Vision Meets Reality

Enterprise Tuesday
19 February 2013

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CEO @ Bicycle Therapeutics

Who am I?

- MD, Internal Medicine and Critical Care Medicine
- PhD, Physical Chemistry
- Executive Development Program at Wharton Business School
- Clinical Research @ Hoechst ➔ Aventis ➔ Sanofi
- Head of global Clinical R&D @ Aventis Behring ➔ CSL
- VP General Manager Business Unit Critical Care @ Aventis Behring
- CEO and COO @ Affimed
- CEO @ Bicycle Therapeutics

From „Vision“ to „Reality“

- Vision
- Strategy
- Implementation
  - Building the Team
  - Funding and Financing
  - The seed phase: Optimising Technology Platform
  - Building the portfolio and business
- Long term perspective/Exit

Vision

"If you want to build a ship, don't drum up people to collect wood and don't assign them tasks and work, but rather teach them to long for the endless immensity of the sea."
(Antoine de Saint Exupéry)

- What you want the organization to be; your dream. What would the company look like in three, five, seven years?
- If you have a clear vision, you will eventually attract the right strategy. If you don't, no strategy will save you.

  ➔*No strategy without vision*

- If the vision is not compelling, you won't have the motivation to stay the course and you won't be able to recruit others to help you.

My Vision of Bicycle

Bicycle to become the most respected innovative biopharmaceutical company to provide new therapies to patients in indications with high unmet medical need where previous approaches have failed.

Bicycles Business Strategy

"A goal without a plan is just a wish."
(Antoine de Saint Exupéry)

- Realise the full potential of the *Bicycle* technology through:
  - Development of an internal pipeline of *Bicycle* drug candidates
  - Collaborative R&D partnerships to explore the technology in additional areas
- Achieve this by:
  - Developing 2-3 internal programmes through to early clinical proof-of-concept
  - Working with collaboration partners to identify *Bicycle* molecules against drug targets of mutual interest

Implementation - The *Bicycle* Team

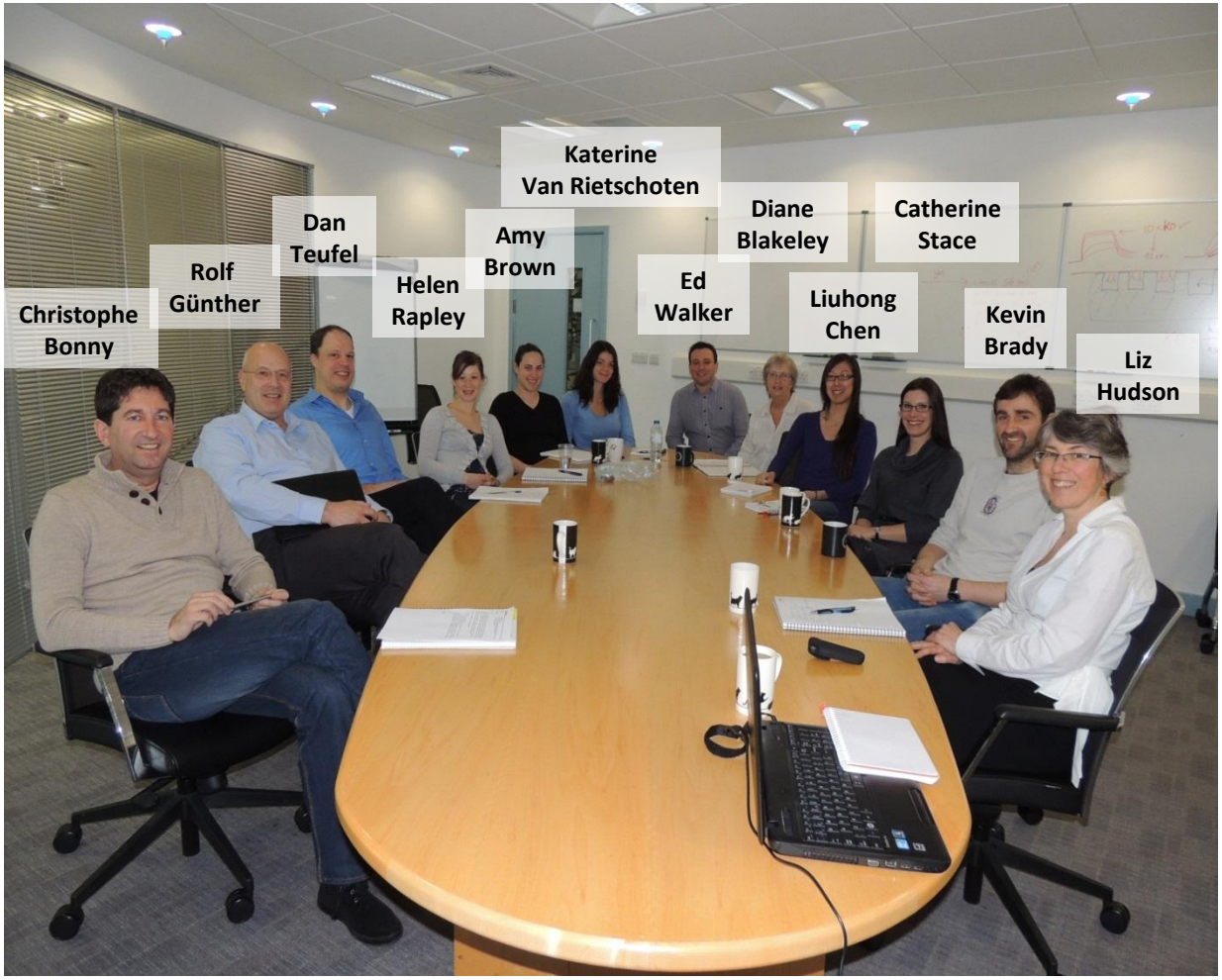
- Founders:
  - Sir Greg Winter (MRC), founder of CAT and Domantis
  - Prof. Christian Heinis (EPFL)

