Invion Limited (ASX:IVX)

Clinical-stage life sciences company targeting chronic inflammation

Investor Presentation
June | 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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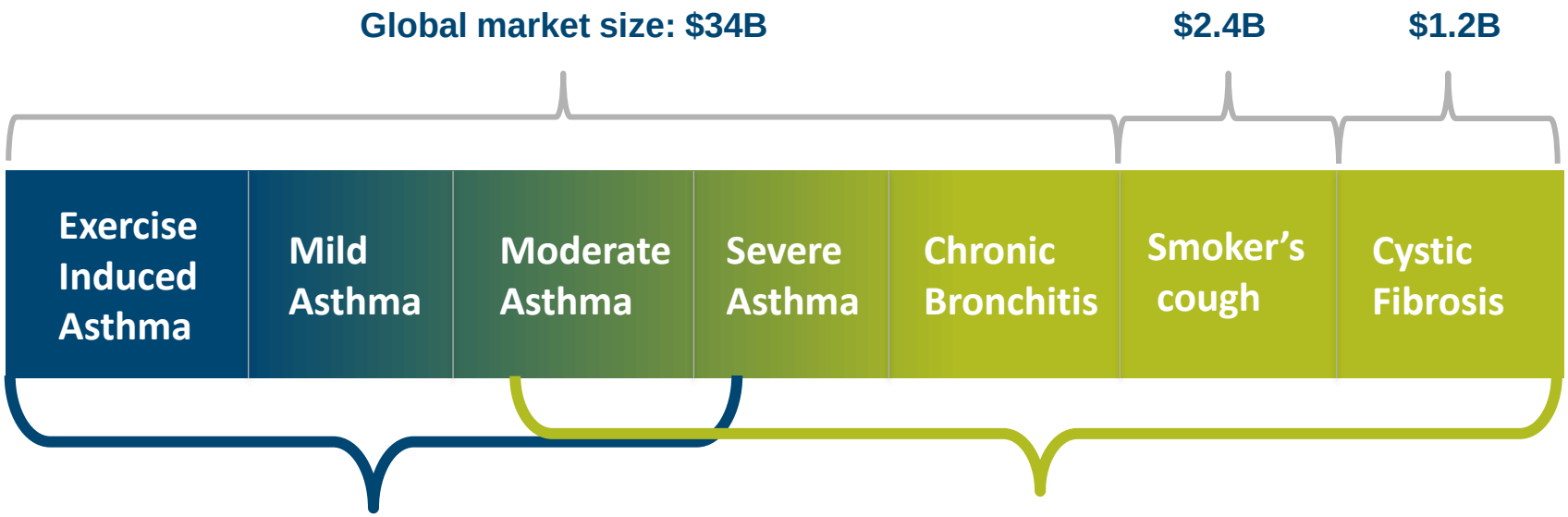
Targeting inflammation

Targeting respiratory disease

INV102 (nadolol) - *unique beta-blocker*

INV104 (zafirlukast) - *leukotriene receptor antagonist*

Spectrum of airway disease and opportunities



Zafirlukast

Monotherapy + combinations

Nadolol

Monotherapy + combinations

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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)"

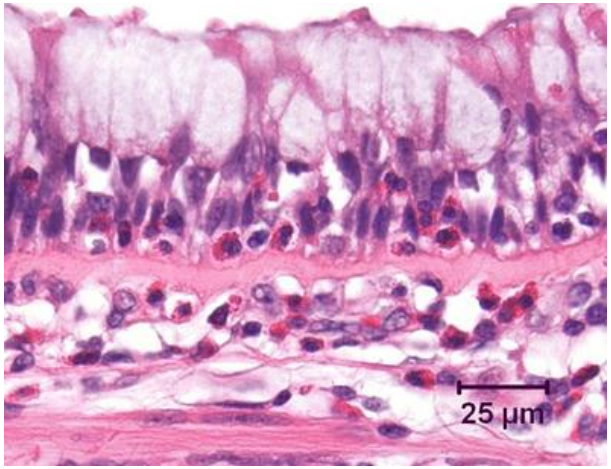
Background

- Beta-Agonists are approved for the treatment of asthma

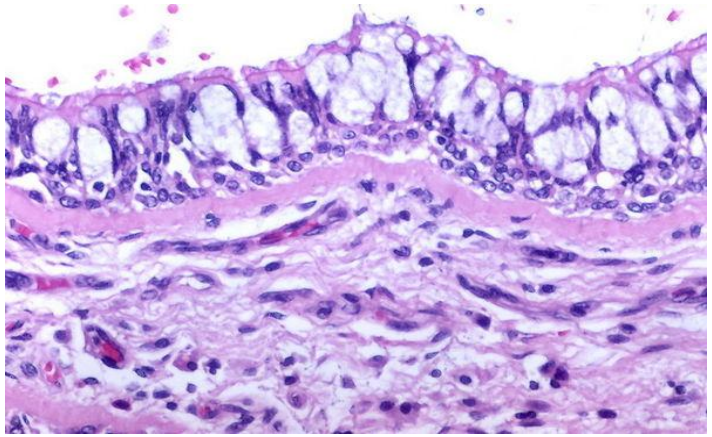
- Acutely, Beta-Agonists are potent bronchodilators, but chronic use can cause loss of asthma control and an increase asthma related mortality

- Beta-Blockers are contraindicated for the treatment of asthma

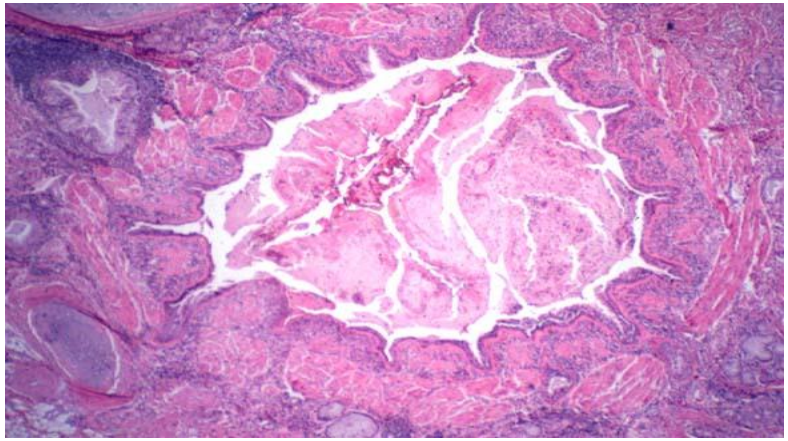
The critical role of the epithelium in the phenotype of severe airway disease



