



**Out-licensing:
A Start-up Company
Perspective**

EuroBio in Lille, France

Sept 24 2009

Carina Schmidt, CEO



A world-class atherosclerosis R&D company, part of Karolinska Development portfolio.

- **Spin-off from Karolinska Institutet**
 - Founded by Professors Johan Frostegård and Ulf de Faire
- **Financed by:**
 - Karolinska Development (public)
 - Baltic Sea Foundation
 - Nutek, ALMI and private investors
- **Key Assets**
 - Access to world class atherosclerosis research
 - Unique access through partnerships to clinical cohorts (10.000+ patients)
 - Strong IP
- **CVDIMMUNE** – highly ranked EU project
 - EU grant of 25 MSEK involving 10 partners
- **Organization**
 - 10 people
 - Pharmaceutical R&D, Business, Test development, Clinical Marketing, Project Management, Quality, Chemistry
- **Partners**
 - Co-development of PC-mAb with Dyax Corp., USA
 - CMC/development and manufacturing of Annexin A5 at Richter-Helm GmbH; Germany
 - Biomarker kit manufacturing at Phadia GmbH; Germany
 - Biomarker kit distributors in UK, Germany and NA.
 - In vivo studies at TNO; The Netherlands
 - In vitro studies at IVS; France

Athera products in Acute Coronary Syndrome (ACS)

Three approaches to treatment and prevention of cardiovascular disease:

- First-in-class biopharmaceuticals targeting Acute Coronary Syndromes (ACS):
 - Annexin A5 – a recombinant protein product to prevent inflammation and new thrombosis.
 - PC-mAb – a monoclonal antibody product to prevent secondary cardiovascular events.
- Biomarker linked to atherosclerosis and ACS:
 - CVDefine® - a CE-marked ELISA kit for detecting IgM antibodies against PC – anti-PC.
 - To select healthy individuals for more active prevention treatment.
 - To select high-risk patients for ACS treatment.

Exit Horizon

Annexin A5

CMC/Development and production
Pharmacology
Interaction

Tox. studies

Phase I

Phase II

Trade Sale/
Licensing

2009

2010

2011

2012

PCmAb

Production In vivo
studies

CD nomination
IND Tox

IND Phase I

Phase II

Trade Sale/
Licensing

2009

2010

2011

2012

Trade Sale or Licensing of Annexin A5 and PC-mAb separately or together

Out-licensing – Preparing the process

- 1) Presenting the case: Carefully carve out a clear positioning that meets medical and industry needs
- 2) Present information on several levels: Non-confidential vs. confidential, teaser and executive briefs vs. complete reports and data documentation
- 3) Team: Champions on both side, back-ups
- 4) Add key competences: Legal, 3rd party opinions on science and IP
- 5) DD process: E-room, prepare possible interviews (inventors, collaborators)
- 6) Key events and time-line: Term sheets to identify issues before agreement!
At critical points - Meet face-to-face with goal to agree
- 7) Communication: Set clear goals, but be flexible! Transparency!

Why Develop New Therapy for Treatment in ACS?

