

OPEN INNOVATION PARTNERSHIPS AT ASTRAZENECA:

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Open Access to Drug Discovery - CATS

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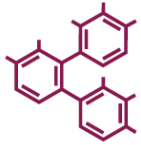
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Advancing research together

Rationale for Open Collaboration

Benefits to external collaborator and AstraZeneca

AstraZeneca



Compounds



Facilities



Drug Discovery Knowledge



External Scientists



Disease Knowledge



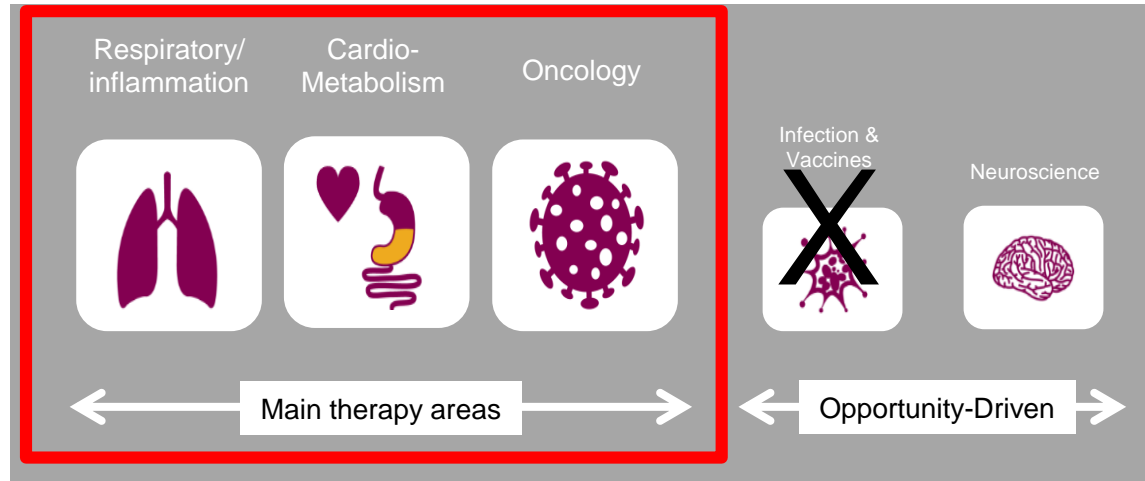
Patients / subpopulations



Technology

**Questions
that
otherwise
could not be
asked**

Key Therapy Areas for AstraZeneca



AstraZeneca Open Innovation 1

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

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Preclinical pharmacology

AZD5213 is potent (Ki 0.5nM; dissociation KB 0.2nM), competitive, rapidly reversible, functional antagonist (inverse agonist; IC₅₀ of 3nM) at the human H3 receptor. It occupies H3 receptors with an in vivo pKi of 8.5, 8.3 and 8.4 (free concentration in brain) for rat, mouse and NHP, respectively. AZD5213 was tested against a broad panel of 335 other receptors and enzymes at 10µM without significant activity (>50% inhibition) for any. *In vivo*, it triggers the release of histamine as well as the neurotransmitters acetylcholine, dopamine and norepinephrine in rat prefrontal cortex following dosing or 0.33mg/kg, po and increased tele-methylhistamine in the CSF of cynomolgus monkeys at 0.1mg/kg, po. At similar dose levels, AZD5213 has been shown to reverse scopolamine-induced memory deficit, increase novel object recognition, and reverse neuropathic in various rodent models.

Safety and tolerability

AZD5213 has been administered orally to healthy volunteers in single doses up to 80mg and multiple doses up to 18mg QD for 10 days. The most frequent and dosing limiting adverse effects were sleep disorder, night sweats, and decreased quantity as well as quality of sleep. Other common AEs include mild to moderate nausea and headache.

Preclinical studies of up to 6 months duration have been performed.

Clinical pharmacology

AZD5213 was rapidly absorbed (T_{max} of 0.7-2.0 hrs) after oral administration with an overall terminal t_{1/2} of 5-7 hours. *In vitro* studies show a low risk for DDIs. PET studies demonstrated saturable, concentration-dependent occupancy of H3 receptors with an estimated Ki,pl of 1.14nM. Receptor occupancy of ~50% was achieved at a dose of 0.1mg.

Suitable for and exclusions

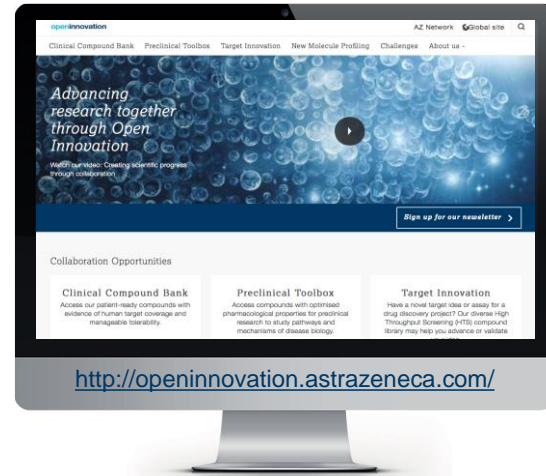
Preclinical reproductive data are available and have not identified any specific risks. Women of child-bearing potential using highly effective contraception can be included.