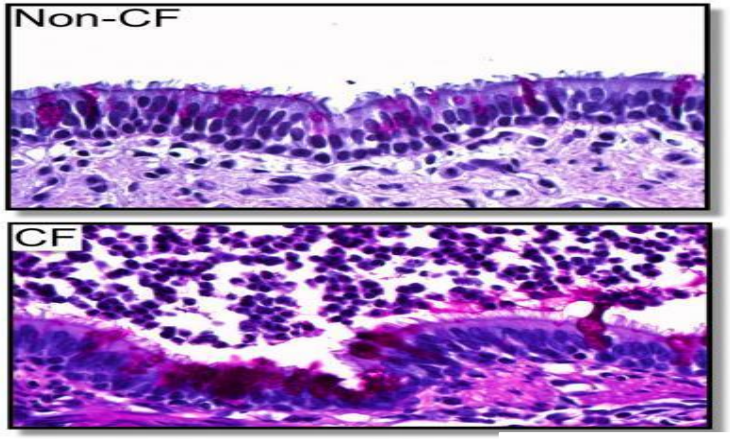
Asthma



COPD

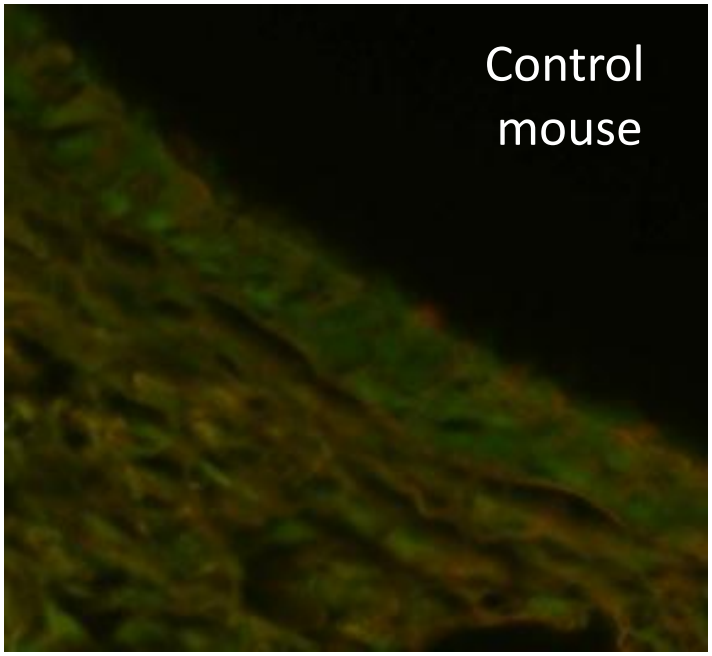


8 y.o. girl treated at Texas Medical Centre



Cystic Fibrosis

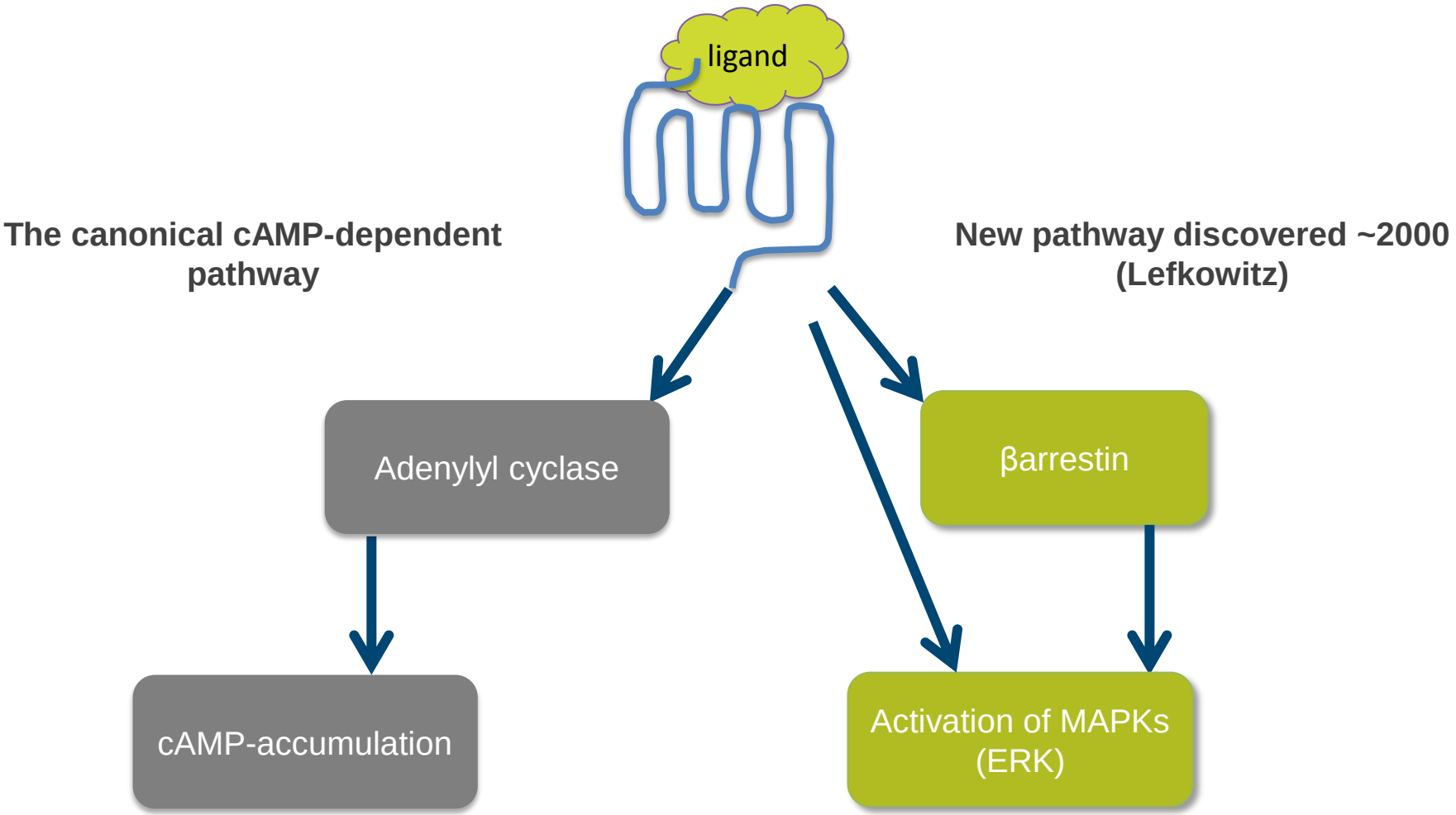
Validity of the preclinical murine model





