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Background

- Incorporated December 2013
  - University of Nottingham spin-out
  - IP from Universities of Nottingham/Bristol/UNSW
  - Closed Seed Round £400,000
- Drug discovery and development company
  - Novel approach to a validated target
  - Alternative splicing of VEGF
  - Lead programme is in ophthalmology
- Flexible capital sparing business model
  - Asset centric investment
  - Academic collaborations
  - Outsource toxicology and manufacture
  - Low cost ophthalmology clinical trail for POC

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Team

- Dr Catherine Beech
  - Chief Executive Officer
- Prof David Bates
  - Chief Scientific Officer
  - Professor of Oncology and Head of Cancer Biology, Division of Oncology at the University of Nottingham
- Prof Steven Harper
  - Consultant Nephrologist
- Dr Lucy Donaldson
  - Associate Professor in the School of Life Sciences
- Dr Jonathan Morris
  - Associate Professor at UNSW (Chemistry)

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“Lean” business model

- Academic Collaborations:
  - Universities of
    - Nottingham
    - New South Wales – medicinal chemistry
- Outsource to CROs when appropriate
  - Chemistry analysis
  - Pre-clinical programme
  - Clinical development

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SPHINX – first in a new class of drug

- VEGF is a validated target
  - well understood by physicians
  - however, novel mechanism of action predicts low side effect profile
- Small molecules not proteins
  - eye drops versus injections –patient preference
  - high penetration into eye
  - non-expensive to manufacture/distribute
- Potential improvement in % visual acuity
- Possible prophylactic use

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Science

- Vascular Endothelial Growth Factor (VEGF)
  - Validated therapeutic target for angiogenesis
  - Targets in AMD, oncology, kidney disease, and pain.
- Exonate –patented novel approach to anti-angiogenesis
  - Switching splicing of VEGF mRNA
  - Alters the process of disease progression
    - From VEGF-A_{165}a - drives angiogenesis
    - To VEGF-A_{165}b - potently anti-angiogenic
  - Development programmes of small molecules
    - May halt blindness using eye drops in wAMD

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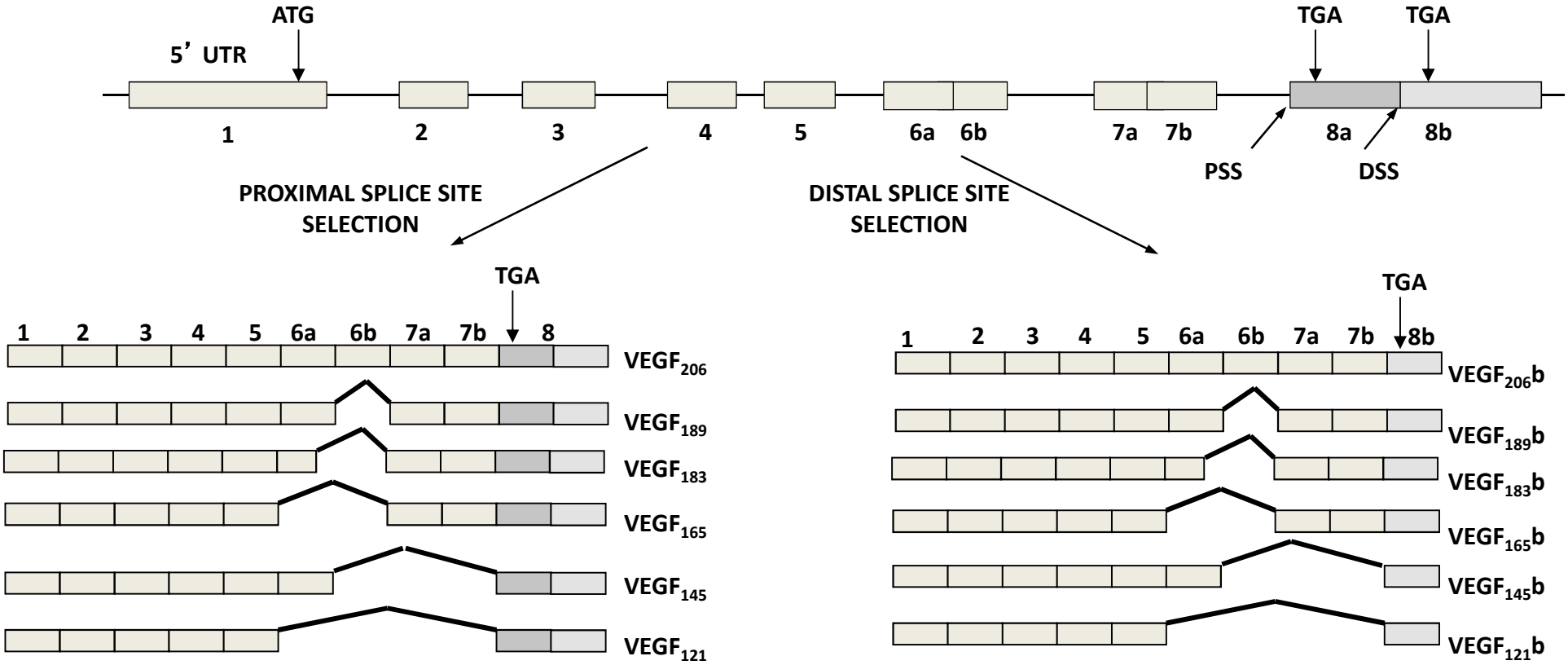
VEGF gene structure and splicing



