
Aquinox
Activate excellence.
Activate innovation.
Activate success.

Development of Targeted Therapeutics for Inflammatory Disease

September 2013

Corporate Overview

Private, venture-backed corporation

- Vancouver, British Columbia, Canada
- SHIP1 discovery made at UBC

Strong investor syndicate

- Baker Brothers, J&J Dev. Corp., Pfizer Ventures, Pharmstandard Investments, and Ventures West
- Closed $18 million Series C March 2013
- ~$60 million raised to-date

Series C proceeds to position for Phase III trials:

- Two Phase II studies: COPD and IC/BPS
- Chronic tox studies
- Large-scale CMC campaign

Highlights

First-in-class program for inflammatory disease

- World leaders developing small molecules that target SHIP1
- Important pathway (PI3K) for cell activation and migration
- Blockbuster and niche/rare clinical opportunities

Strong lead compound - AQX-1125

- ADME properties suitable for oral, once daily dosing
- Potent *in vitro* and broad *in vivo* efficacy data
- Multi-part Phase I study complete: well-tolerated with dose-proportional PK
- Two Phase IIa studies complete: primary endpoint met in both studies
- Decisive data from two Phase II trials (COPD & IC/BPS) available Q4 2014

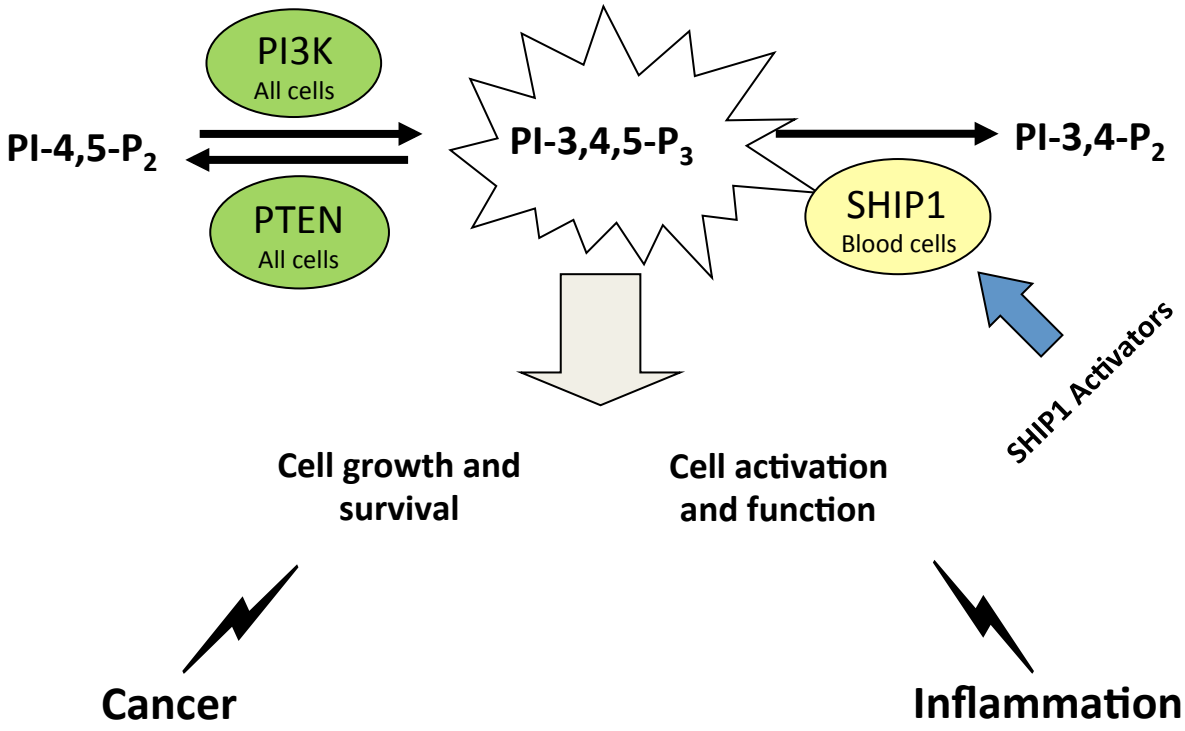
Well-protected intellectual property

- Issued COM claims to AQX-1125 in the US and Europe
- Chemical space is free of prior art