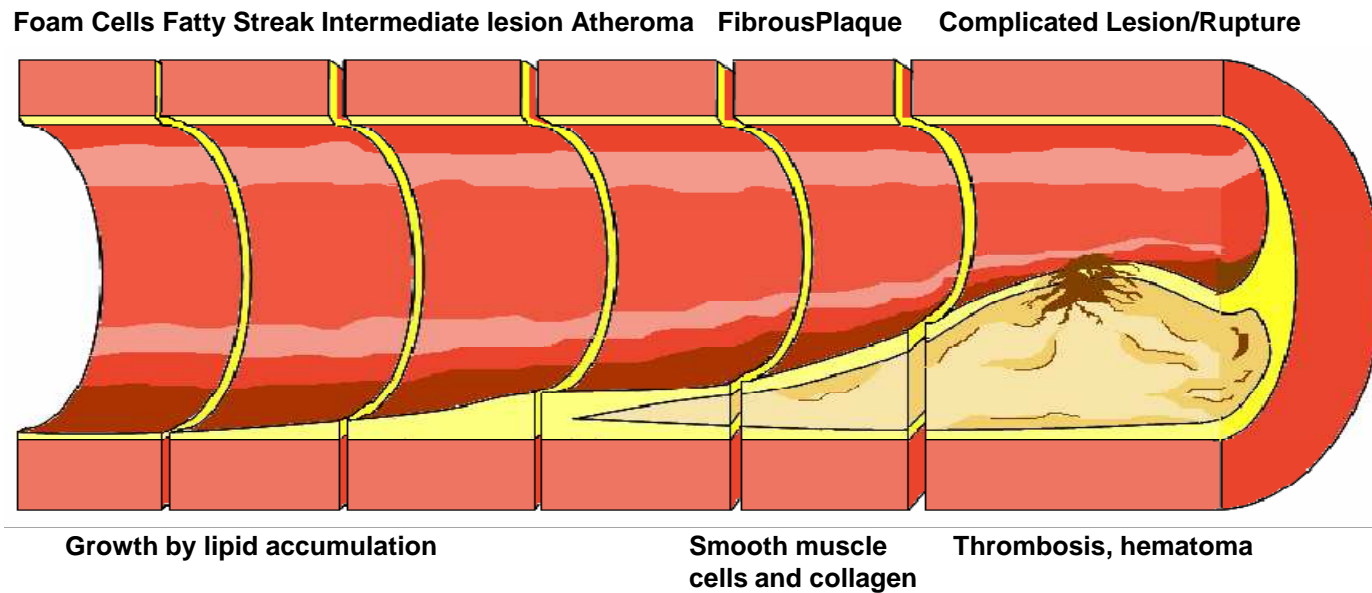
- ACS (Angina and Myocardial Infarction) and stroke is the #1 killer in the world
- ACS incidence approximately 3.6 million in US and 2.2 million in Europe
(Business Insights, 2005)
- ACS is caused by atherosclerosis i.e. plaque formation in intima.

Atherosclerosis is an inflammatory disease.

There are no marketed drugs against ACS targeting inflammation.

**ACS is caused by atherosclerosis
i.e. plaque formation in intima.**

Pathogenesis of a plaque leading to rupture



(Data Monitor, DMHC 2347, 12/2007)

Athera Biotechnologies – Partnering Highlights

- Large unmet medical need –
Cardiovascular disease No 1 killer
- Atherosclerosis related disease and inflammatory targets is number 1 priority for the pharma industry
- Athera's know-how on novel immunological mechanisms opens new treatment approaches
- Direct link between treatment and relevant biomarkers
- Solid scientific concept with strong IP
- Experienced management, experts and advisors
- Access to well characterized clinical cohorts



Out-licensing – Preparing the process



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Out-licensing – Partner selection

- 1) Pipe-line gap:
Unmet medical need: A hygiene factor
Industry needs: Clinical situation, molecule, administration, duration
Stage of development
- 2) Technology
- 3) Complementing competences
- 4) Resources
- 5) Market access
- 6) Authority access
- 7) Access!

Dyax Corp – Partner for co-development of PC-mAb



Develops novel biotherapeutics - inflammatory and oncology focus.
Listed on NASDAQ, market cap. close to \$ 300 million and 164 FTEs.

= Match in therapeutics focus

DX-88 and pipeline compounds are identified using patented phage display technology.

Over 70 revenue generating licenses and collaborations.

Status in August 2009: 1 approved product and 15 clinical-stage candidates.

= Match in technology

= Active and collaboration driven team

Lead candidate DX-88 (ecallantide, a recombinant small protein) is being evaluated in two indications (HAE and on-pump heart surgery).

= Complementing competences

Access

Out-licensing – The Options

Agreement alternatives :

- 1) Co-development partnerships
- 2) Licensing of projects: Target, pre-clinical or clinical stages (Phase IIa)
- 3) Contract research
- 4) Technology licensing
- 5) Mergers and acquisitions

Out-licensing – Validating deals in CVD

BI-204 (now also RG 7418)

Monoclonal antibody against oxLDL (apoB100) for prevention of CVD – potential for secondary prevention in high-risk patients

Phase I study (May 2009) showed that BI-204 is safe and well tolerated. Decision to start Phase II studies expected shortly.

Agreement Jan 2007 between Bioinvent and Genentech to develop and commercialize BI-204 (at pre-clinical stage at the time) in North America. Upfront \$ 15 million, plus milestone fees \$ 175 million and double digit royalty (NA).

Agreement for world-wide rights outside NA expected to time with start of Phase II. Expected to have a higher value, est. upfront \$ 30-50 million, plus milestone fees \$ 300-500 million and double digit royalties.

Out-licensing – The timing

Dilemma of maximizing value and securing resources to move forward:

- 1) Target or discovery stage licensing increasingly difficult and values are low
- 2) Pre-clinical stages possible, but extremely data driven
Pharmacology and Tox desired
- 3) Proof-of-concept studies in man (Phase IIa) common request
- 4) Beyond Phase IIa: Few biotech's manage the transition

Prepare and initiate process early – even “simple” agreements take time!

