



Drug Reposition & Open Innovation Initiatives: potential paths to new therapies and advancing medical science

“Together we can ...”



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Rationale for Drug Repositioning Partnerships

Maximizing the Therapeutic Potential for Optimized Compounds

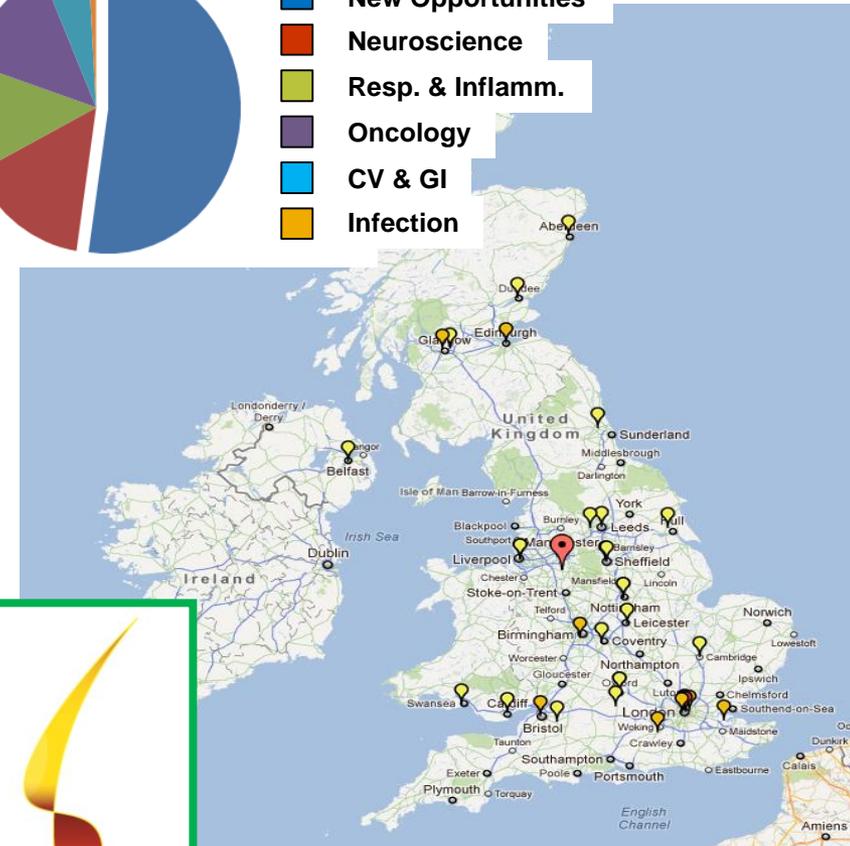
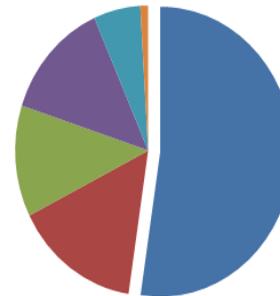
- 'Patient-ready' compounds offered an unique opportunity for clinical and translational research into diseases of significant unsatisfied medical need
- Finite limits in budget, manpower, expert disease insight, and patent-life inhibit pharmaceutical companies from pursuing all, or even perhaps most, of the meritorious indications for these optimized compounds
- Most (>75%) of marketed drugs are approved for indications different from or in addition to those for which they were initially designed ¹
- To combat these limitations and leverage the opportunity, AstraZeneca (AZ) is inviting disease expert physician and basic scientists to partner with each other and AZ to brainstorm, design, and execute preclinical, clinical and/or translational research on optimized AZ compounds
- **We believe medical breakthroughs may await**