- Directors and Management Team
  - *Chairman:* Andy Sandham (Experienced biotech CEO/Chairman; currently CEO Kymab; previously venture partner at Abingworth)
  - *CEO:* Rolf Günther (Affimed, Aventis-Behring, Hoechst)
  - *CSO:* Christophe Bonny, PhD (Xigen, University of Lausanne)
  - *BD*: Jonathan Savidge, PhD (Evotec, UCL, Novartis)

- Scientific team of 12 in total

The pessimist sees difficulty in every opportunity. The optimist sees the opportunity in every difficulty.“ (Winston Churchill)

Thanks to the team:



Also Jonathan Savidge (BD), Theresa Lander and Andrew Muncey (Finance)

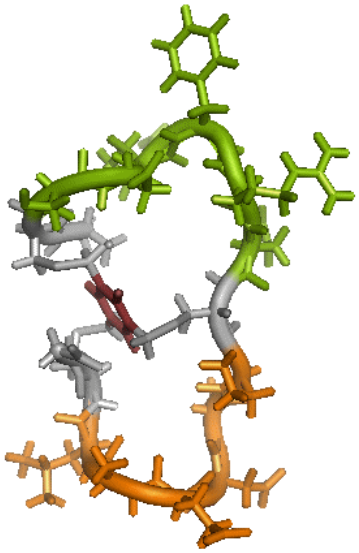
Implementation - Bicycle's Investors

- Top tier investors
  - Astellas Venture Fund
  - Atlas Venture
  - Novartis Venture Fund
  - SR·one
  - SVLS
- Seed financing £7.7M, series A planned 2014

Implementation - Confirmation of Key Features

"However beautiful the strategy, you should occasionally look at the results."
(Winston Churchill)

- ✓ High throughput selection of lead molecules (typically < 2 months)
- ✓ Successful generation of Bicycles against >20 targets in different target classes
- ✓ Affinities in low to sub-nanomolar range and very high selectivity similar to antibodies
- ✓ New properties through chemical modification and addition of functional groups via linkers without affecting affinity
- ✓ Creation of bi-functional molecules through conjugation of two *Bicycle* molecules with different specificities



