AstraZeneca and Open Innovation

Can no longer work in ‘silos’

Share, discuss and develop ideas in a flexible environment

Create environments that reward innovation, encourage engagement

Build, manage and maintain eco-systems for co-created solutions
# Clinical Pipeline

**February 2013**

<table>
<thead>
<tr>
<th>Pre-Clinical</th>
<th>Phase I</th>
<th>Phase II</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZD9874 / EGFR-CD2</td>
<td>AZD2811 / AUR-NANO</td>
<td>Volitinib</td>
</tr>
<tr>
<td>AZD3759 / EGFR BM</td>
<td>AZD5312 - ISIS - AR</td>
<td>AZD8835 / PI3Kα,δ</td>
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<td>AZD1775 / Wee1</td>
<td>AZD9291 / EGFRm</td>
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<td>AZD2014 / TOR</td>
<td>AZD4547 / FGFR</td>
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<td>AZD5363 / AKT</td>
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</table>

**Projects**

- Pre-Project
- Back-up
- Alliance / BD
- Phase III

**Clinical Candidates**

- Olaparib / PARP
- Selumetinib / MEK
- AZD9874 / EGFR-CD2
- AZD2811 / AUR-NANO
- AZD3759 / EGFR BM
- AZD5312 - ISIS - AR
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- AZD2014 / TOR
- AZD4547 / FGFR
Topics of interest

Translational research on Asian cancers*

- Identification of **driver oncogenic & immune pathways** and effects of pharmacological modulation in **preclinical models**, particularly explants, representative of Asian cancers* (PTEN, Ras-Raf-MEK, FGFR, cMET, EGFR, DNA damage response, and BIM pathways are of particular interest)

- Mechanisms of **innate and acquired resistance to targeted agents** (EGFR inhibition in NSCLC, MEK pathway in lung, FGFR and cMET in GC and LC are of particular interest)

- Understanding key **metabolic pathways and dependencies in Asian cancers*** (HCC, GC would be of particular interest)

- **Molecular profiling of Asian cancers*** including BTC, ECF, sqNSCLC to understand the genetic diversity and key genomic drivers & immunity, angiogenesis and interrelationships

- Understanding the **genetic diversity that develops during disease progression and implications for** therapeutic intervention for GC, NSCLC, BC, BTC.

- **Determinants** of response and resistance to **chemotherapy** in GC and PC.

- **Preclinical models** of premenopausal BC

*Asian Cancers* : cancers such as **BC** (breast cancer), **BTC** (biliary tract cancer), **ECF** (gastroesophageal cancer), **GC** (gastric cancer), **HCC** (hepatocellular carcinoma), **NSCLC** (non-small cell lung cancer), **PC** (pancreatic cancer)
AstraZeneca and Open Innovation portal
openinnovation.astrazeneca.com
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Receptor Tyrosine Kinase signaling

RTK inhibitors:
- CSF1R
- EphB4
- Trk
- FGFR
- AnLK

AZD8931
AZD5582
AZD8055
AZD2014
AZD9291
AZD0530
AZ12823138
AZ12419304
Selumetinib

For discussion only: Do not duplicate or distribute
Cell Cycle Control

AZD5363

DNA Repair

AZD6738

AZD7762

For discussion only: Do not duplicate or distribute

Cell Signaling Technologies
AstraZeneca and Open Innovation portal
openinnovation.astrazeneca.com
# Clinical Table of Compounds

The compounds available for clinical and/or preclinical research proposals are listed below. This table can be filtered to only display those compounds with a specific originating disease area (e.g., oncology), type of proposal invited (e.g., preclinical only), or CNS penetrant (e.g., yes). The header of each column sorts the information in alphabetical order. The compound number is linked to a summary description of the properties, including the preclinical and, if available, clinical experience.

Additional marketed compounds, biologics, and those in late-stage clinical development are offered via the AstraZeneca [Externally Sponsored Scientific Research](https://www.astrazeneca.com/) portal.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Mechanism of Action</th>
<th>Target Class</th>
<th>Originating Disease</th>
<th>Original Indication</th>
<th>Types of Proposals</th>
<th>Route</th>
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<tr>
<td>AZD2014</td>
<td>Mammalian target of rapamycin (mTOR) serine/threonine kinase (dual TORC1 and TORC2) inhibitor</td>
<td>Kinase</td>
<td>Oncology</td>
<td>Solid Tumours</td>
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<tr>
<td>Sotrastaurin (AZD6244; ARBJ)</td>
<td>Mitogen-activated protein kinase kinase (MEK or MAPK/ERK kinase) 4 and 1 inhibitor</td>
<td>Kinase</td>
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**Mechanism of Action:** Epidermal growth factor receptor (EGFR) tyrosine kinase sensitising and T790M resistance mutations inhibitor

AZD9291 is a potent, selective, irreversible inhibitor of both EGFR sensitising and T790M resistance mutations with less activity towards wild-type EGFR. It inhibits phosphorylation of mutant-EGFR and wild-type EGFR in cells in vitro with IC₅₀ potencies < 100nM and 0.5 – 2 µM, respectively. AZD9291 exhibits moderate potency against erbB2: it remains to be determined whether sufficient clinical exposure will be achieved to target erbB2. AZD9291 inhibited proliferation of mutant-EGFR cell lines in vitro with a potency of <50 nM. AZD9291 is highly selective, only significantly inhibiting ~10 other protein kinases when tested across a kinome panel of ~280 protein kinases at 1 µM.

