finding the next super STAR medicine!

Trevor Perrior
Britain’s Got Talent!

- Specialising in Translational Research
- The Domainex Platform
- A case study
- The Domainex STAR Award
- Decision-making
Specialists in Translational Research

- Basic Research Knowledge
- Translational Research
- New Health Products
- Commercialisation
- Patients and Clinicians

Drugs

- Successful track-record in Drug Discovery
- Experienced in research funding
- Strong scientific background
- Wide-ranging disease know-how
- Good platform technology fit
- Flexible and collaborative
- Extensive academic networks

- Founded in 2001
- Based on Cambridge Science Park
- About 40 staff
Full integration of drug discovery sciences

- Protein Science
- Structural Biology
- Medicinal Chemistry
- Cell biology and Pharmacology
- Compound optimisation
- Candidate selection
- Hit finding
- Biochemistry and Biophysics
- DMPK
Excellence in drug discovery

**Laurence Pearl laboratory**

**LeadBuilder**
- Virtual and fragment screening

**Ruthless Design**
- ‘Every compound counts’

**Protein Science**

**Structural Biology**

**Medicinal Chemistry**

**Compound optimisation**

**Candidate selection**

**Cell biology and Pharmacology**

**DMPK**

**Biochemistry and Biophysics**

**Combinatorial Domain Hunting**
- rapid expression of difficult proteins

**In collaboration with**

pharmidex
A case study
Tankyrase inhibitors for treatment of cancer

Tankyrase:
- Member of PARP family - a novel target involved in:
  - Wnt signalling
  - Regulation of telomere length

Clinical setting:
- Oral administration
- Wnt-dependent tumours, e.g. colorectal carcinoma
- Triple-negative breast cancer

£3.9m SDDI grant

Drug discovery know-how

Alan Ashworth and Chris Lord
Tankyrase project evolution

Domainex
*LeadBuilder*
Virtual screen against homology model

Several hit series
1-10μM

Potent inhibitors with excellent cell activity

Enzyme: <10nM potency
Cell: Low nM suppression of Wnt signalling

Candidate drug nominated, follow-on programme

Hit to candidate:
<400 compounds
Whole programme:
4-5 medchem FTE < 3 yrs

Riffell *et al*, NRDD, 2012, 11, 923
STAR Award: Supporting Translational Academic Research

Bridging the **first** Valley of Death...

**Domainex STAR award**

- Drug discovery advice
- Virtual screening
- Medicinal Chemistry strategy

First awardee: Prof Vilmos Fulip (Univ of Warwick)
“*A new treatment for Chagas Disease – a life-threatening tropical disease*”

Next call for applications: **September 2014**
Decision-making in Translational Research

Exploitation

Execution
- Capitalise on the project strengths
- Identify the key problems...
  ... and solve them!

Identify funding
- University PoC Funds, Domainex STAR Award
- Wellcome Trust, MRC, Technology Strategy Board

Select projects
- Medical need/commercial opportunity
- Target validation
- Scientific tractability

Build networks
- Academic partnerships
- Complementary technologies

Establish a powerful technology platform
- Combinatorial Domain Hunting
- LeadBuilder
- Ruthless Chemistry
Conclusion

- Integrated drug discovery
- Highly-innovative and scientifically-driven
- Full service solution
- Efficient
  "Every compound counts"
- Effective
  Superb track-record in Translational Drug Discovery

Ideal fit of platform technologies

Fast and flexible