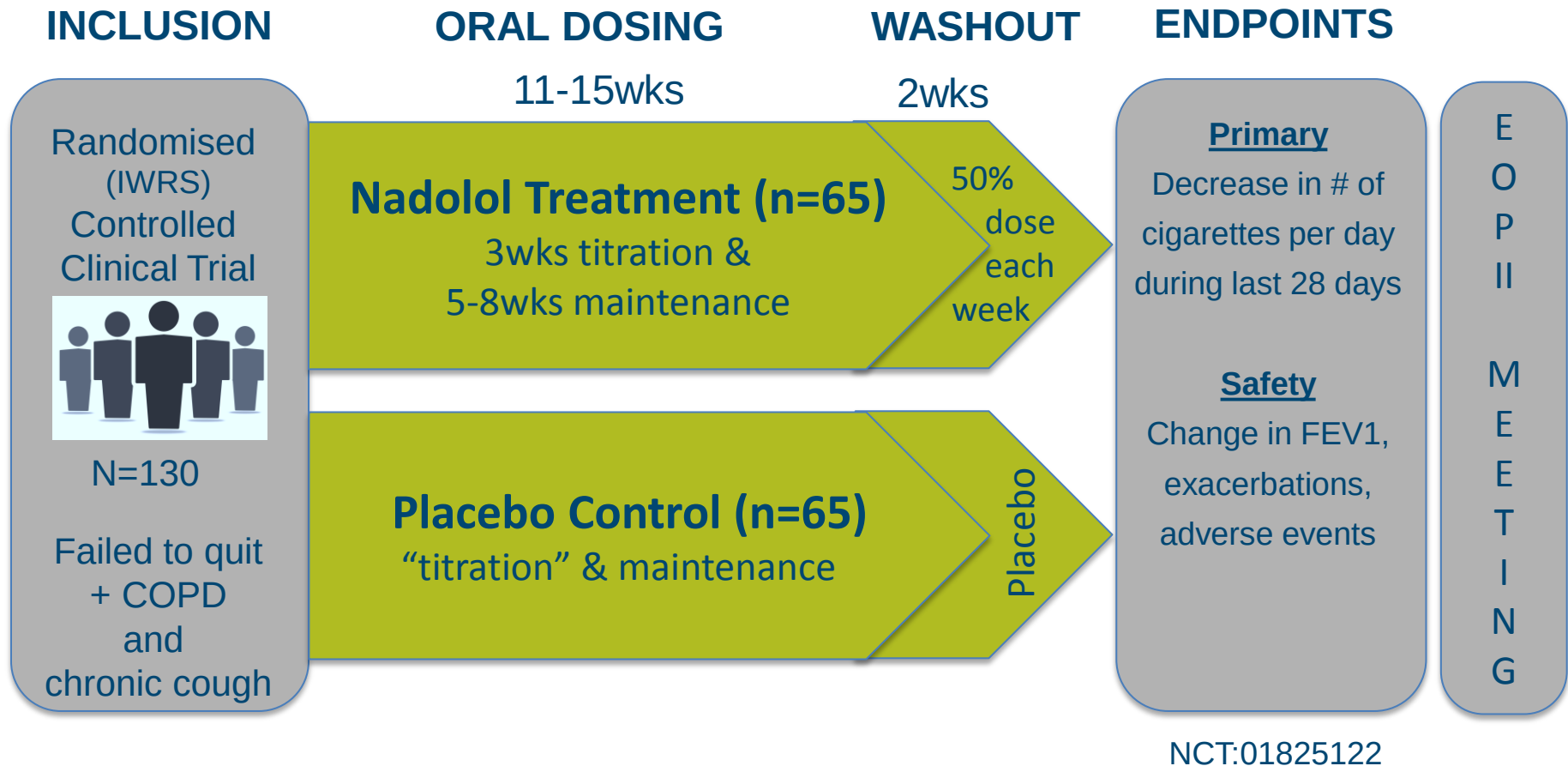
INV102: phase II trial design - mild asthma



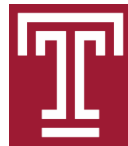
PI & Protocol Chair:
Nicola Hanania, MD
Active clinical trial
sites include:



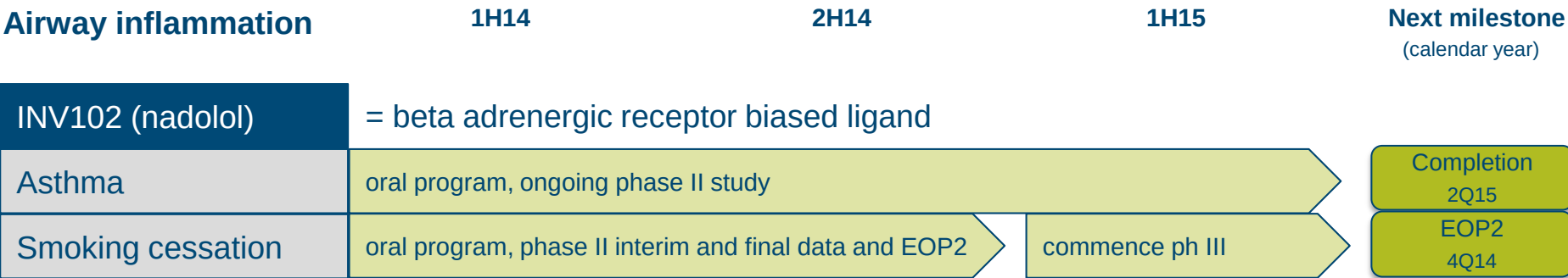
INV102: phase II trial design - smoking cessation



PI: Mario Castro, MD
Active clinical trial
sites include:



INV102 (nadolol): oral program





Targeting inflammation

Respiratory therapeutics: inhaled program

INV102 (nadolol) in COPD & cystic fibrosis

INV104 (zafirlukast) in asthma

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



INV102 (nadolol): comparison oral vs inhaled

Target Product Profile

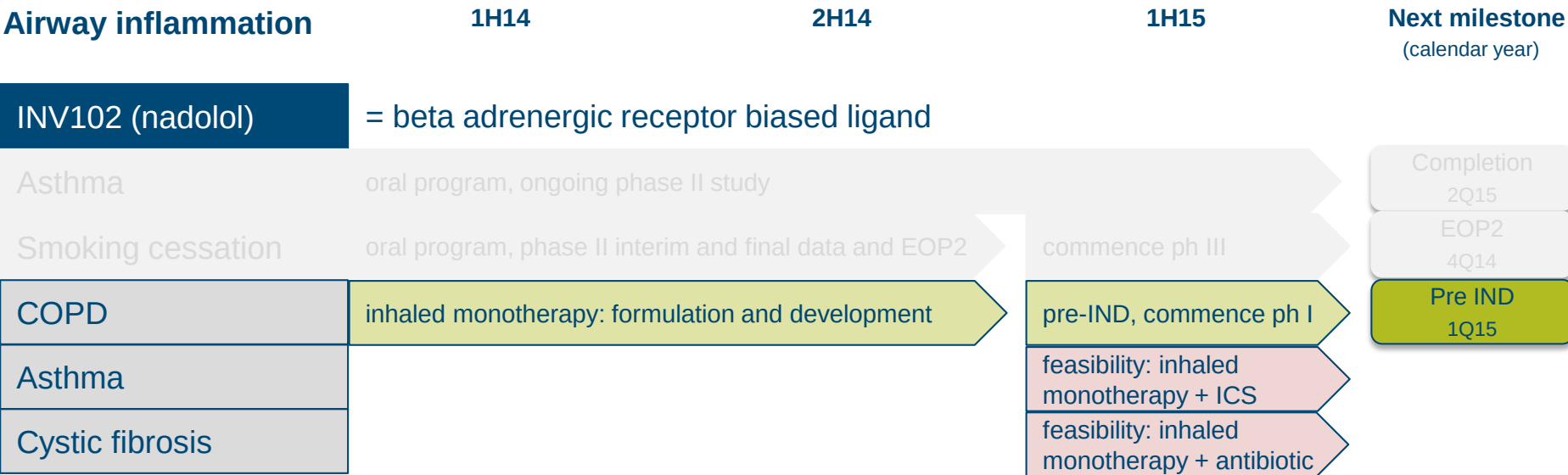
Oral

- > IP protection: titration and method of use (USA)
- > Once daily dosing including titration to avoid systemic side effects
- > Invion phase II and III data limited to 13 weeks for smoking cessation
- > **New indication limited to smoking cessation**
- > No efficacy data on concomitant use of inhaled corticosteroids (severe asthma) or antibiotics (CF)
- > Limited data on reducing cough, sputum production, “smoker’s cough”, avoiding use of steroids or preventing/ameliorating exacerbations

Inhaled

- > IP protection based on 3M formulation and device
- > Once daily dosing with no need for titration and no systemic side effects
- > Safe for long term regular use for chronic airway diseases
- > **Approved for long term use in COPD, severe asthma and cystic fibrosis**
- > Safety and efficacy data in combination with LABA + ICS (Asthma), antibiotics (CF), and LAMA + ICS (COPD)
- > Indicated for reducing cough, sputum production, “smokers’ cough”, decreasing use of steroids or preventing/ameliorating exacerbations