From start-up biotech to integrated pharma

Millennium Pharmaceuticals - Founded in 1993

Early years: Genome mapping science and target discovery.

Created more than 20 strategic alliances with leading pharmaceutical and biotechnology companies, that provided close to \$2 billion of funding.

Mergers and acquisitions:

Leukosite in 1999 to add drug close to market, Campath®, and more in clinical trials.

Cambridge Discovery Chemistry in 2000 to add presence in Europe and expertise in chemistry.

COR Therapeutics in 2002 to take leading biopharma role and create strong pipeline of novel therapeutics (CVD) and add pipe-line to other key therapeutic areas: oncology and inflammation. The merger brought INTEGRILIN® and VELCADE®.

Acquired by Takeda for \$ 8.8 billion in 2008

Now: Millennium The Takeda Oncology Company

A 15 year long transition! – Start in time and remember,...

... the noise level is high out there!



Thank you for listening!

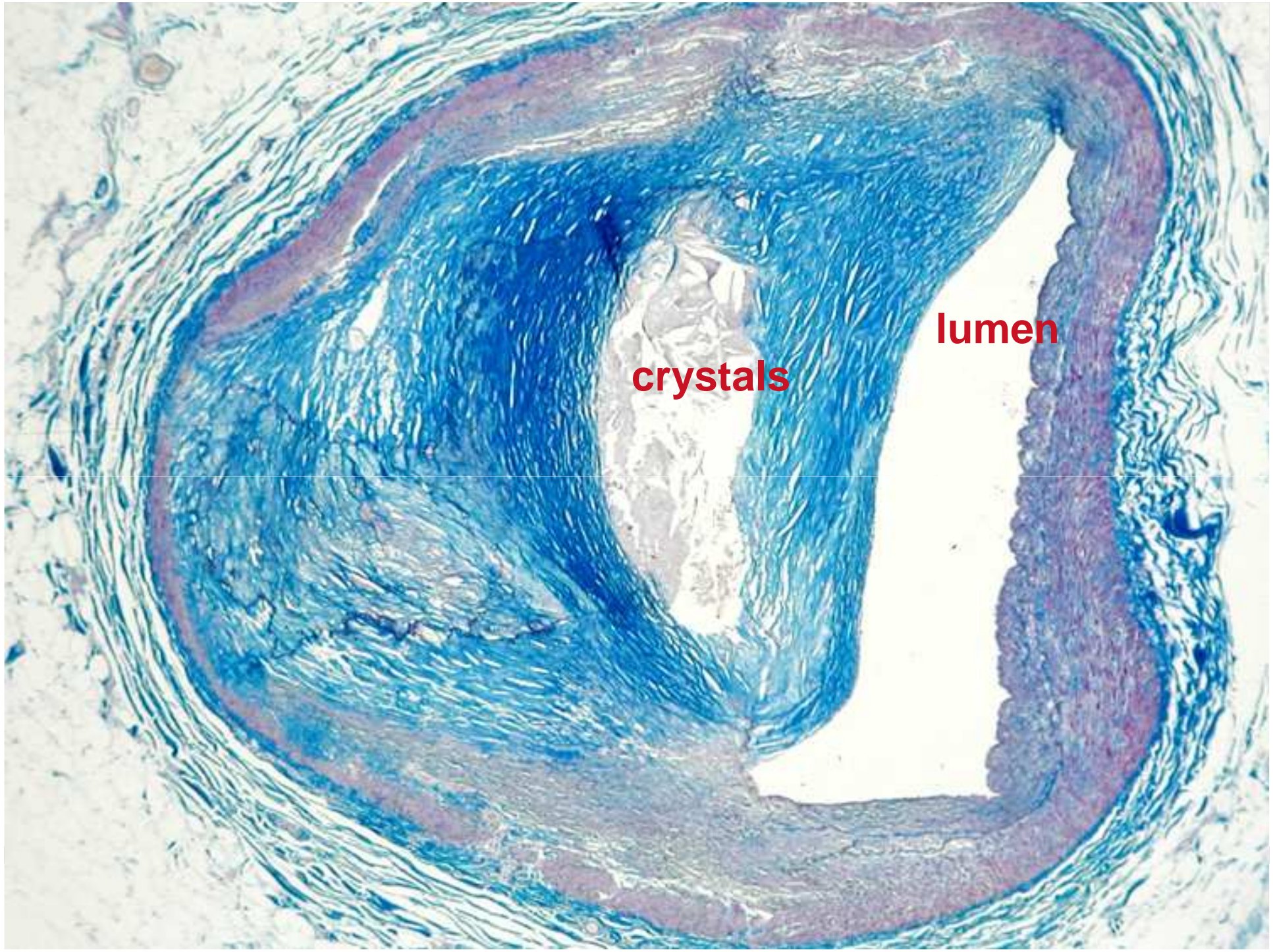
Athera is the lead singer in Susperia *Black metal band from Oslo*