Large, diverse library of 2nd generation compounds (incl. oncology)

SHIP1 is an Ideal Drug Target

SHIP1 is nature's way to regulate PI3K in immune cells



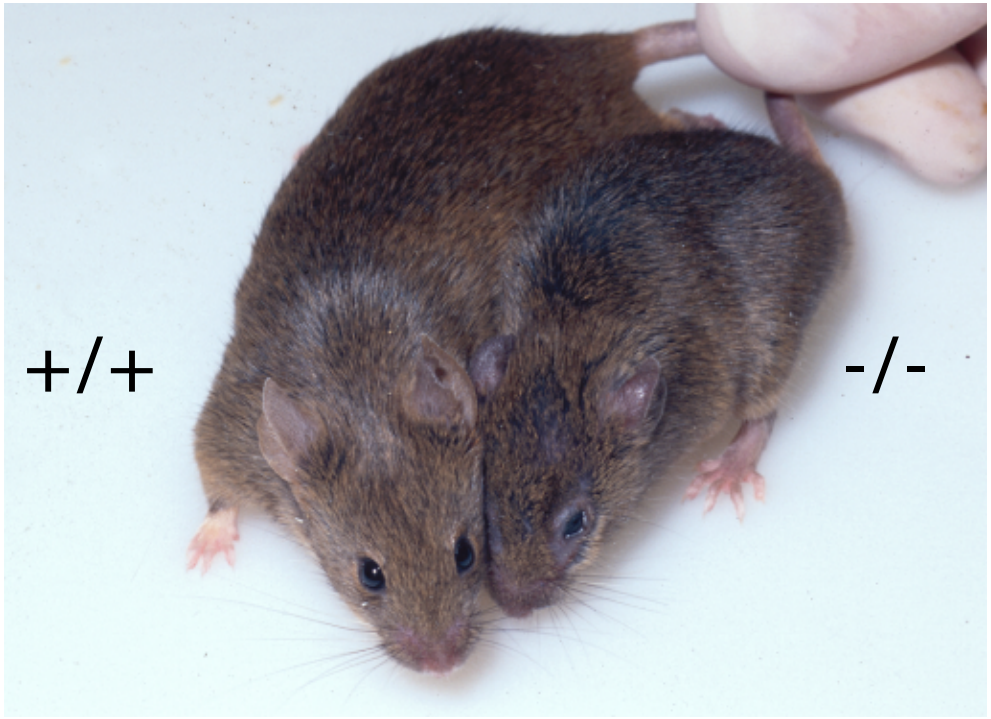
- ✓ Restricted expression to hematopoietic derived cells limits off tissue toxicity
- ✓ Plays key role in regulating cell migration and activation
- ✓ SHIP1 activators redirect signalling, not block it
- ✓ Non-catalytic binding site imparts target selectivity and limits off target toxicity
- ✓ Small molecule - oral dosing

SHIP1 activators have the potential to become the next generation anti-inflammatory drugs

Features of SHIP1 -/- Mice

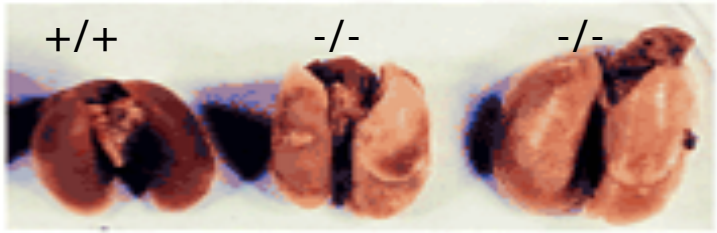
Roadmap for Clinical Indications – Airway, GI, Bladder

A



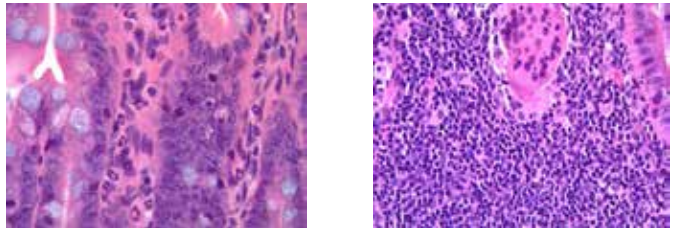
- Viable & fertile, ~40% survival by 14 weeks