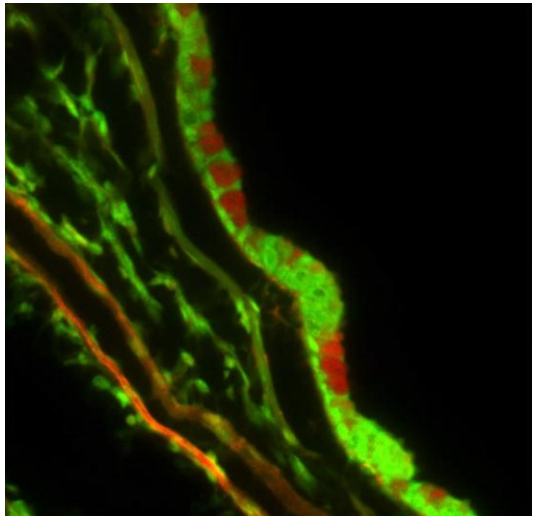
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β_2-adrenoceptor signaling pathways

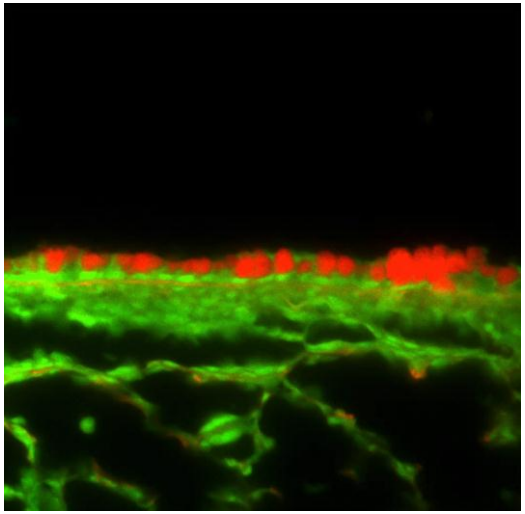


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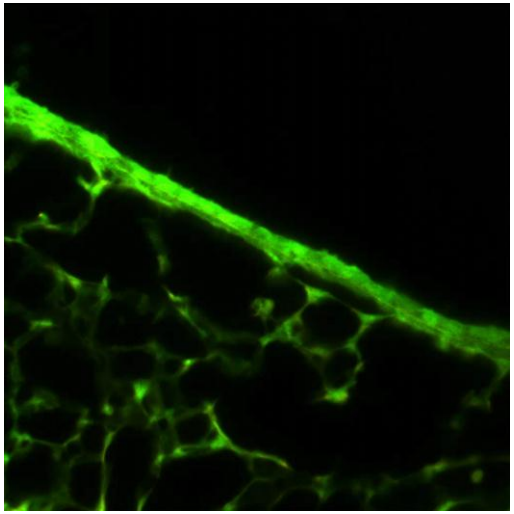
Effects of different beta-blockers on mucous in mouse asthma model