¹ Gelijns *et al.* *New Engl J Med* 1998; **339**:693

Case Study #1

MRC – “Mechanisms of Disease” program

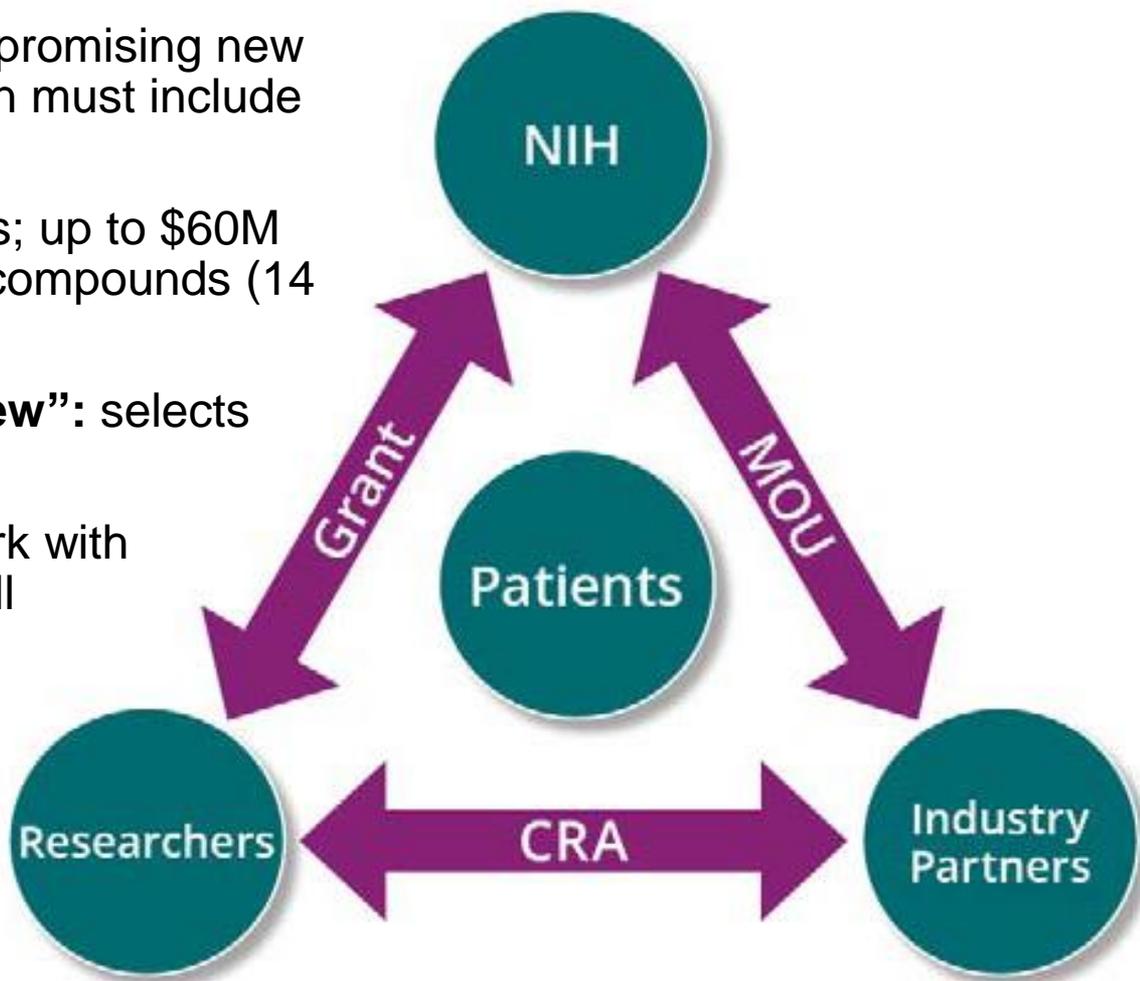
- 22 AstraZeneca compounds
- >100 clinical and pre-clinical proposals from 37 UK institutions
- Proposals submitted on all compounds & across a broad span of disease areas
- MRC funded \$11M over 3 yrs
- 15 collaborative proposals funded across multiple disease areas