B



- Increased GM progenitors
- Infiltration of lungs with macrophages/neutrophils
- Airway remodeling/fibrosis

C



- Mixed inflammatory infiltrates
- Granuloma
- Fibrosis
- Colitis phenotype

Helgason *et al*, Genes & Development, 1998, 12: 1610-1620.
Oh *et al*, Journal of Allergy and Clinical Immunology, 2007, 119: 123-131.
Kerr *et al*, Gut, 2011, 60: 177-188.
McLarren *et al*, American Journal of Pathology, 2011, 179: 180-188.

AQX-1125 Positive *In Vivo* Data

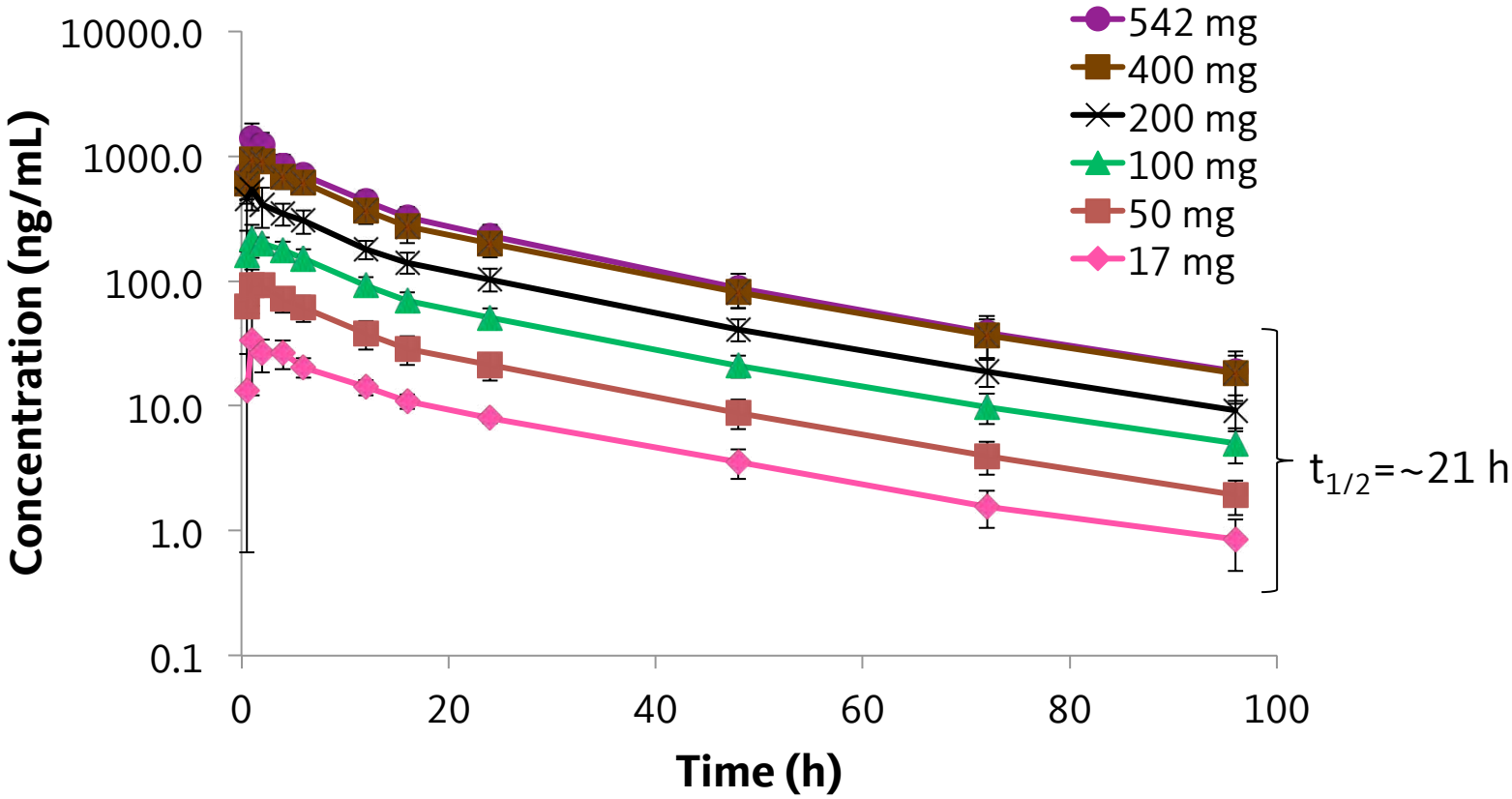
Clinical Indication	Animal Model	Endpoint
COPD / Respiratory	LPS Airway Inflammation (Rat)	↓ neutrophils
	Ovalbumin Airway Inflammation (Rat)	↓ eosinophils
	Smoke Airway Inflammation (Mouse)	↓ neutrophils
	Bleomycin Fibrosis (Mouse)	↓ collagen ↑ survival
Interstitial Cystitis / Bladder Pain Syndrome	Cyclophosphamide Bladder Cystitis (Rat)	↓ inflammatory pain ↓ hemorrhage
	Carrageenan Paw Edema (Mouse)	↓ edema
IBD	TNBS IBD (Rat)	↓ adhesions/strictures ↓ inflammation

