



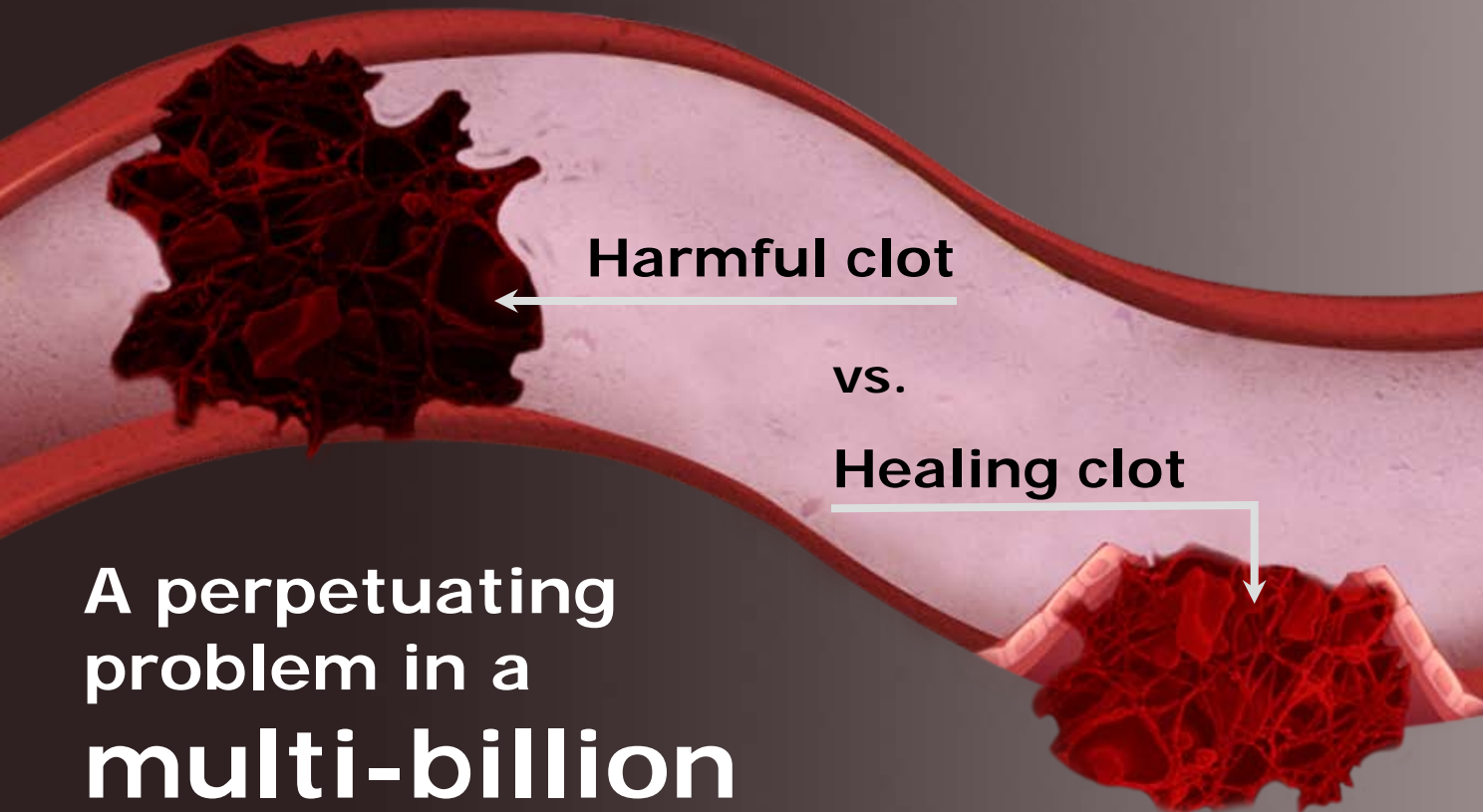
Taking Science to Heart™

Pioneering innovative
antithrombotic treatments

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President and CEO

September 2010

The antithrombotic conundrum



A perpetuating problem in a multi-billion dollar market

PCI

CABG

VTE prophylaxis
surgical, chronic
medical, cancer

Stroke

Catheter
ablation

Coronary
ischemia

Peripheral
arterial disease

DVT/VTE
treatment

Hemodialysis

Current antithrombotic use: A compromising medical decision

Prevent Bleeding

Low dose
antithrombotic

1 in 15
chance of
bleeding



Increased risk of
ischemia

Prevent Ischemia

Standard dose
antithrombotic

1 in 5
chance of
bleeding



Increased risk of
bleeding

Standard
dose optimal
antithrombotic

Minimize risk of
ischemia and
bleeding

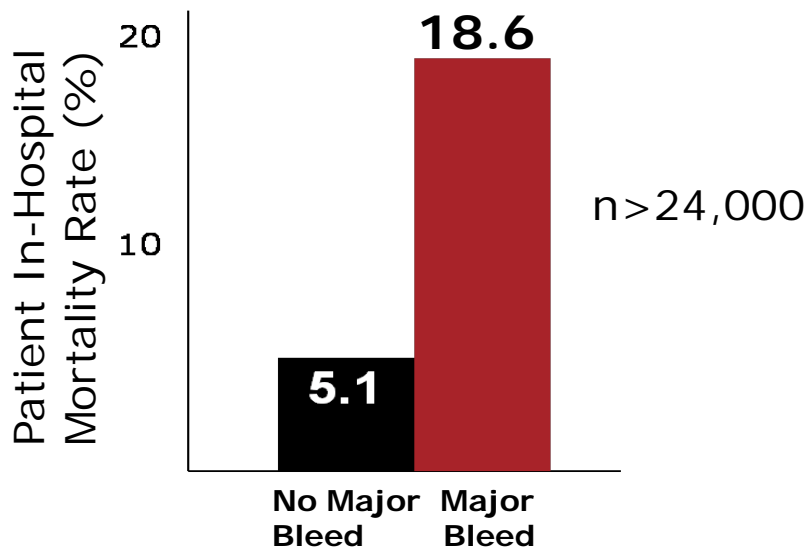
Bleeding can be as medically serious and as costly as ischemia

Medical cost

ACS-PCI:

Major bleeds are associated with a ~4x increase in mortality and ~5x increase in recurrent MI at 30 days

JP Bassand, 9th Annual Maseri-Florio International Lecture, ACC Annual Mtg., Atlanta, March 2010



Moscucci et al., Eur Heart J 2003;24:1815-23

Rao SV, et al. Am J Cardiol. 2005

Economic cost

PCI associated:

\$266 - \$973 GPIIb/IIIa inhibitors¹

\$200 - \$250 Closure device²