In xenograft studies in vivo, daily oral dosing of AZD9291 causes regression leading to complete and sustained macroscopic response in both sensitising-mutant EGFR model (PC-9) and T790M model (H1975), at low 5 and 25 mg/kg doses. Similarly, such doses lead to significant regression in lung transgenic tumour models of mutant-EGFR. Tumour growth inhibition is associated with significantly reduced phosphorylation of EGFR and downstream signalling markers (e.g., pERK and pAKT).

**Safety and Tolerability**
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### FILTER BY:

- [Oncology](#)
- [Clinical and/or Preclinical](#)
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<td>Sultematinib</td>
<td>Mitogen-activated protein kinase kinase (MEK) or MARK1245 inhibitors</td>
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Welcome to AstraZeneca/MedImmune Externally Sponsored Scientific Research Operations System

Externally Sponsored Scientific Research is designed and managed by a qualified external investigator/researcher, Medical Institution, or Collaborative Research Organization having the legal and regulatory responsibility for the conduct and management of the research.

Types of Externally Sponsored Scientific Research we support:

Investigator Initiated Sponsored Research (IISR)

IISR is independent clinical research involving company products or therapeutic areas of interest. This research is supported by the Company through the provision of drug and/or funding for qualifying clinical studies. IISRs are different from Company sponsored research because the researcher, not AstraZeneca/MedImmune, holds the legal and regulatory accountability for the initiation, design, conduct, and reporting of the research, and the Company is not involved in Sponsor-related activities.

Externally Sponsored Collaborative Research (ESCR)

ESCR is research that typically involves company products currently under investigation (e.g. are not yet marketed commercially) and where the company may have some defined involvement with Sponsor risk and other responsibilities.
To submit a study idea, you will need the following info:

- A current Curriculum Vitae (CV)
- Medical license, if applicable
- Preliminary budget proposal*, (if funding is requested)
- Study hypothesis/rationale
- Objective(s)/endpoint(s)
- Treatment (if applicable)
- Sample size
- Subject eligibility
- Statistical plan

* Please use the budget template in the ESROS Resource Center to expedite the review of your idea.
## AstraZeneca and Open Innovation portal

### Open Innovation Partnerships

Representative examples (not comprehensive)

<table>
<thead>
<tr>
<th>Oncology ISS (Worldwide)</th>
<th>Discovery</th>
<th>Pre-Clinical</th>
<th>Clinical</th>
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<tbody>
<tr>
<td>Selumetinib Thyroid Case Study</td>
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<tr>
<td>Gefitinib Case Study</td>
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<td>MANTA Case Study</td>
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<td>Olaparib and Eribulin in Recurrent/Metastatic Triple Negative Breast Cancer Case Study</td>
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<th>NIH / NCATS (US)</th>
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<tr>
<td>NIH/NCATS partners with AstraZeneca and seven other companies to make 58 discontinued compounds available for this pioneering ‘pilot’ program</td>
<td></td>
<td></td>
<td>3 Projects</td>
</tr>
<tr>
<td><a href="#">Read more</a></td>
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<td><a href="#">NIH/NCATS</a></td>
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### MRC (UK)

Free-of-charge compounds available to UK medical researchers following a landmark agreement with the MRC

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<td>8 Projects</td>
<td>7 Projects</td>
<td></td>
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</table>

**Drug repurposing programs**
AstraZeneca and Open Innovation
Identify new indications for clinical assets

Medical Research Council (UK)
• 22 ‘de-prioritised ‘AstraZeneca compounds
• MRC will provide funding up to £10M
• 106 applications submitted from 37 UK institutions
• 15 proposals funded
  – e.g. zibotentan repositioned from prostate cancer to Alzheimer's disease
AstraZeneca and Open Innovation
Identify new indications for clinical assets

National Center for Advancing Translational Sciences (US)

• Initiated by AstraZeneca and other MNC pharma leveraging 14 ‘de-prioritised’ AstraZeneca compounds (out of total 58)

• Modelled on MRC programme

• NIH/NCATS to fund $20M a year over 3 years

• 9 projects selected (3 AZ compounds)
  e.g. Saracatinib repositioned from oncology into a progressive lung disease (Lymphagioleiomyomatosis)
We seek partnerships spanning all stages of drug discovery and development.
LET'S WORK TOGETHER