Case Study #2

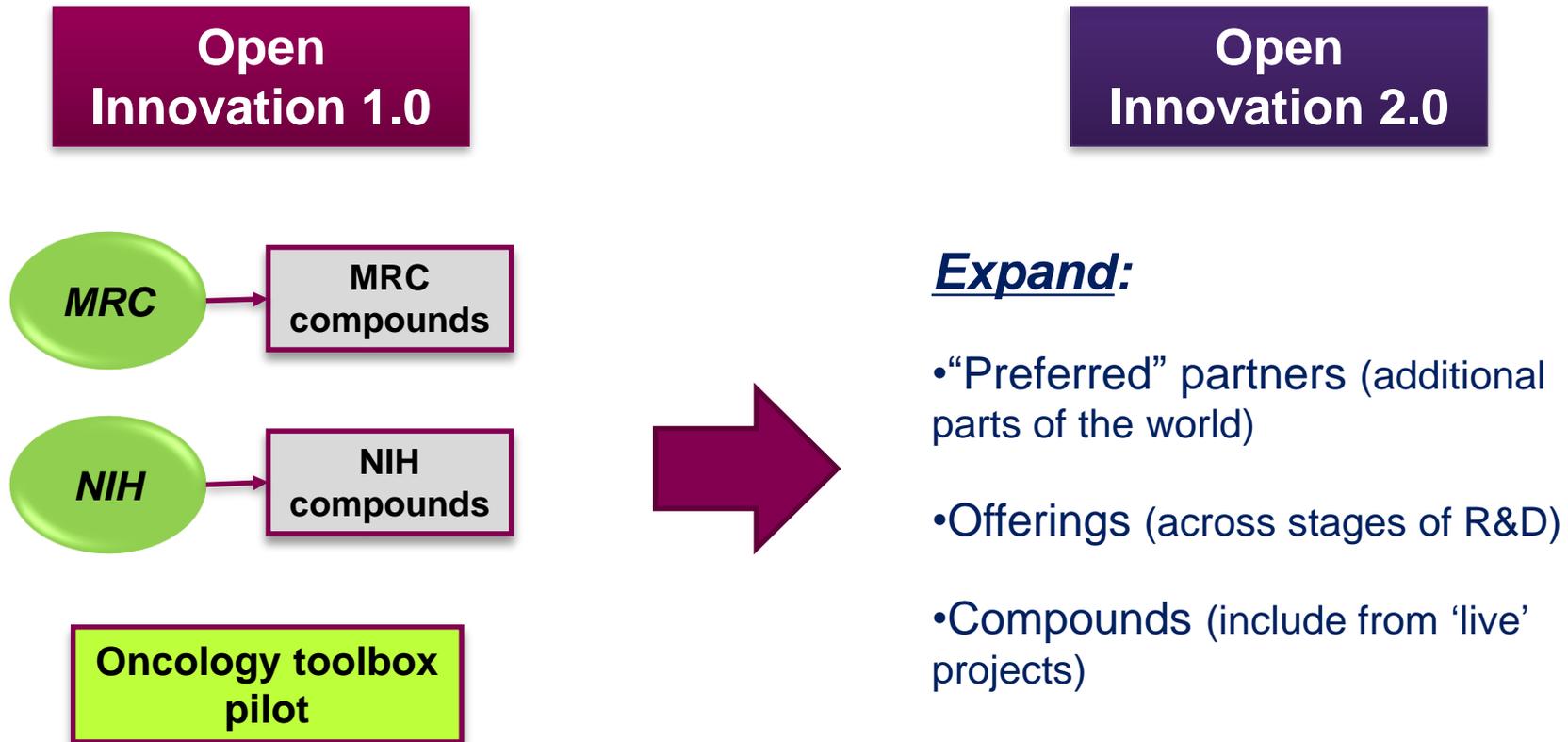
NIH/NCATS – “Discovering New Therapeutic Uses for Existing Molecules” program

- **Ultimate goal** of identifying promising new treatments for patients – plan must include clinical Ph 2 validation
- **Pilot Program:** 8 companies; up to \$60M over 3 yrs; 58 discontinued compounds (14 from AZ)
- **NCATS RFA** → “Peer Review”: selects best “Concept Proposals”
- **Co-create:** investigators work with Pharma Co. to generate “Full Application”
- **NCATS funds** 9 projects; 3 with a AZ compound
- **Additional projects** stimulated by RFA and discussions