Implementation - From Features to Applications

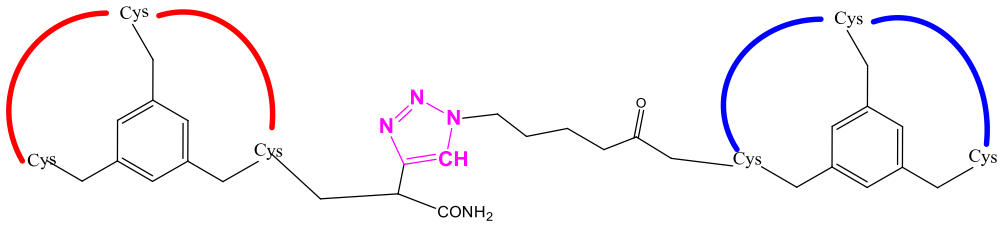
- Highly constrained bicyclic peptides
  - ➔ high affinity binding and high selectivity
  - ➔ potential to address targets not easily tractable with small molecules e.g PPIs
- Small size
  - ➔ potential for good tissue distribution and options of different formulations for various routes of administation
  - ➔ possibility for topical and pulmonary routes of delivery and slow release formulations (subcutaneous, ophthalmic)
- Ease of chemical modification without affecting target binding
  - ➔ Modulation of pharmacokinetic properties
  - ➔ Chemical conjugation with payloads (radionuclides, cytotoxic drugs)
  - ➔ Conjugation of two *Bicycle* molecules to produce a single bi-specific molecule

Bicycle is exploring applications where the features of Bicycle molecules provide differentiation from other modalities

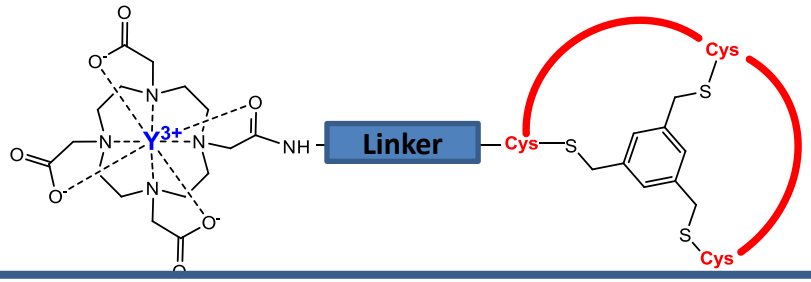
Translation into Products

Extension of half life by conjugation with albumin binders

Generation of bi-specific molecules by joining two *Bicycles*

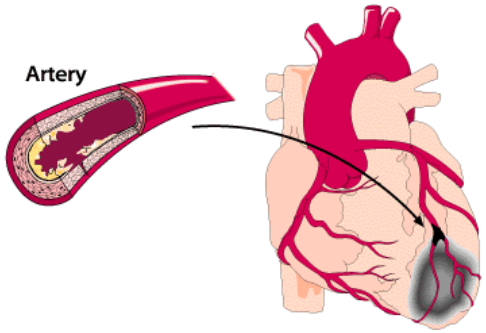
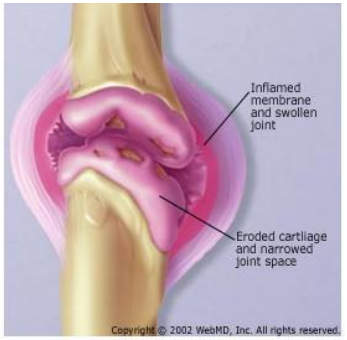


Conjugation with radionuclide chelators or cytotoxic drugs with a cleavable linker



Optimising Drug Like Properties

- Multiple formats to tune drug for disease setting
- Tune bicycle PK through chemical modifications

Disease: Myocardial Infarction	Diabetes	Rheumatoid Arthritis
		
Management: Acute	Daily	Chronic
None – ‘Simple’ bicycles for acute settings	Binding to Albumin - Once daily administration	Slow release formulations