AQX-1125 not active in models of RA, MS, nor Uveitis

Activity in models consistent with phenotype of SHIP1 knock-out mouse

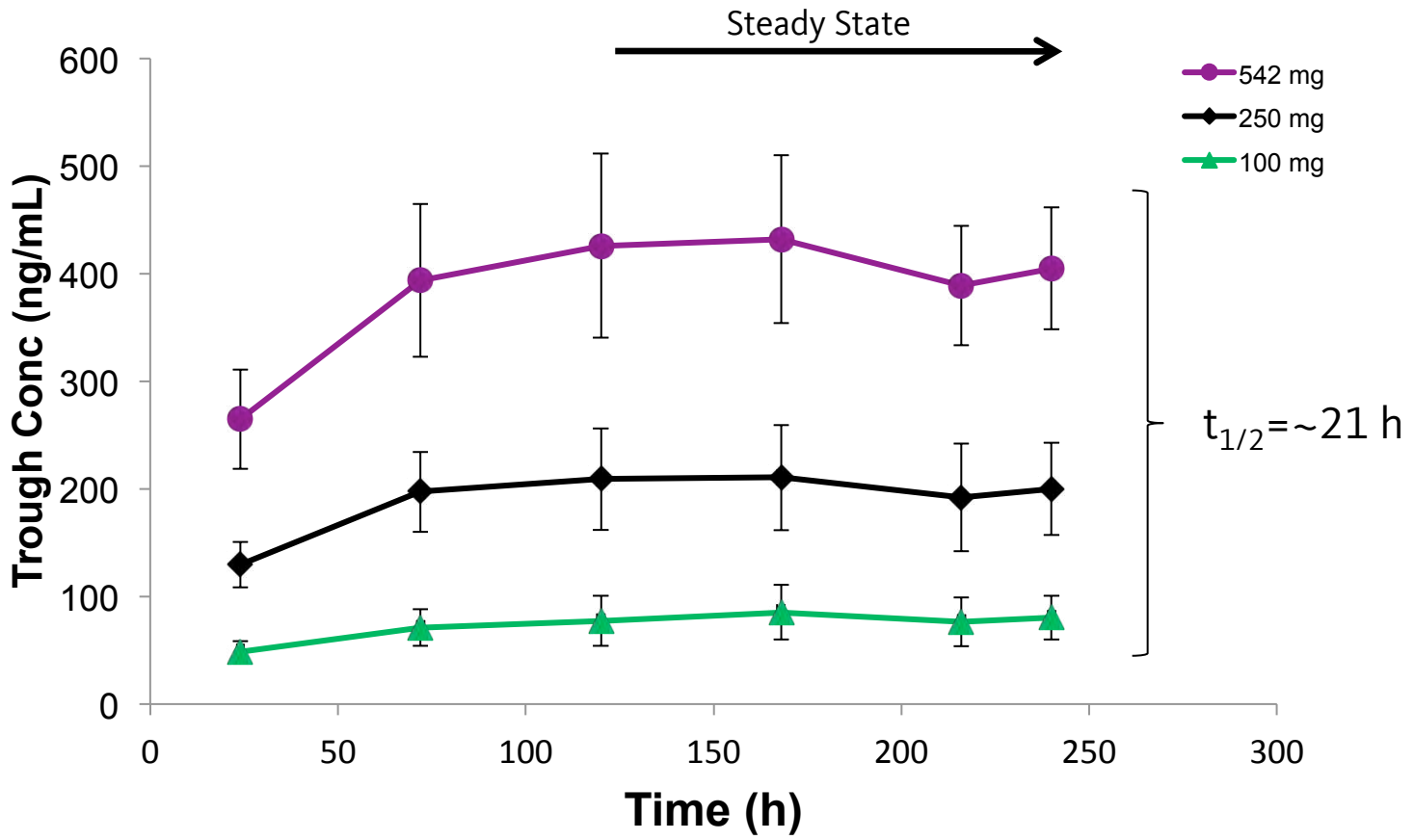
AQX-1125 Phase I and IIa Clinical Summary

