

# Respiratory Disease



## Asthma & COPD

### THE CHALLENGE

#### Exacerbations in Asthma and COPD

Viral infections are reportedly responsible for approximately 65-80% of asthma and 40% of COPD exacerbations and occur despite appropriate treatments including inhaled corticosteroids (ICS). Recent evidence suggests, particularly in asthma, that allergic airway inflammation driven by TH2 cytokines is induced in the airway during human rhinovirus "HRV" related symptom worsening; with suppressed anti-viral immunity linked to exacerbation severity.

### HVIVO CHALLENGE MODELS IN EARLY RESPIRATORY CLINICAL DEVELOPMENT

#### hVIVO can help with respiratory human challenge in both asthma and chronic obstructive pulmonary disease (COPD)

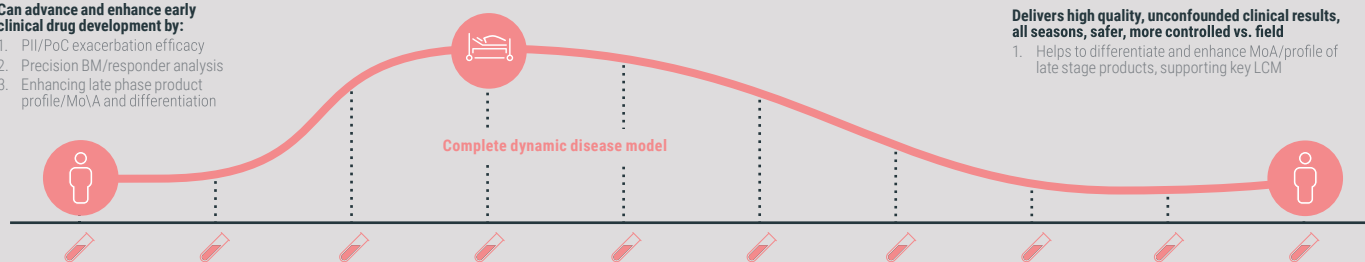
Human challenge models have, for many decades, enabled early proof of concept studies to include evaluable efficacy endpoints that can inform subsequent field trials. For many respiratory diseases, exacerbations are the key drivers of patient morbidity, mortality and increased healthcare costs; and therefore, remains a crucial target in the development of new and novel therapies. **hVIVO has been at the forefront of human challenge models for over 15 years and can offer a suite of challenge models that can expedite and inform clinical development.**

#### Can advance and enhance early clinical drug development by:

1. PII/PoC exacerbation efficacy
2. Precision BM/responder analysis
3. Enhancing late phase product profile/MoA and differentiation

#### Delivers high quality, unconfounded clinical results, all seasons, safer, more controlled vs. field

1. Helps to differentiate and enhance MoA/profile of late stage products, supporting key LCM



The VC model provides unique opportunities for illuminating the pathophysiology and testing of novel drugs through the entire time course of an exacerbation

### MONOCLONAL ANTIBODIES / IMMUNOGLOBULINS

#### CONCEPTUAL OVERVIEW / CHALLENGE

Immunoglobulins can target the host or the virus itself

A precise approach matching the drug MoA, patient population and study design, including selection of appropriate endpoints in an established viral challenge model is central to maximising trial success

#### UTILISING HVIVO'S HRV CHALLENGE MODEL

##### Towards a deeper understanding

##### ENABLES:

- Precise and dynamic measurement of asthma/COPD exacerbation physiology and drug MoA/efficacy
- Provide direct evidence / rationale for MoA and pathway cytokine suppression link to restoration of anti-viral immunity
- Demonstrate direct effect on most common (i.e. viral) cause of asthma exacerbations
- Provide data in patients with mild and/or moderate to severe asthma / COPD to support future strategic development of mAb / immunoglobulins
- Drug efficacy (symptom reduction, preventing reductions in lung function)
- Direct comparison of TH2 high vs. TH2 low asthma, identifying different clinical and biomarker responses in the subtype of patients
- Effect of non-TH2 inhibitors on viral induced exacerbations

### ANTI-INFLAMMATORIES

#### CONCEPTUAL OVERVIEW / CHALLENGE

The concept of human challenge models has been recognised for many years in the field of anti-inflammatory drug development