Contacts and More Information

www.athera.se

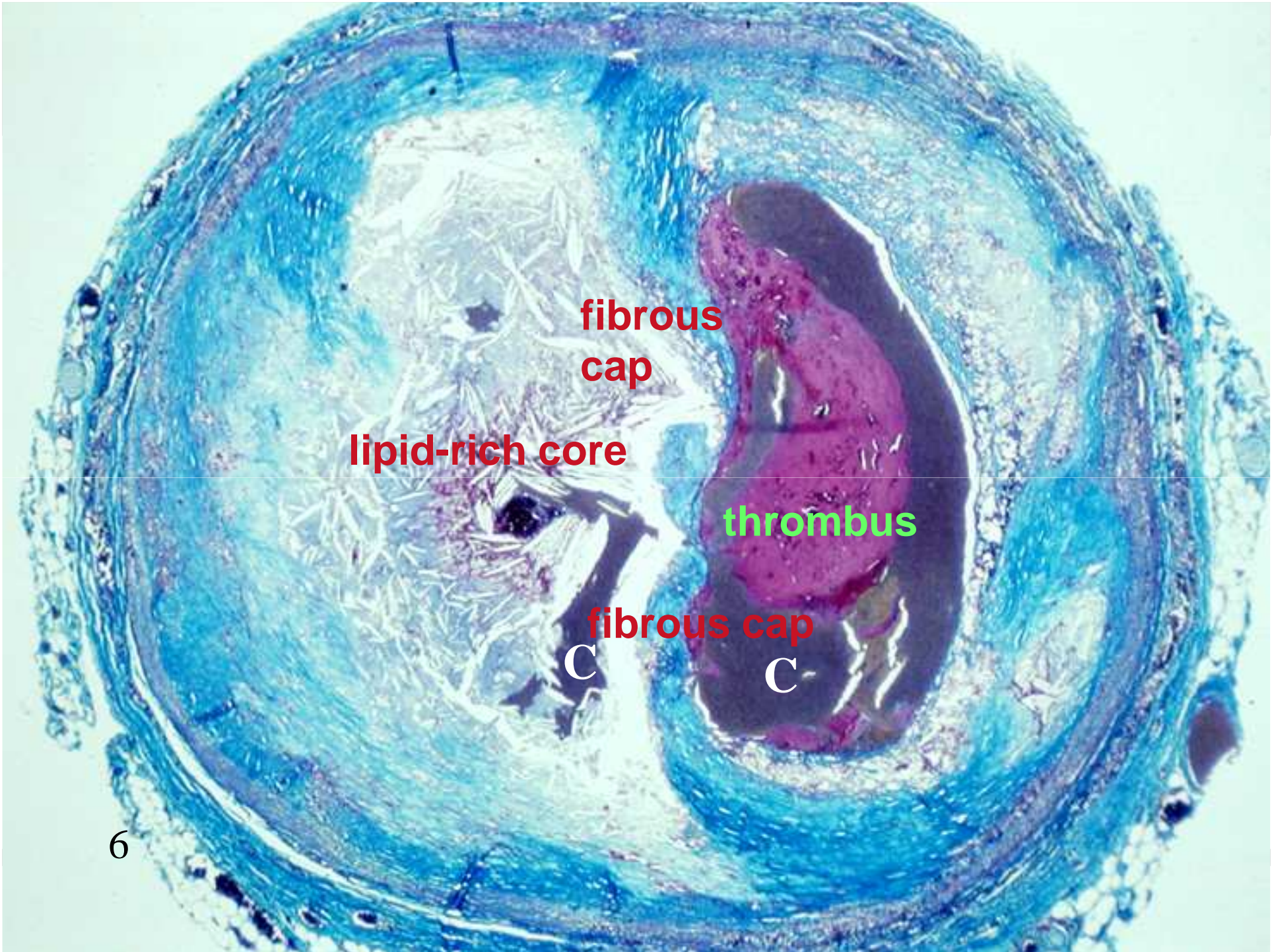
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crystals