Phase I: SAD PK



AQX-1125 exhibits ideal PK suitable for once-a-day oral dosing

Phase I: MAD PK



Human exposure above preclinical target coverage

Phase IIa: Proof-of-Concept Studies

Evaluation of preclinical translation and distinct inflammatory challenges

Allergen Challenge (Asthma POC)

- Respiratory Clinical Trials Group, London, UK – PI's: Drs. Leaker & O'Connor
- Cross-over study (450 mg vs. placebo); 22 mild asthmatics, QD x 7
- Lung function (powered to p=0.05), sputum leukocytes and analyte endpoints
- **Achieved primary endpoint: 20% Inhibition of Late Asthmatic Response (LAR) (p=0.027)**

LPS Challenge (COPD POC)

- Celerion, Belfast, UK – PI's: Drs. Smith & Elborn
- Cross-over study (450 mg vs. placebo); 20 NH volunteers, QD x 7
- Sputum leukocytes (powered to p=0.1) and analyte endpoints
- Known steroid refractory challenge
- **Achieved primary endpoint: 62% Inhibition of sputum neutrophils (p=0.067)**

SHIP1 is an active target in humans

AQX-1125 Phase I and IIa Summary

Near ideal PK and ADME properties

- Dose proportional PK with limited variability
- Rapid and complete oral absorption
- $T_{1/2}$ ~ 21 hrs = Once-daily dosing

Well tolerated at all doses studied

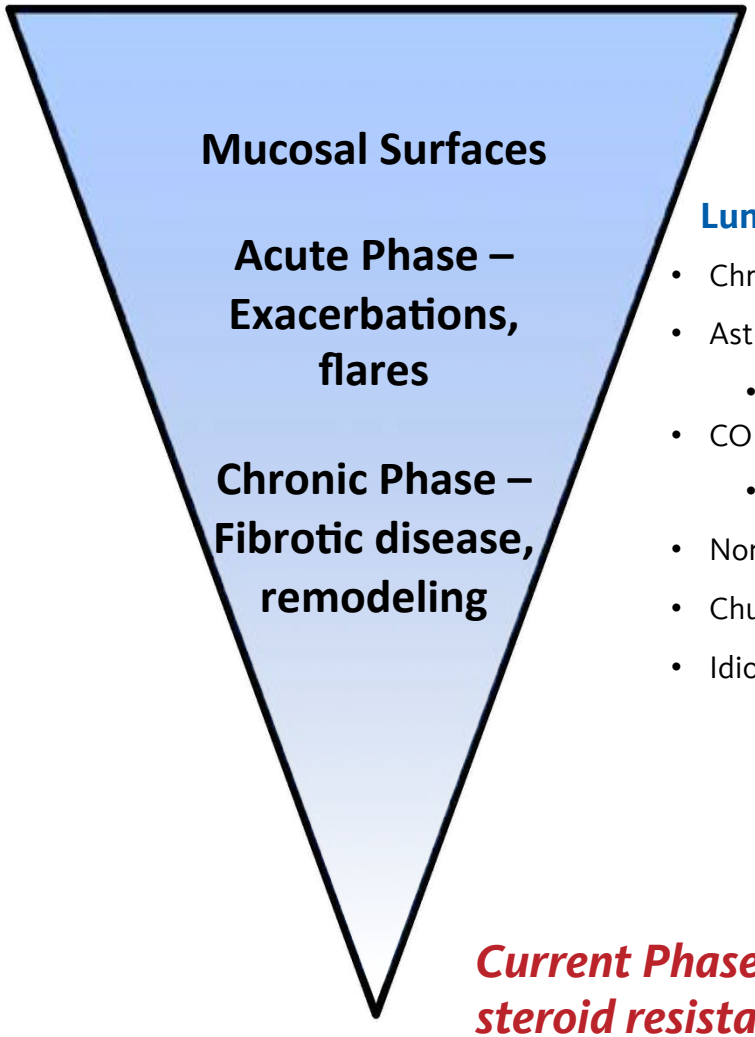
- Doses ≤ 200mg equivalent to placebo
- Doses > 200mg mild GI upset ameliorated by food
- No noted peripheral blood count effects