Alprenolol



Carvedilol

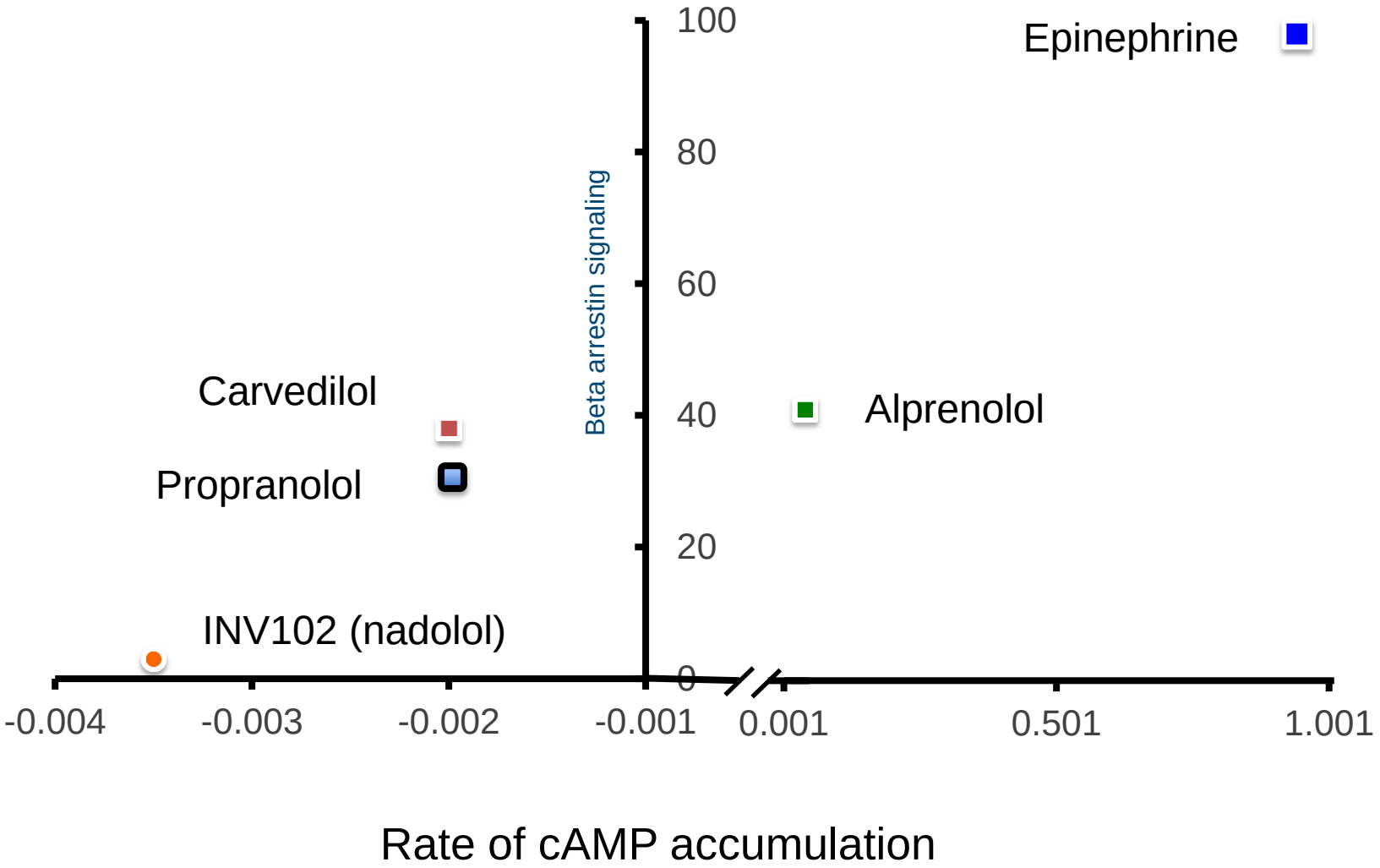


INV102 (nadolol)

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

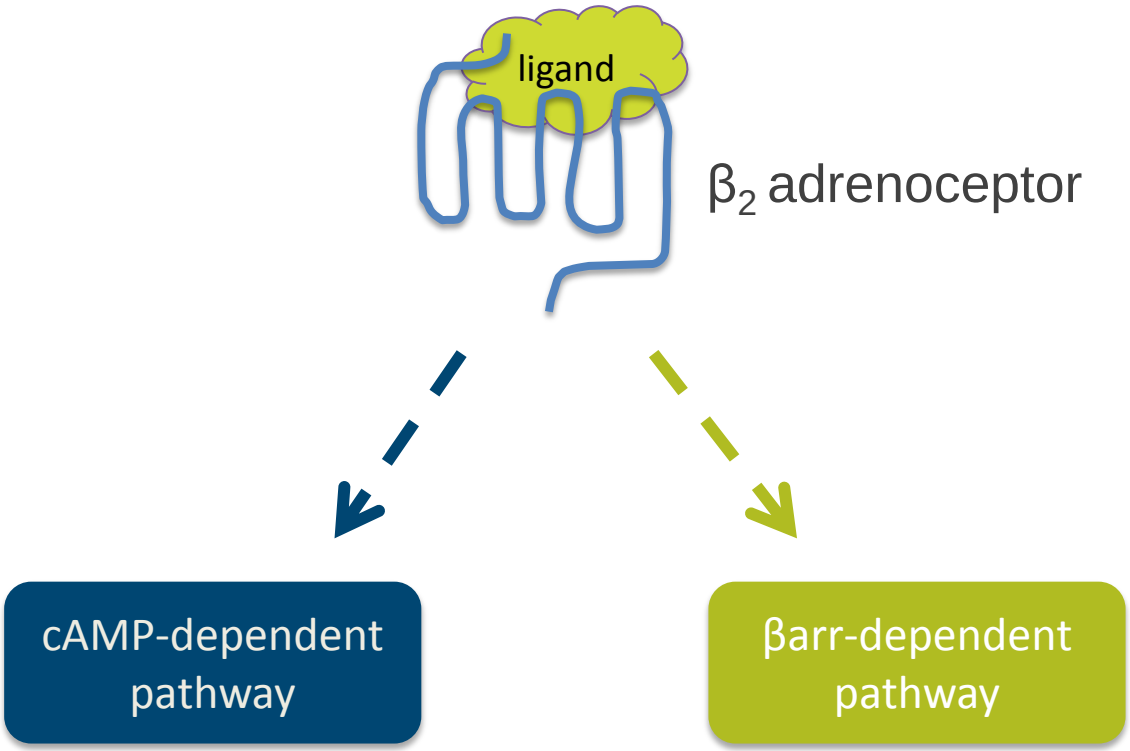
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Nadolol is different from other beta-blockers



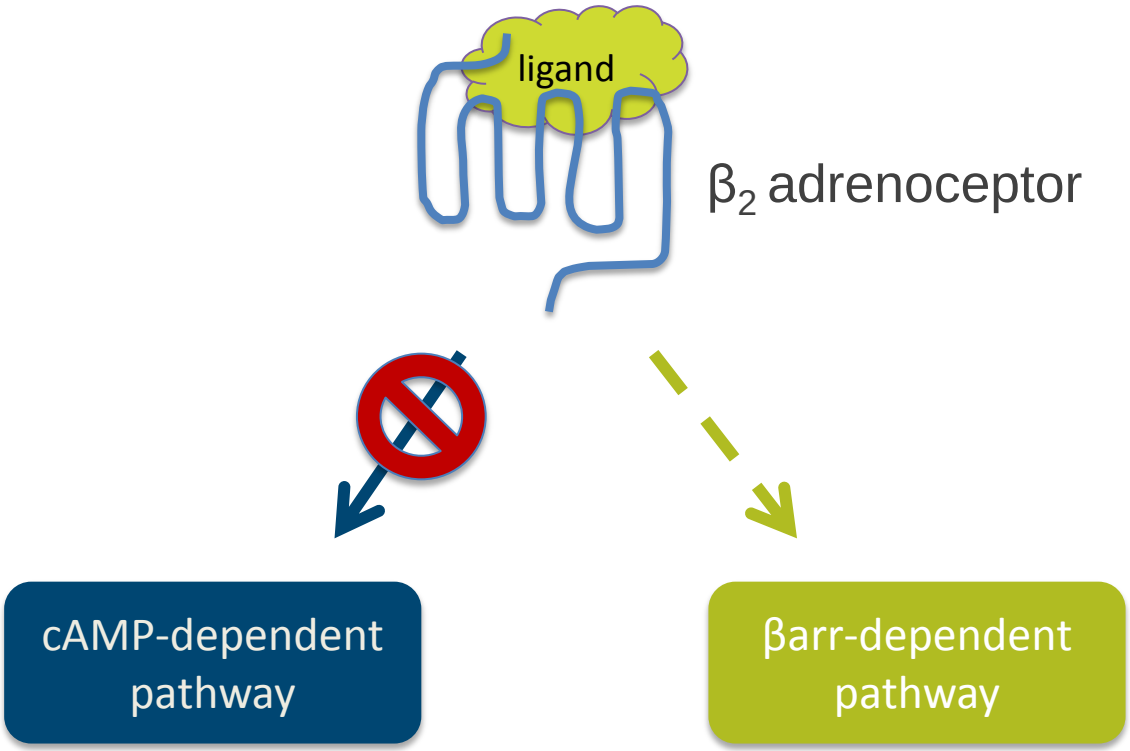
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Alprenolol