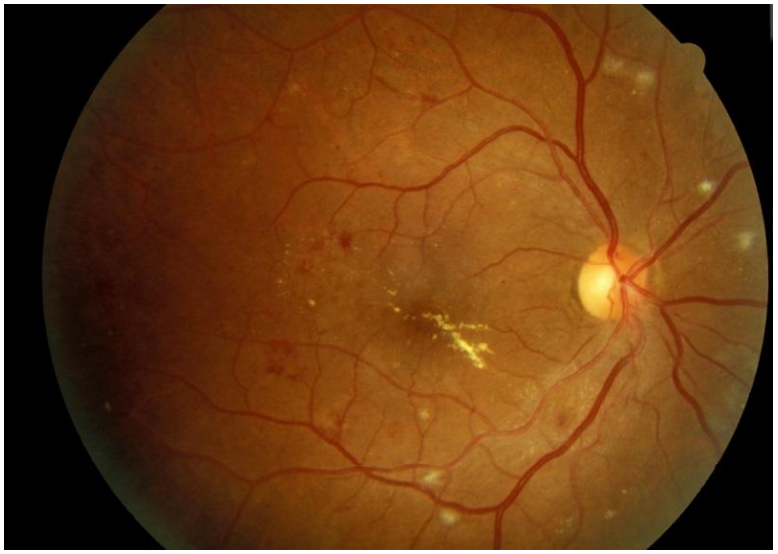
Building the Portfolio and the Business

"We are continually faced by great opportunities brilliantly disguised as insoluble problems." (Lee Iacocca)

- First look at the opportunities, then
- Balance opportunities versus risks
- Proactively manage risks
  „Good managers manage risks, poor managers manage problems"
- Manage expectations
- Implement business develoment and partnering strategies
- Accept (initial) resistance and setbacks, your time will come, it is your vision....

Diabetic Macular Oedema (DMO)

- 2,342,951*people with diabetes in the UK in 2010
- 166,325 (7.12%) had DMO in one or both eyes
- 64,725 clinically significant DMO
- £116,296,038 overall health and social care costs*
- Treatment options:
  - Prevention - Management of Diabetes
  - Laser photocoagulation
  - Vitrectomy
  - Anti-VEGF treatment; monthly intravitreal injections
- Success rate <50%
- New pathologic pathway: Kallikrein
- Development of bispecific Bicycle targeting Kallikrein with 70pM potency and VEGF
- Slow release formulation intreavitreal injections ever 6 months

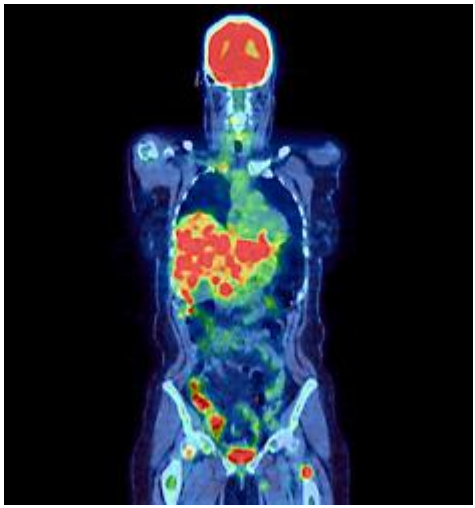


* Br J Ophthalmol. 2012 Mar;96(3):345-9. Epub 2011 May 20.

Radioimmunotherapy in Oncology

- Bicycle with short half-life for in-vivo diagnostics
  - High penetration due to small size
  - High retention due to high affinity to tumour tissue
  - Low background due to fast clearance (increased tumour/blood ratio)

  ➔ Superior tumour imaging anticipated



- Bicycle with longer half-life for therapy
  - Enhanced tissue penetration anticipated due to small molecular size
  - Lower toxicity anticipated due to faster clearance versus radio-labelled antibodies

  ➔ Superior efficacy and safety

Long Term Perspective/Exit

- Become „Apple“ or „Genentech“ (very tough)
- Build profitable, long term sustainable business (difficult)
- IPO (currently difficult)
- Trade sale
- Failure

“It is hard to fail, but it is worse never to have tried to succeed.“
(Theodore Roosevelt)

Thank you!

Questions?