INV102 (nadolol): inhaled program

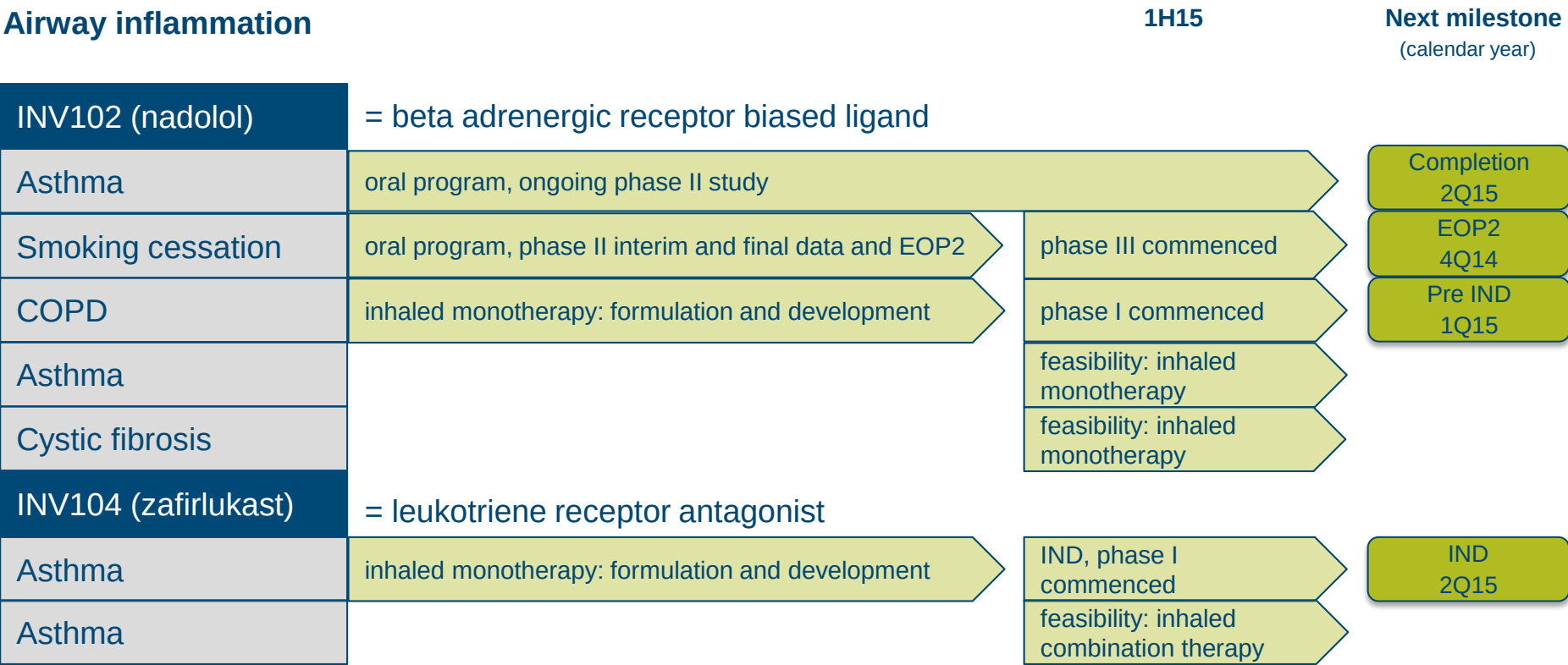


Invion: 3 drugs in development

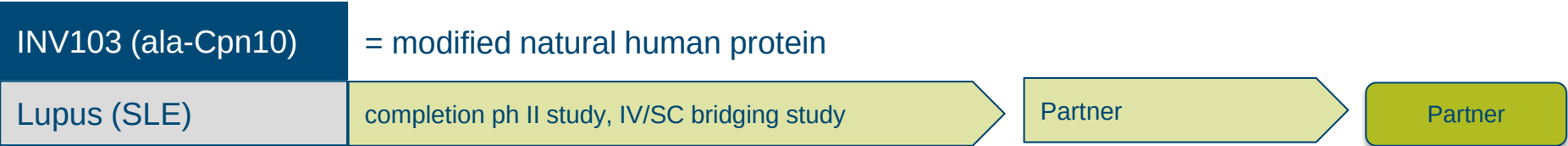
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Pipeline: 12-18 month outlook

Airway inflammation



Autoimmune disease





Targeting inflammation

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



Targeting inflammation

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Investor Presentation
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