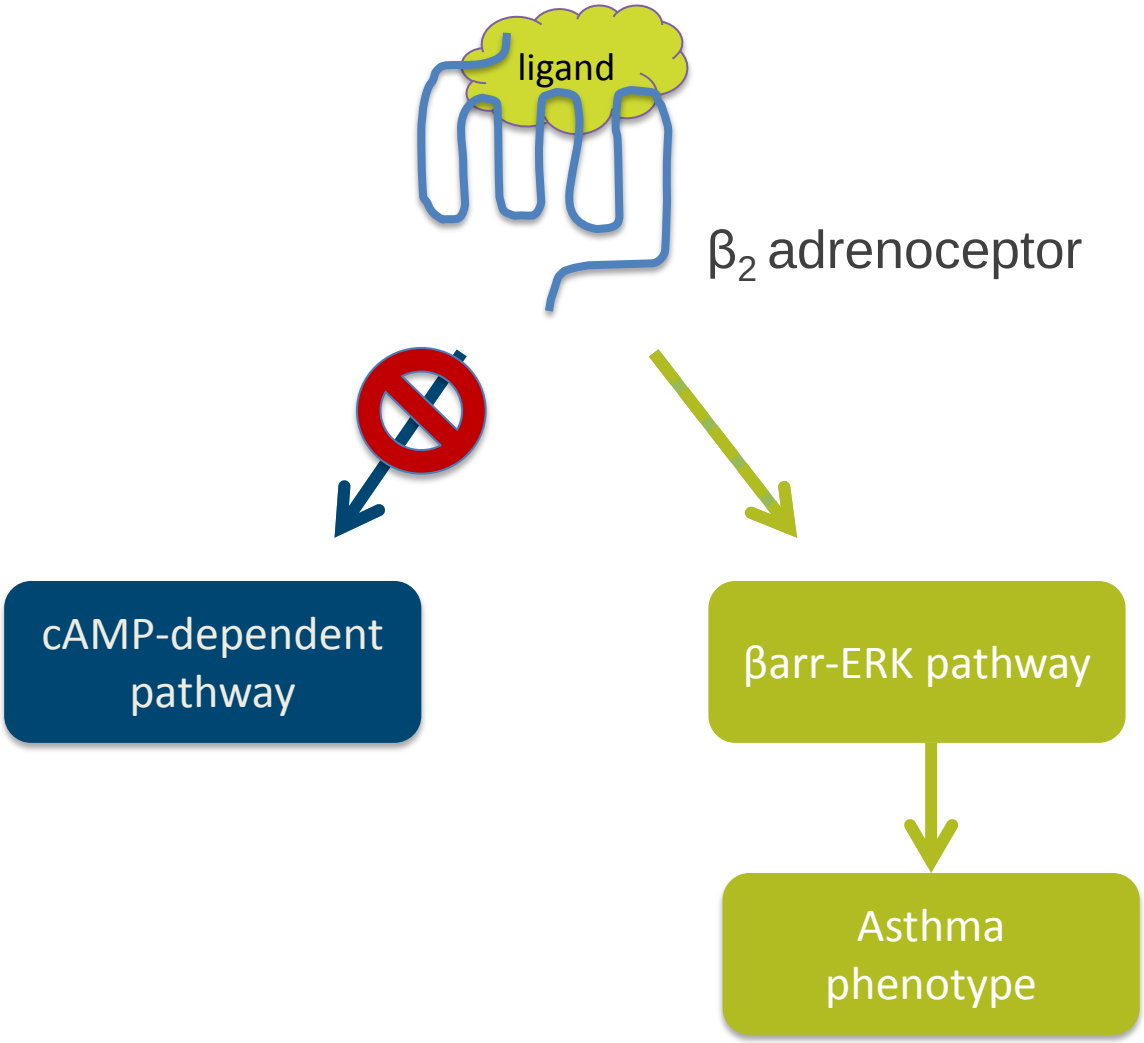
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Carvedilol



