OPEN INNOVATION PARTNERSHIPS AT ASTRAZENECA:

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Open Access to Drug Discovery - CATS

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Rationale for Open Collaboration

Benefits to external collaborator and AstraZeneca

AstraZeneca

- Compounds
- Facilities
- Drug Discovery Knowledge

External Scientists

- Disease Knowledge
- Patients / subpopulations
- Technology

Questions that otherwise could not be asked
Key Therapy Areas for AstraZeneca

Main therapy areas

- Respiratory/inflammation
- Cardio-Metabolism
- Oncology

Opportunity-Driven

- Infection & Vaccines
- Neuroscience

Personalised healthcare capabilities

- Biologics
- Small molecules
- Immuno-therapies
- Protein engineering
- Devices
Clinical Compound Bank
Access our patient-ready compounds with evidence of human target coverage and manageable tolerability.

Delivered:
• **30** ISS clinical validation studies

Disease indication agnostic

Preclinical Toolbox
Access compounds with optimised pharmacological properties for preclinical research to study pathways and mechanisms of disease biology.

Delivered:
• **150+** projects approved

Primarily in AZ main therapy areas

Target Innovation
Have a novel target idea or assay for a drug discovery project? Our diverse High Throughput Screening (HTS) compound library may help you advance or validate your idea.

Delivered:
• **62** projects on-going/complete

Now aligned to AZ R&D focus areas
AstraZeneca Open Innovation 2

New Molecule Profiling
Explore the properties and therapeutic potential of your novel compounds by leveraging our cheminformatic and screening technologies.

Delivered:
• 30,000 natural product compounds added to AZ’s HTS library

Challenges
Offer and be rewarded for your innovative ideas and research expertise to help overcome difficult R&D barriers.

Delivered:
• 17 challenges run
• 2 collaborations delivered solutions

Data Library
Access preclinical data sets on our early development compounds for data mining and research purposes. to enhance understanding of translation to human efficacy and safety.

Launched June 2017
• Preclinical safety data
• Oncology combinations data
Preclinical Toolbox & Clinical Compound Bank

How does it work?

AZ Open Innovation web portal provides:

- List of available compounds
- Mechanism of action / target class
- Original disease area / indication(s)
- Route of administration
- CNS penetration

AZD5213 is potent (IC50 0.05mM, dissociation half 0.2 h), competitive, rapidly reversible, functional antagonist (inverse agonist) (IC50 of 3nM) at the human H3 receptor. It suppresses H3 receptors with an in vivo pIC50 of 6.8, 6.3 and 6.4 (free concentration in brain) for rat, mouse and NIH, respectively. AZD5213 was tested against a broad panel of 125 other receptors and enzymes at 10μM without significant activity (>100% inhibition) for any. In vivo, it triggers the release of histamine as well as the neurotransmitters acetylcholine, dopamine and noradrenaline in rat prefrontal cortex following dosing at 0.33mg/kg, po and increased tail-methylhistamine in the CSF of syngeneic monkeys at 0.5mg/kg, po. At similar dose levels, AZD5213 has been shown to reverse scopolamine-induced memory deficit, increase novel object recognition, and reverse neuropathy in various rodent models.

Safety and tolerability

AZD5213 has been administered orally to healthy volunteers in single doses up to 50mg and multiple doses up to 15mg QD for 10 days. The most frequent and dose-limiting adverse effects were sleep disorder, night sweats, and decreased appetite as well as quality of sleep. Other common AEs include mild to moderate nausea and headache. Pretreatment studies of up to 6 months duration have been performed.

Clinical pharmacology

AZD5213 was rapidly absorbed (Tmax 0-2.0 h) after oral administration with an overall terminal t1/2 of 6.7 hours. In vivo studies showed a low risk for COXs. PET studies demonstrated saturable, concentration-dependent occupancy of H3 receptors with an estimated K1/2 of 6.14nM. Receptor occupancy ≥50% was achieved at a dose of 0.5mg.

Suitable for and exclusions

Preclinical neurotoxicology data are available and have not identified any specific risk. Women of child-bearing potential using highly effective contraception can be included.

Indications and dosing regimen should consider the potential for and optimization of efficacy while minimizing the mechanism-based adverse effect on sleep. Given the strong association between dose, plasma concentration and brain receptor occupancy as well as the rapid absorption and recovery shortlives, data is available to potentially optimize benefit (delay time, efficacy) versus risk (night time sleep disturbance).
Applications to AZ Open Innovation

Guiding Principles

• Review what we offer
• Submit a non-confidential proposal
• If mutual interest ⇒ discuss further (CDA, MTA)
• If positive results ⇒ AZ option to negotiate license

More details:
• Pre-existing IP remains with original owner
• New IP – ownership framework taking into account the contribution of each party. Generally data belongs to academic partner and AZ only claims compounds developed by AZ
• Publication encouraged

http://openinnovation.astrazeneca.com/
Data Library

- New data library module launched June 2017
- Only pharma company openly sharing large amounts of preclinical data
- Oncology combinations and preclinical safety data currently available; more coming later in 2017
Target Innovation: External Partnership Screening Set

EPEC - a flexible screening set for external partnerships

- Includes compounds of sufficient volume, without current project activity constraints; no ELF set, or AZ patent compounds
- **External screening partners** can access sets of up to 250k compounds in 50k tranches
- AZ also screens this set as part of our HTS strategy
- Allows external screening partners broad coverage of AZ collection’s chemical space

**EPEC COMPOUNDS** (approved for external use)

**LIMITED COMPOUNDS** (Active projects, AZ patents etc)
More screening collections available

**Fragments**
- >17K fragments
- Average 15 heavy atoms
- Average cLogP = 1.3.
- The set can be screened as a whole or as a subset that can be cherry-picked depending on the throughput of the assay technology

**Annotated Phenotypic Library**
- 14K well annotated tool compounds.
- Compounds that have an affinity of < 100 nM on > 1200 human targets.
  - Pre- and clinical candidates
  - Compounds profiled extensively in selectivity panels,
  - Tool compounds
  - Marketed drugs
  - Many compounds not commercially available
- Powerful chem- and bioinformatics methods can be applied to identify a preliminary target list
But most importantly please talk to us:
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