Unique MOA, broad *in vivo* and cellular response

- Potent in models of mucosal inflammation
- Active against two distinct inflammatory challenges in humans
- Active in steroid resistant indication(s)
- Anti-fibrotic activity

Successful translation of preclinical to clinical results

AQX-1125 Development Strategy/Opportunities



Lung/Airway

- Chronic Rhinosinusitis (CRS) – **(Orphan)**
- Asthma:
  - Steroid unresponsive, Moderate-severe
- COPD:
  - Moderate-severe
- Non-CF Bronchiectasis (NCFBE) – **(Orphan)**
- Churg-Strauss Syndrome (CSS) – **(Orphan)**
- Idiopathic Pulmonary Fibrosis (IPF)

Urinary Tract

- Lupus Nephritis
- Non-infectious Nephritis
- Renal Fibrosis
- Interstitial Cystitis / Bladder Pain Syndrome

GI

- Eosinophilic Esophagitis – (**Orphan)**
- Crohn's
- Ulcerative Colitis (UC)

Current Phase II studies: COPD and IC/BPS – steroid resistant indications with acute phase

AQX-1125 Phase II
Current Development

Interstitial Cystitis/Bladder Pain Syndrome

Disease driven by chronic inflammation and pain following damage to bladder lining

3-8 million women affected in the US

IC/BPS amongst most challenging urologic conditions

Current approach = direct instillation for short-term relief + symptomatic (analgesics) etc.

US economic burden of ~$30-$70 billion/year (IC Assoc)

AQX-1125's biodistribution, anti-inflammatory and pain reducing properties make it compelling for IC/BPS investigation

LEADERSHIP Study: Summary

Objective: Evaluate effects of AQX-1125 on pain in subjects with IC/BPS utilizing eDiaries

- ~70 moderate to severe IC/BPS patients will be enrolled and randomized
- ~15 sites in Canada

Estimated completion date: Q4/2014

Chronic Obstructive Pulmonary Disease (COPD)

High unmet need for effective anti-inflammatories that reduce exacerbations and slow/prevent disease progression

- Exacerbations driven by viral and bacterial infections resulting in high mucus (neutrophil) production
- Chronic inflammation leads to fibrosis and reduced lung function
- Bronchodilators reaching maximum effect
- Inhaled steroids ineffective and increase pneumonia risk