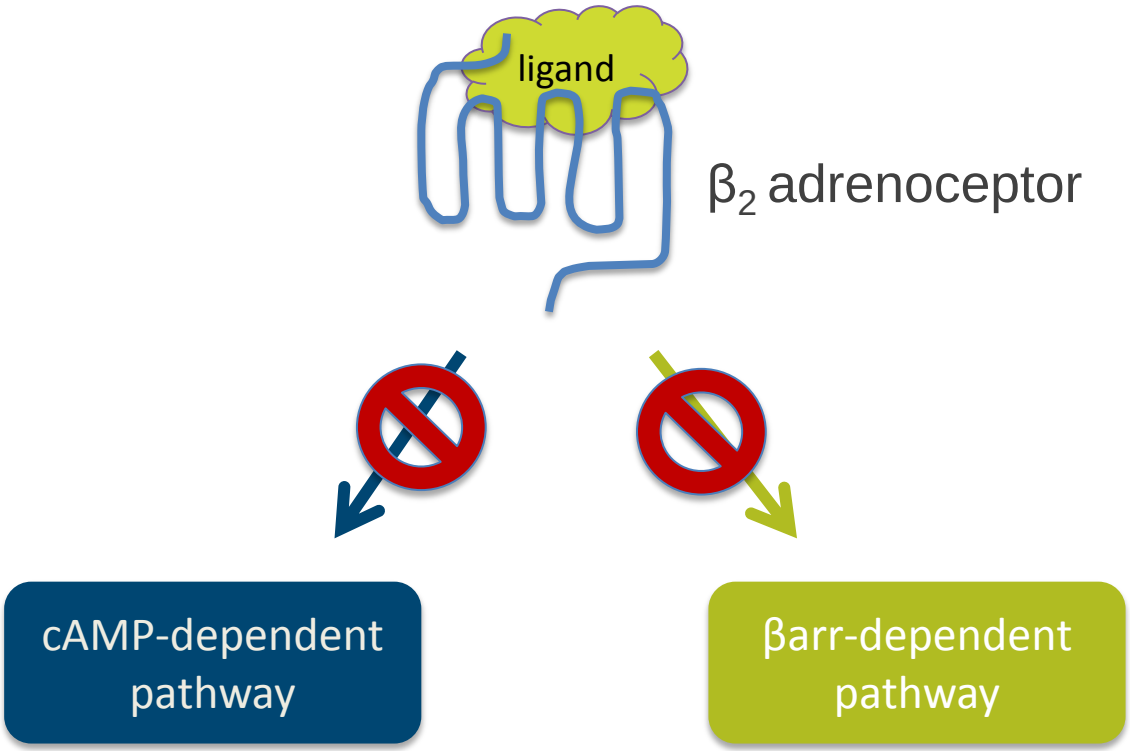
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Carvedilol and alprenolol did not work



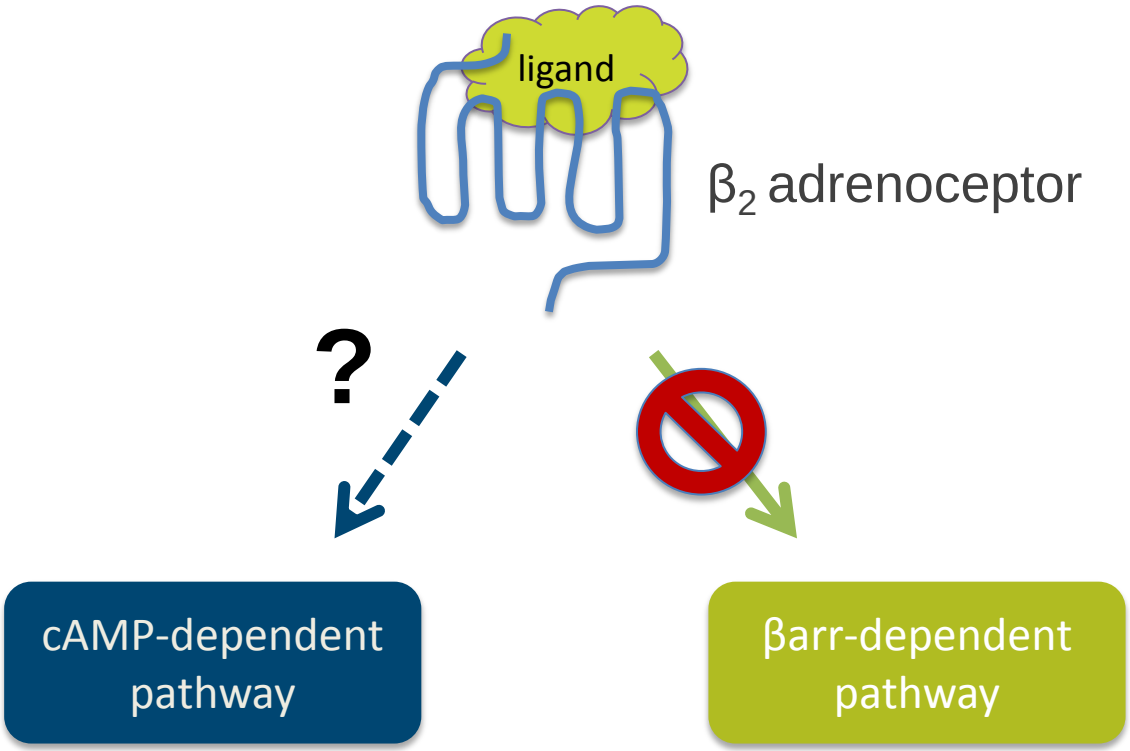
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Nadalol (acute)