Proximal Splice Site - $VEGF_{xxx}$
Angiogenic
(Discovered UCSF/Genentech, Harvard 1989)

Distal Splice Site - $VEGF_{xxx}b$
(Discovered by Exonate founders in 2001)

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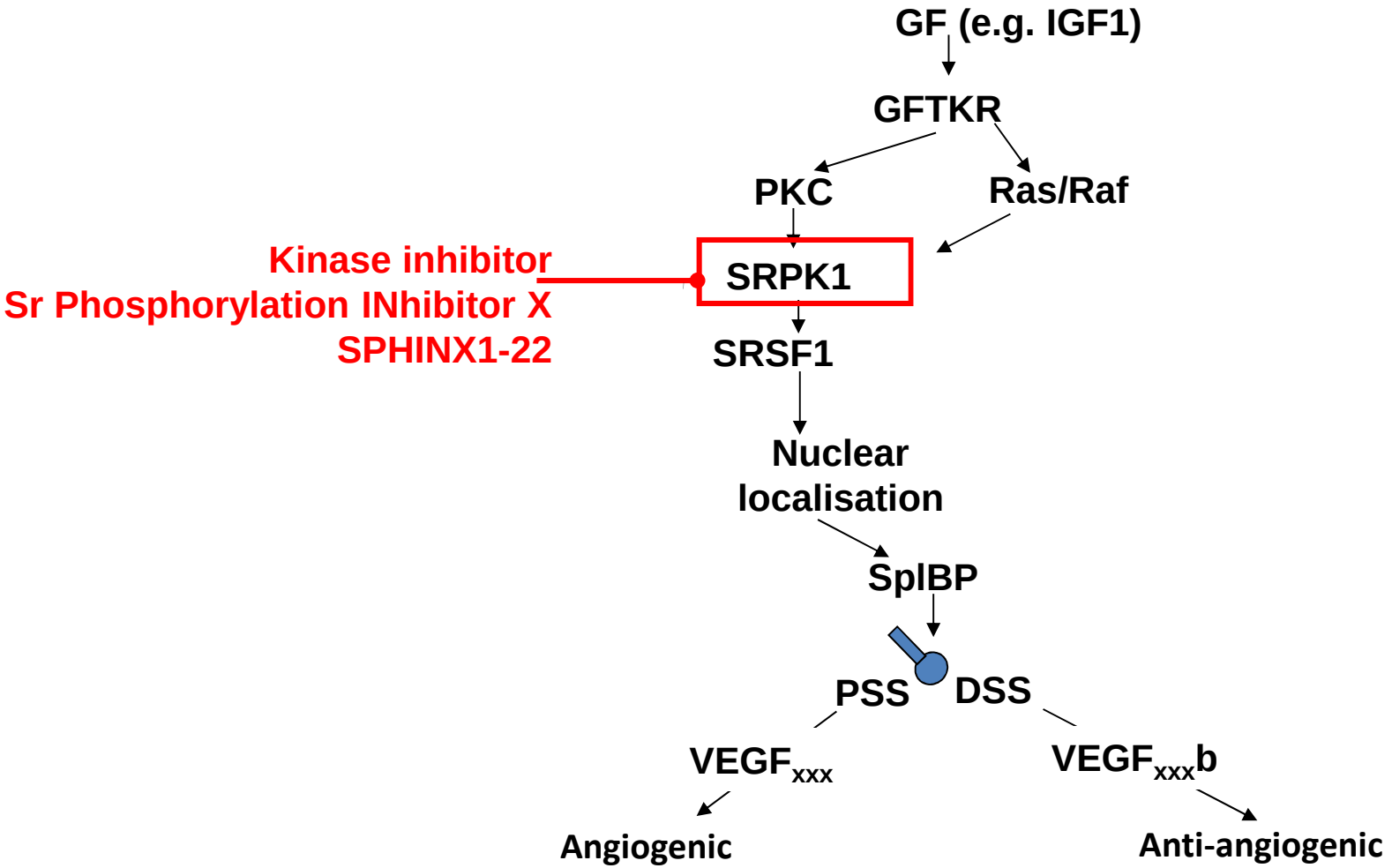
Multiple targets to hit VEGF splicing