Indications and dosing regimen should consider the potential for and optimisation 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 relatively short t_{1/2}, data is available to potentially optimise benefit (day 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 \Rightarrow discuss further (CDA, MTA)
- If positive results \Rightarrow AZ option to negotiate license



More details:

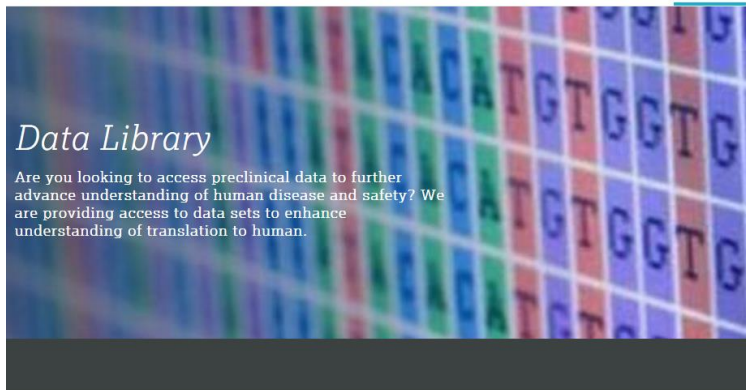
- Pre-existing IP remains with original owner
- New IP – ownership framework taking into account the contribution of each party. Generally data belongs to academic partner and AZ only claims compounds developed by AZ
Publication encouraged

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

New Data Library Module Launched

[Clinical Compound Bank](#) [Preclinical Toolbox](#) [Target Innovation](#) [New Molecule Profiling](#) [Challenges](#) [Data Library](#)



Jump to section

- ☑ [What we offer](#)
- ☑ [Preclinical safety data](#)
- ☑ [Oncology combinations data](#)

We offer access to preclinical data sets on our early development compounds for data mining and research purposes. The aim is to enhance understanding of translation to human efficacy and safety.

Available data sets:

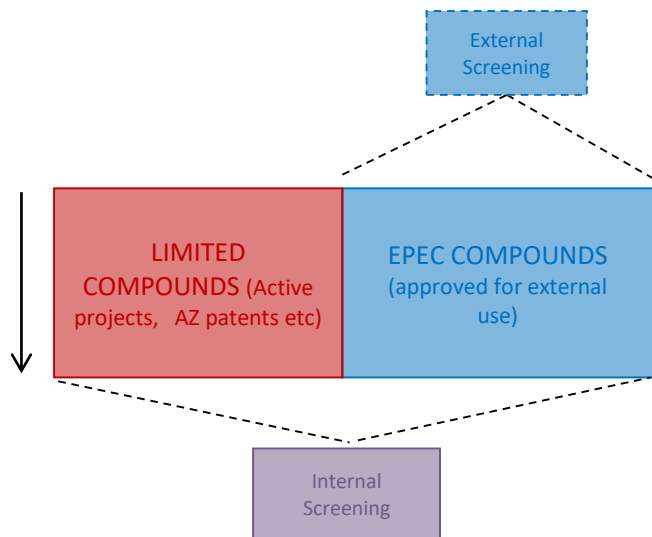
- Preclinical safety data: contains in vivo data in standard models to provide insight into compounds and explore relationships in data to better understand preclinical safety profiles and translation to human safety
- Oncology combinations data: contains 11,000 data points from over 100 oncology drugs tested in combination, for the purpose of assessing and predicting drug combination synergies.

Interested investigators are invited to:

- Learn more about the available data sets through the information on this site
- Submit a brief proposal on how you intend to use the data set
- Access our data once your application has been approved



Target Innovation: External Partnership Screening Set



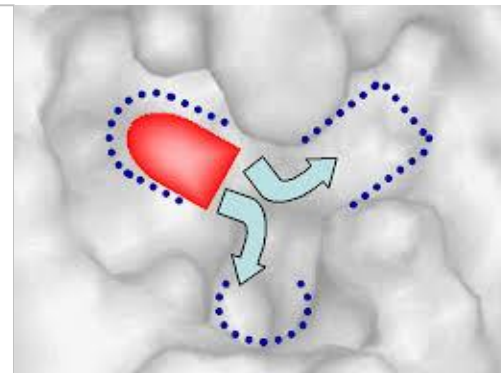
EPEC- a flexible screening set for external partnerships

- 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

More screening collections available

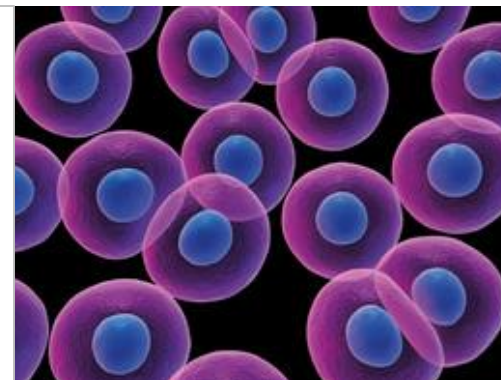
Fragments

- >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



Discover more at
openinnovation.astrazeneca.com

and

<https://www.astrazeneca.com/partnering/externally-sponsored-scientific-research.html>

But most importantly please talk to us:

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