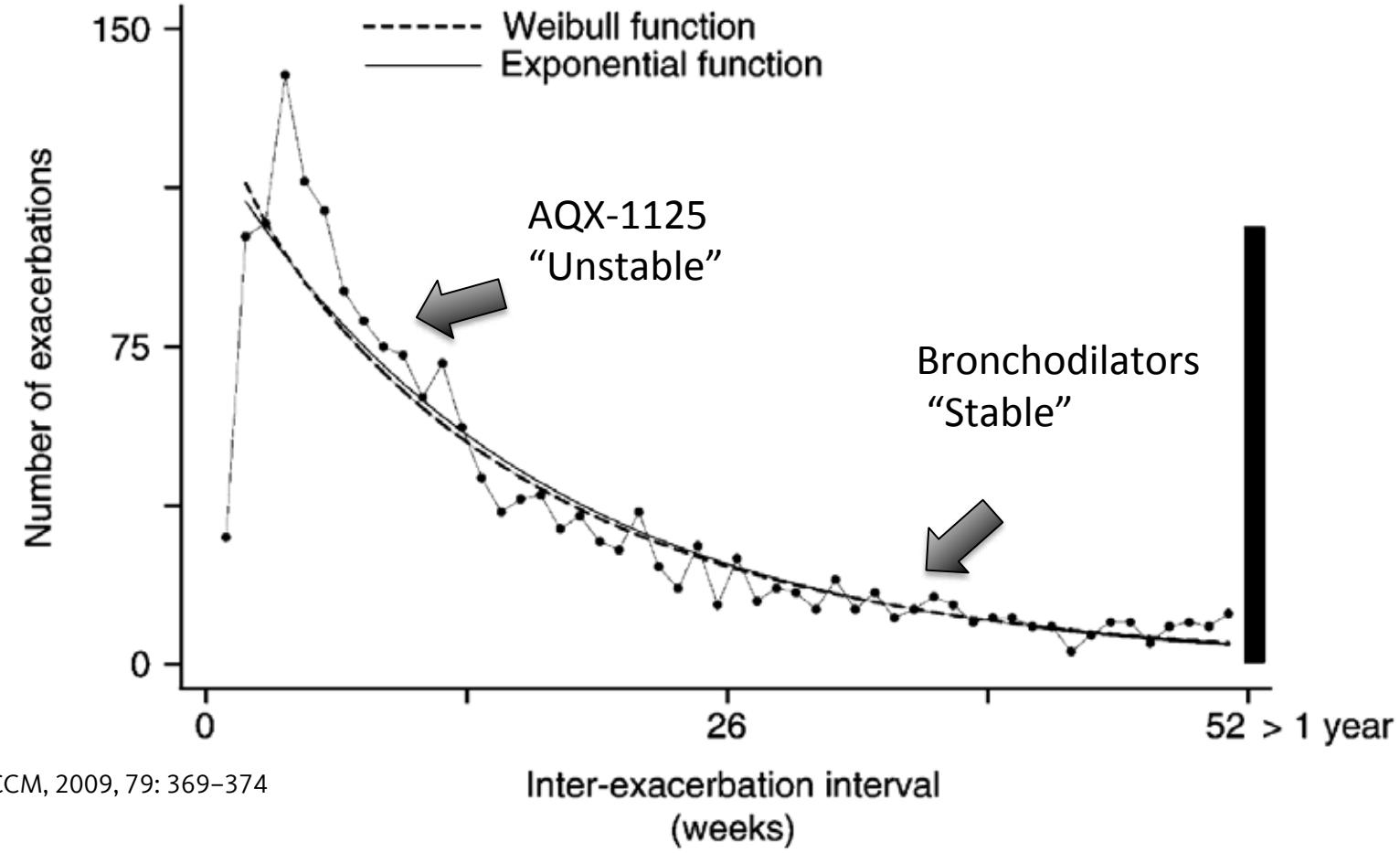
600 million affected and 4th leading cause of death globally

Leading cause of urgent hospitalisations in many countries

Global economic burden >$100 billion

AQX-1125's anti-inflammatory and anti-fibrotic properties in steroid-refractory models provide clear competitive differentiation

COPD: Exacerbations Cause Morbidity and Mortality



Hurst *et al*, AJRCCM, 2009, 79: 369–374

Pioneering AQX FLAGSHIP study in unstable population

FLAGSHIP Study: Summary

Objective: Evaluate effects of AQX-1125 on resolution and exacerbation rates in "at risk" COPD population

- ~350-400 moderate to severe COPD patients

Immediately following (hospitalized), or with (outpatient) COPD exacerbation

- ~30-40 sites in Northern/Central Europe

Estimated completion date: Q4/2014

Highlights

Novel target platform w/ near ideal lead candidate in Phase II

Unencumbered once-daily oral product for blockbuster and niche indications

Strong translation from preclinical to clinical results

Decisive near-term Phase II clinical data: Q4/2014

Focused on under-invested areas; limited competition

Well-protected intellectual property

Large, diverse library of potential backup and next generation compounds

Experienced management and strong investors

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