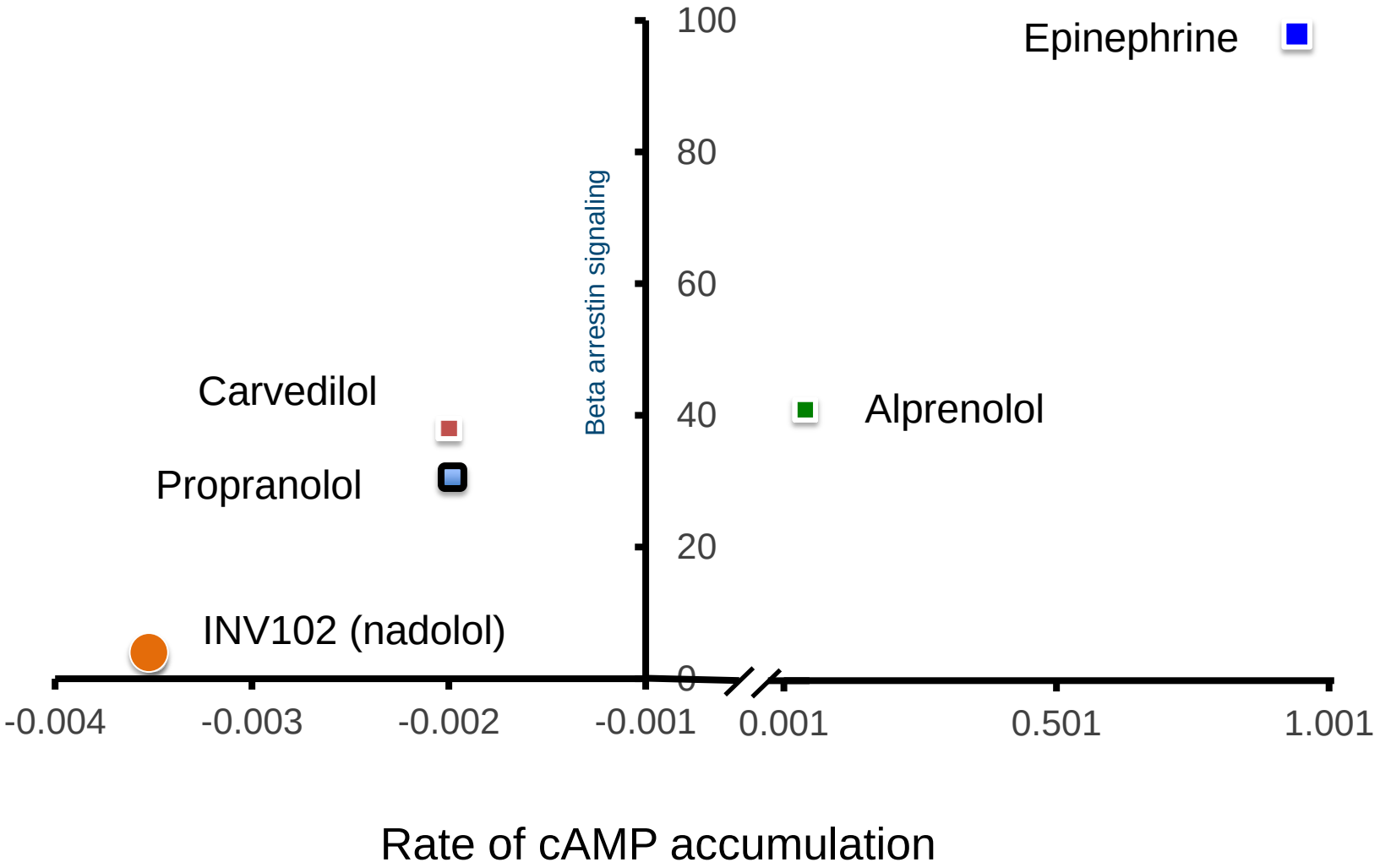
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Nadolol (chronic)



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Nadolol is different from other beta-blockers



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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

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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. 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

INCLUSION

Randomised Controlled Clinical Trial



N=60

Mild persistent asthma

NIH Sponsored

ORAL DOSING

26wks

Randomize

Nadolol Treatment
Titration & Tolerability
(N=30, 1:1 Placebo: Active)

Placebo

Randomize

Bronchoscopy Substudy
(n=30, 1:1 Placebo: Active)

Placebo

WITHDRAWAL

4wks

ENDPOINTS

Efficacy

Improved airway hyper-responsiveness

Safety

Titration and bronchoscopy tolerated over 6 mo dosing

NCT:01804218

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

BCM Baylor College of Medicine

Washington University in St. Louis

Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

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INV102: phase II trial design - smoking cessation

INCLUSION

Randomised (IWRS) Controlled Clinical Trial



N=130

Failed to quit + COPD and chronic cough

ORAL DOSING

11-15wks

Nadolol Treatment (n=65)

3wks titration &
5-8wks maintenance

Placebo Control (n=65)

"titration" & maintenance

WASHOUT

2wks

50% dose each week

Placebo

ENDPOINTS

Primary

Decrease in # of cigarettes per day during last 28 days

Safety

Change in FEV1, exacerbations, adverse events

EOPII MEETING

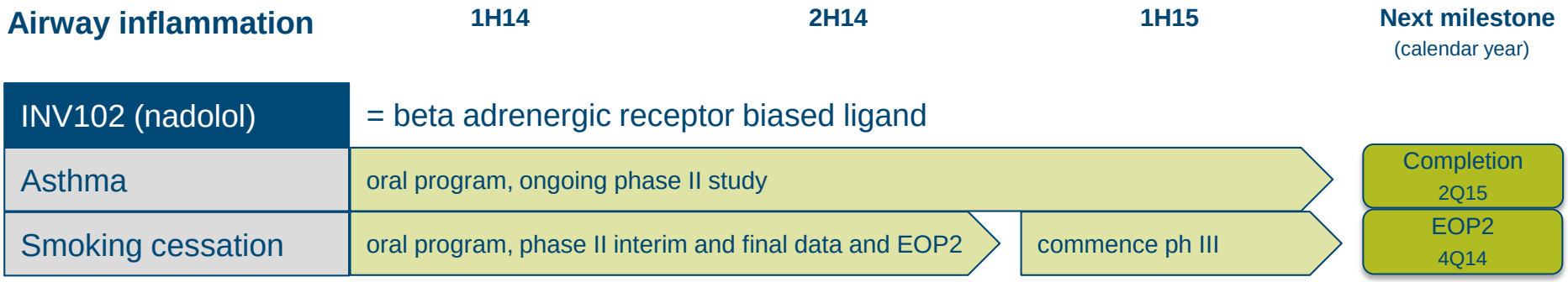
NCT:01825122

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

Birmingham, Alabama

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INV102 (nadolol): oral program



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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