Bronchial allergen challenge is a well-established model with decades of data supporting its use for confirming specific efficacy of anti-inflammatory as add on therapies in allergic asthma and related exacerbations

The viral exacerbation challenge has been studied extensively over the last 30 years with potential for evaluating the effect anti-inflammatories can have on virally induced exacerbations

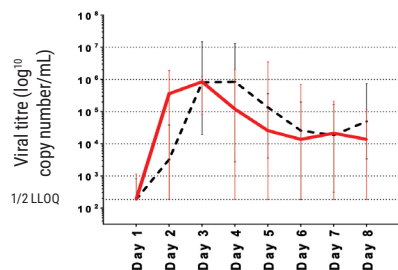
#### UTILISING HVIVO'S HRV CHALLENGE MODEL

##### Towards a deeper understanding

##### ENABLES:

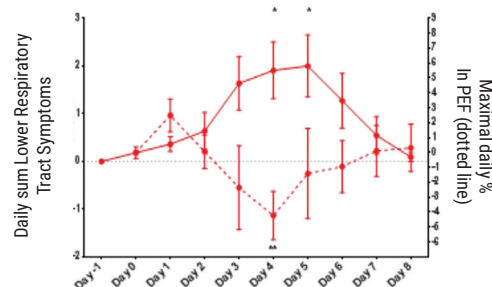
- Efficacy evaluation of disease biomarkers, symptom severity and exacerbation frequency / reduction
- Understanding of biomarker modulation in the context of human disease: protein / transcriptomics pathway modulation
- Analysis of target engagement in human disease model

### Viral shedding subsequent to HRV inoculation in mild atopic asthma



Median HRV viral loads in infected asthmatics (pink, n=11) and healthy controls from a previous study (black, n=6). (median; interquartile range)

### Increase in LRTS mirrors time course of lung function fall post HRV16 inoculation



Solid lines = LRTS; Dashed lines = Maximal daily % fall in PEF; Red = Infected (n=11)

## HVIVO HUMAN CHALLENGE MODELS FOR RESPIRATORY

### VIRAL

#### HRV-16

Asthma HRV challenge in adults aged 18-60 years old

COPD HRV challenge in adults aged 40+ years old

### NON-VIRAL:

- Bronchial Allergen
- LPS
- Histamine/Methacholine
- Adenosine Mono-Phosphate
- Adenosine Tri-Phosphate
- Mannitol

### HVIVO'S HUMAN CHALLENGE MODEL AGENTS

hVIVO can offer a suite of viruses for use within human challenge models. These viruses have been used in numerous clinical trials with over 2500 patients/volunteers having been safely inoculated to date. We maintain a virus dossier as part of our commitment to safety and regulatory transparency.

hVIVO also has an extensive database of patient/volunteer virology and disease profile data giving us the ability to offer a unique insight into the human viral challenge model and has been, and will continue to be, a core part of our successful trial designs and client relationships.



- HRV-16
- HRV-39
- RSV Memphis-37
- FLU H3N2

### HVIVO SERVICES FOR RESPIRATORY



#### Respiratory Diagnostics / Monitoring

Lung function (FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC, FEF<sub>25-75</sub>, IC, SVC)

Reversibility

Forced Oscillation Technique

Cough Monitoring



#### Inflammation Sampling / Monitoring

Induced sputum

Fractional Exhaled Nitric Oxide (FeNO)

Nasosorption

Nasal Scrape

### ABOUT HVIVO

Established in 1989 as a spin out from Queen Mary University, London, hVIVO is a trusted partner and industry leading clinical development services business pioneering human disease models based upon viral challenge. Using human challenge studies to establish early proof of concept, hVIVO's clinical trial platform can accelerate drug and vaccine development in respiratory and infectious diseases

specifically leveraging hVIVO's established human disease challenge models in influenza 'flu', respiratory syncytial virus 'RSV' and human rhinovirus 'HRV' and more recently the expansion and development of these models in other respiratory indications for asthma, chronic obstructive pulmonary disease "COPD", cough and related new therapies and in special populations.



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\* human rhinovirus (HRV) and respiratory syncytial virus