Evolution of Open Innovation in AstraZeneca

Building on past experiences / learnings



Cornerstones for Success

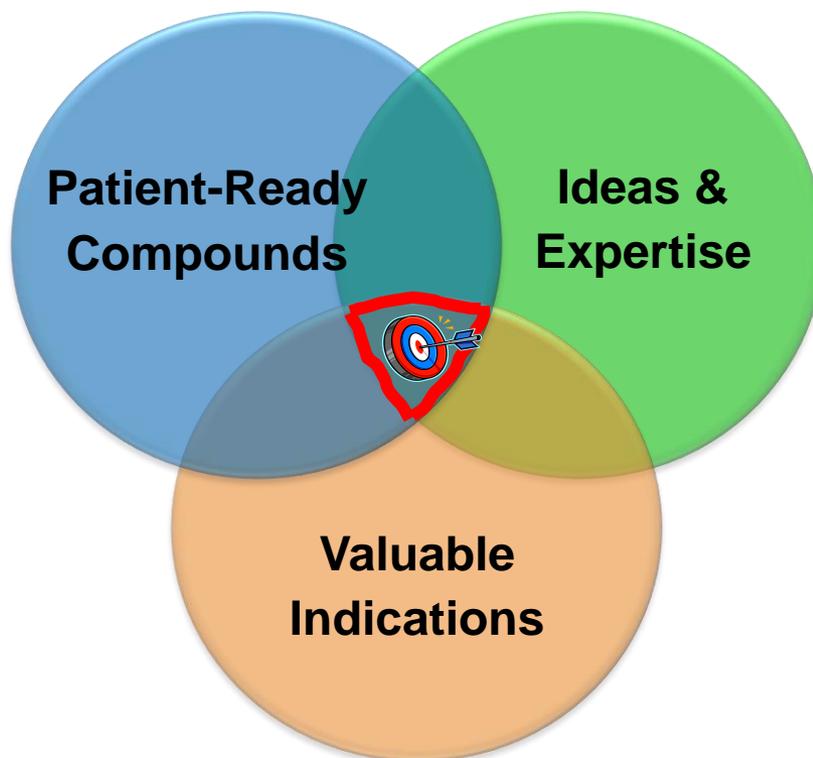
Both parties must open-up and benefit

1. Open Collaboration – Creating Partnerships that Work
 - a. AZ makes first gesture by opening up our Research pipeline and tools
 - b. IP friendly, fair and common/universal Template Agreements
 - c. Invite “*Concept Proposals*” to initiate project discussions → co-author “*Full Project Proposal*” to facilitate ‘courtship’ before ‘marriage’
2. Both Parties Empowered – full flexibility to say No! or accelerate!
3. Resource Efficient – leverage existing tools/skills & public funding
4. Transparent & Effective Engagement (‘dating’) Process

Challenges

Two key hurdles to be scaled

1. Traditions of the past: financial contracts → scientific collaborations
2. Small intersection for quality ideas:



**Select
the Best**

Summary

Together we can ..., but are we willing?

- Unlocking the collective power of industry/academic/public partnership will advance medical science and, consequently, benefit patients
- Open collaboration and a broad outreach are required
- Pioneering partnerships have piloted the path – but most still stuck in the traditions of the past
- **Bold steps are necessary, but parties seem ready**



"Your proposal is innovative. Unfortunately, we won't be able to use it because we've never tried something like that before."

AstraZeneca openinnovation



Mene Pangalos

“At AstraZeneca, we have great scientists doing some really ground-breaking research. However, more than ever, we need to access the very best science wherever it’s happening in order to deliver the next generation of medicines. To make this happen we need to find new ways to break through the barriers that exist to working collaboratively with great scientists in other organisations who share our passion for patients and who can bring different perspectives to our research.”

“Sharing our compound libraries and cheminformatics to support the generation of quality lead series for important and novel drug targets are just part of AstraZeneca’s efforts to link industry and academia, to help advance the discovery of potential new medicines in a broad range of disease areas for patients who desperately need them.”



Mike Snowden



Back-ups

Additional or New Indication Examples

Benefit for Patients Realized Across Therapeutic Areas

VEGF mAb	Cancer → Ophthalmology	Initial Indication: Cancer (Avastin®) Additional Value: AMD (Lucentis)
DOPA decarboxylase carbidopa	CVD → Neurosciences	Initial development: Hypertension True Value: Parkinson's disease (Sinemet®)
PDE5 inhibitor sildenafil	CVD → Endocrinology	Initial development: Angina Additional Value: ED (Viagra®) <u>and</u> PAH (Revatio®)
5α-reductase inh. finasteride	Urology → Dermatology	Initial development: BPH (Proscar®) Additional Value: Male pattern baldness (Propecia®)
NK1 antagonist aprepitant	Psychiatry → Cancer	Initial development: Depression True Value: Nausea and Vomiting (Emend®)
α2δ agonist gabapentin	Neurology → Pain	Initial Indication: Epilepsy (Neurontin®) Additional Value: Neuropathic Pain, Fibromyalgia
TNF mAb etanercept	Critical Care → Rheumatology	Initial Indication: Sepsis Additional Value: RA, Crohn's, Psoriasis (Embrel®)

Why Open Innovation

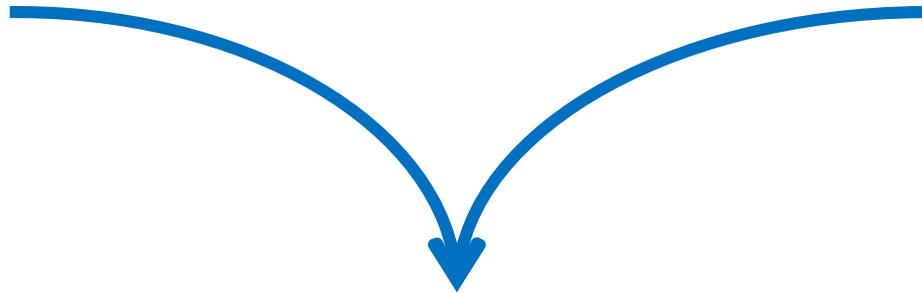
Truly open exchange, debate, collaboration

Basic & Physician-Scientists

have unique insight to patients,
disease, mechanisms and technologies
but
have limited access to novel
patient-ready compounds

Pharma Company Scientists

have state-of-the-art compounds
and drug R&D expertise
but
limited by focus on a single or
small number of indications



Synergy (i.e., $2 + 2 \gg 5$)

if ideas, tools, technology, expertise are shared openly

Patients Health (and advancing medical science) Connect Us