lumen



**fibrous
cap**

lipid-rich core

thrombus

fibrous cap

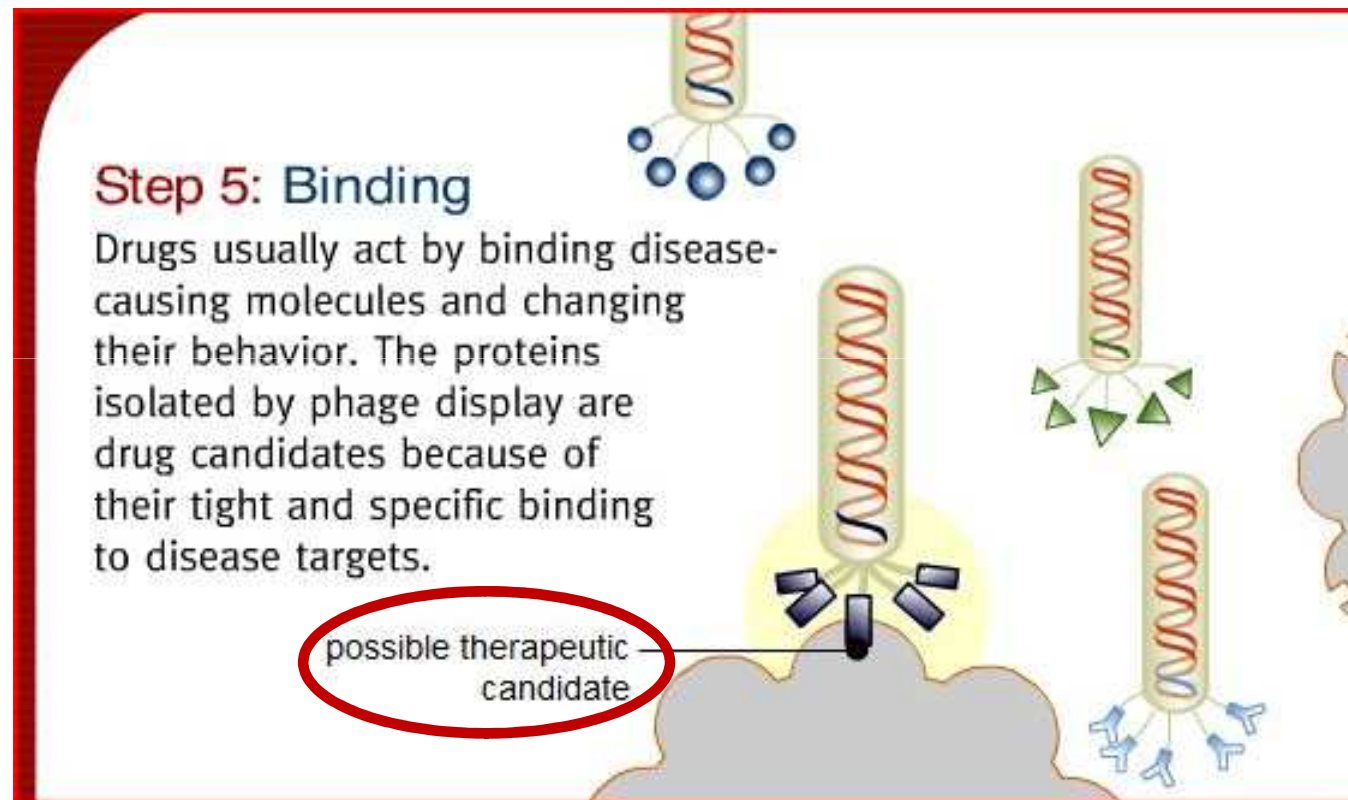
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Partner selection technology access

Phage Display



Out-licensing – Typical deal terms in Biotech

	Preclinical	Phase I	Phase II	Phase III*	Vs. 5 Yrs Ago
Upfront	\$3-10M	\$5-15M	\$10-25M	\$40-100M	3 x
IND	\$2-5M	NA	NA	NA	3 x
Ph II Start	\$3-8M	\$5-10M	NA	NA	
Ph III Start	\$10M	\$10-15M	\$25M	NA	
NDA Filing	\$5M	\$5M	\$10M	\$30M	2-3 x
1 st Approval	\$5M	\$10M	\$30M	\$50M	
2 nd -3 rd Approval	\$10M	\$20M	\$45M	\$70M	
Royalty Tiers	9-13%	12-15%	14-20%	18-26%	1.2 x

* + Supply, Profit Split, Carve-outs, Co-Promote, etc.

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