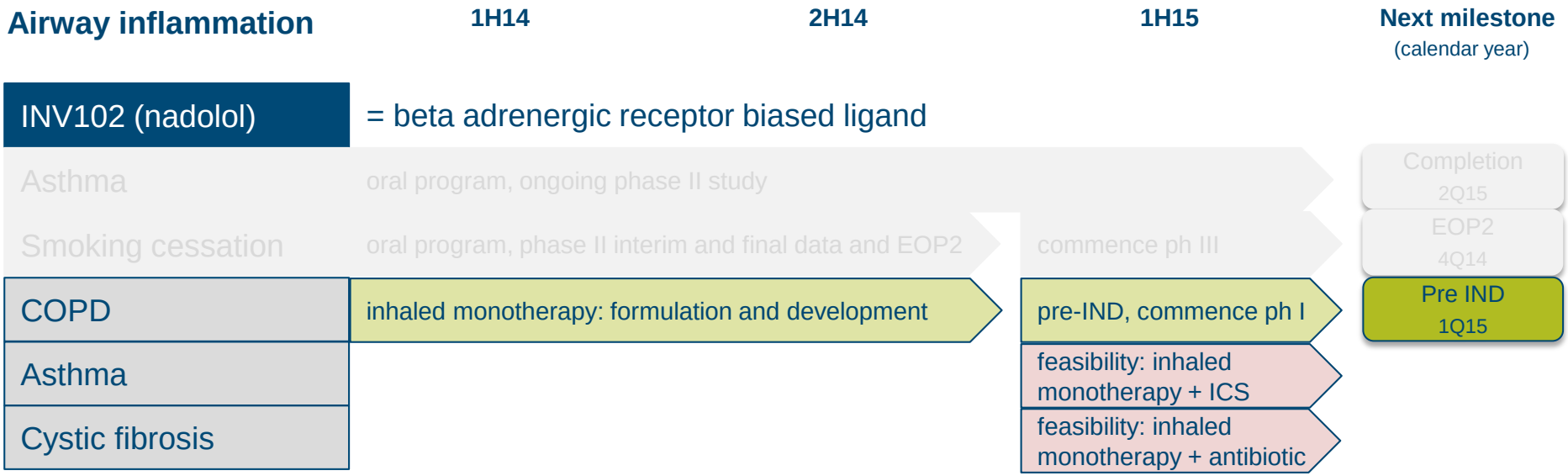
- Collaboration with 3M Drug Delivery systems
- Inhalation development expertise
- Proprietary formulation and device
- Works will assess the feasibility of inhaled INV102 (nadolol) and INV104 (zafirlukast) delivered using 3M's proprietary pressurised metered dose inhalation (pMDI) technology
- Collaboration 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	**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	> Safe for 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



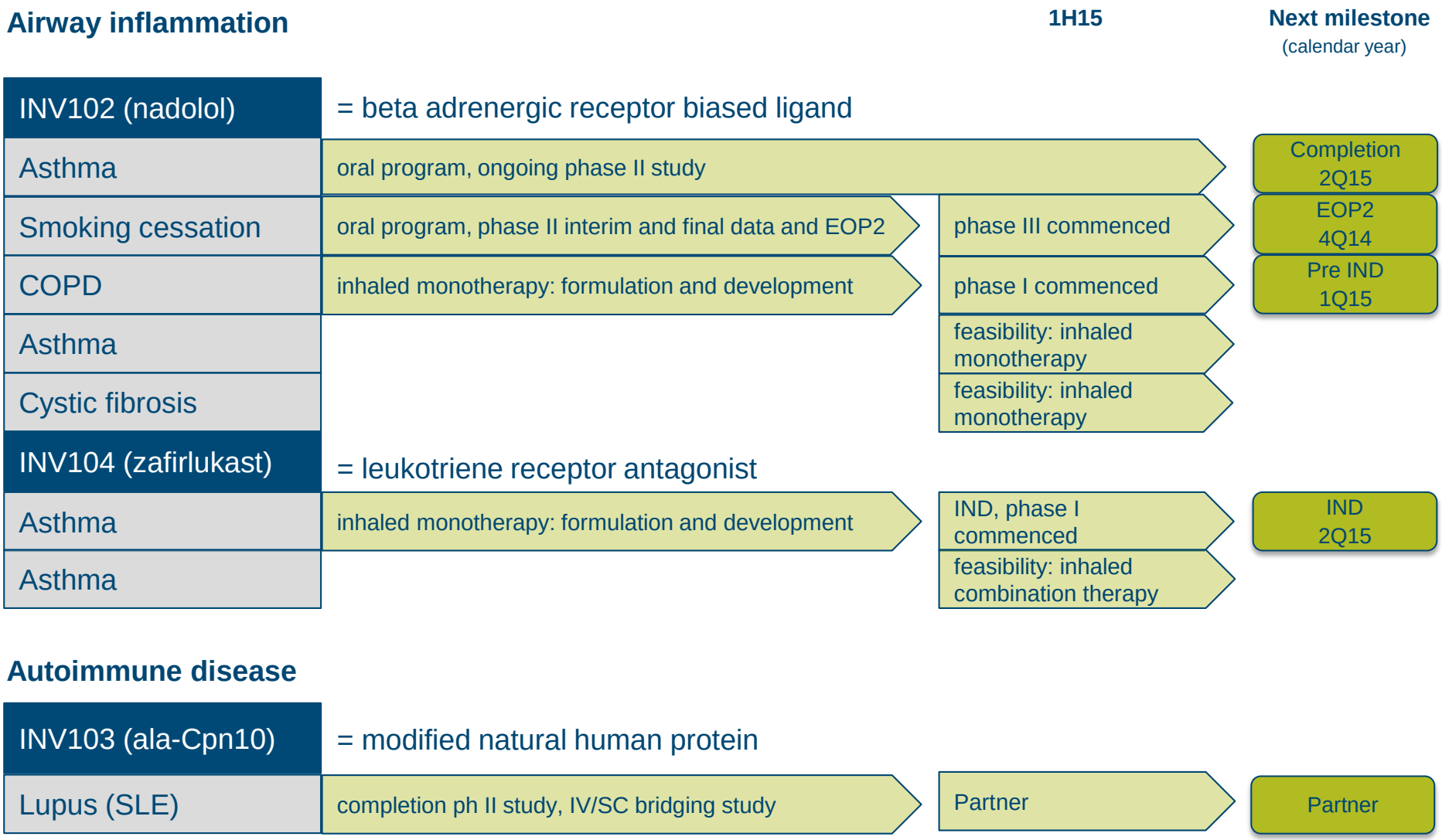
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Invion: 3 drugs in development

- Developing two new respiratory franchises
  - **INV102 (nadolol)**: *beta-blocker* being repurposed to treat inflammatory airway diseases including COPD and cystic fibrosis
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Pipeline: 12-18 month outlook



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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

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