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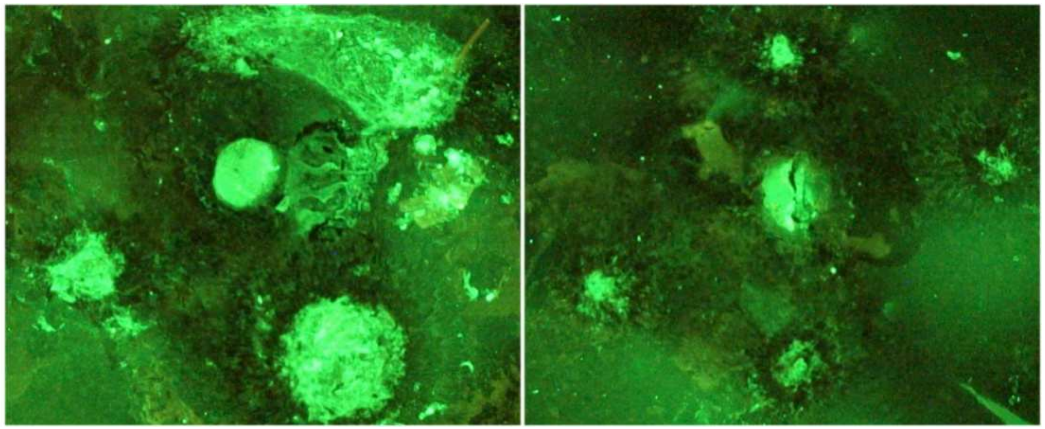
CNV mouse model

Untreated

SPHINX7 eyedrops



Replaces injections into the eye
Keeps retinal cells protected

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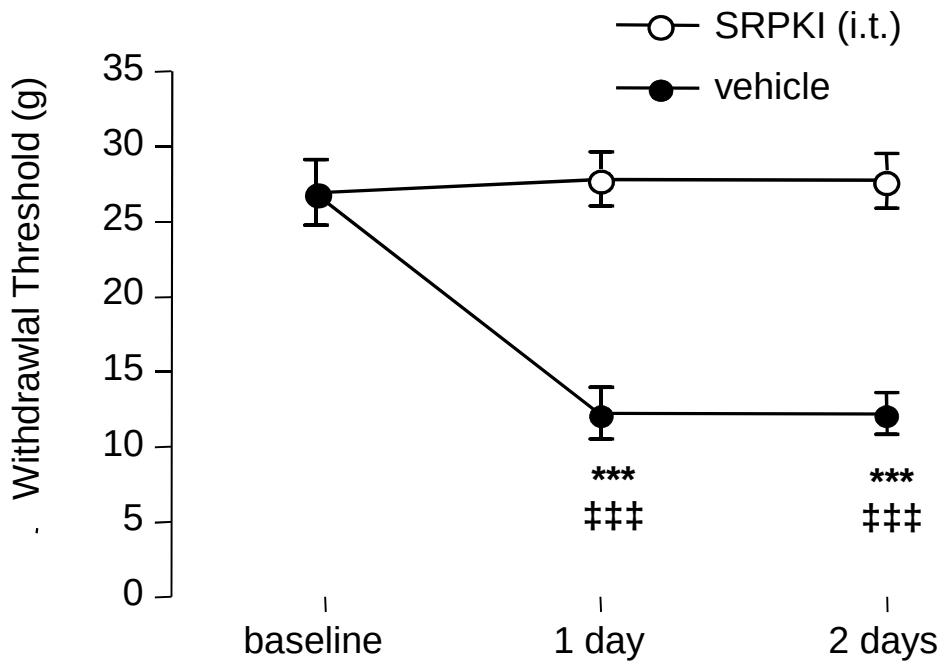
Pain



Chronic pain model (Donaldson labs)

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Scientific objectives

- **2014**
  - Nominate lead compound
  - Plan lead optimisation and pre-clinical programme
- **2015**
  - Start pre-clinical ophthalmology programme
  - Plan clinical development programme
  - Evaluate further therapeutic indications under pipeline agreement
  - Seek pharmaceutical partner
- **2016**
  - Apply for IND
  - Build a successful drug discovery company with several programmes

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Competition in w AMD

- Only anti-VEGF therapies available at present
  - Generate global sales in excess of $4.7 billion
  - Stabilize sight in more than 90% of patients -10% fail
  - Only improve vision in 30-40% of patients
- Therefore a need for new drugs
  - At least 43 drugs being actively developed for wet AMD
- Approaches taken
  - Novel mechanism of action
    - Platelet-derived growth factor (PDGF) inhibiters
    - VEGF/PDGF combinations
  - Improved delivery methods
    - Better PK profile of existing drugs
    - Reformulate VEGF inhibitors as eye drops

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Business development

- Seeking early partnership deals
  - Post phase IIa in ophthalmology
  - During preclinical development for other programme
- Structure - Usual for industry
  - Up-front payments
  - Milestone payments
  - Royalty payments
- Discussions around ophthalmic opportunity starting

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IP position

- Strong IP position
  - Originated at Bristol/UNSW - assigned via UoN
  - Portfolio of 6 patents (2 granted)
  - Covers platform for VEGF isoforms
  - Composition of matter on SPHINX molecules (2013)
  - Composition of matter on SPHINX molecules (2014)

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A Nottingham University Spin-out