\$1,300 - \$15,200 Bleeding^{2,3}

\$1,000 - \$2,700 Hospital recovery

ACS-NSTEMI

\$7,400 - \$52,300 Bleeding⁴

CABG

\$8,200 Major bleeding

¹ Red book AWP

² Primary Market Research 2008; NCI Analysis

³ Milkovich, Am. J. Health-Syst. Pharm. 2003

⁴ Rao, Am. Heart J Vol 155

We are solving the conundrum with
active, specific control,
tailoring therapy to patient's needs

Not clotting
Preventing
ischemia

Clotting
Preventing
bleeding



Opportunities for the optimal anticoagulant

Open Heart Surgery*			
Catheter ablation*			
Hemodialysis*			
DVT/VTE treatment*			
VTE prophylaxis surgical, chronic medical, cancer			
Coronary ischemia*			
PCI*			
	Bivalirudin	Low molecular weight heparin	REG1/REG2

*Heparin used off-label

REG1 – arterial thrombosis

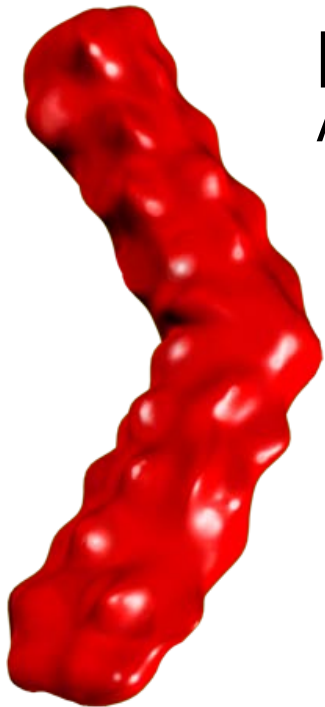


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**Acute Coronary Syndrome -
Percutaneous Coronary
Intervention (ACS-PCI)**

REG1: The optimal anticoagulant system

- Synthetic, single-strand oligonucleotides
- COGs more similar to those of small molecules than those of biologics
- Administered by IV bolus
- Metabolized by nucleases in the blood with no active metabolites
- No protein binding



pegnivacogin Anticoagulant aptamer

- Specific affinity for Factor IXa
- 31 nucleotides + 40 kDa PEG
- Long half life (>24hr)

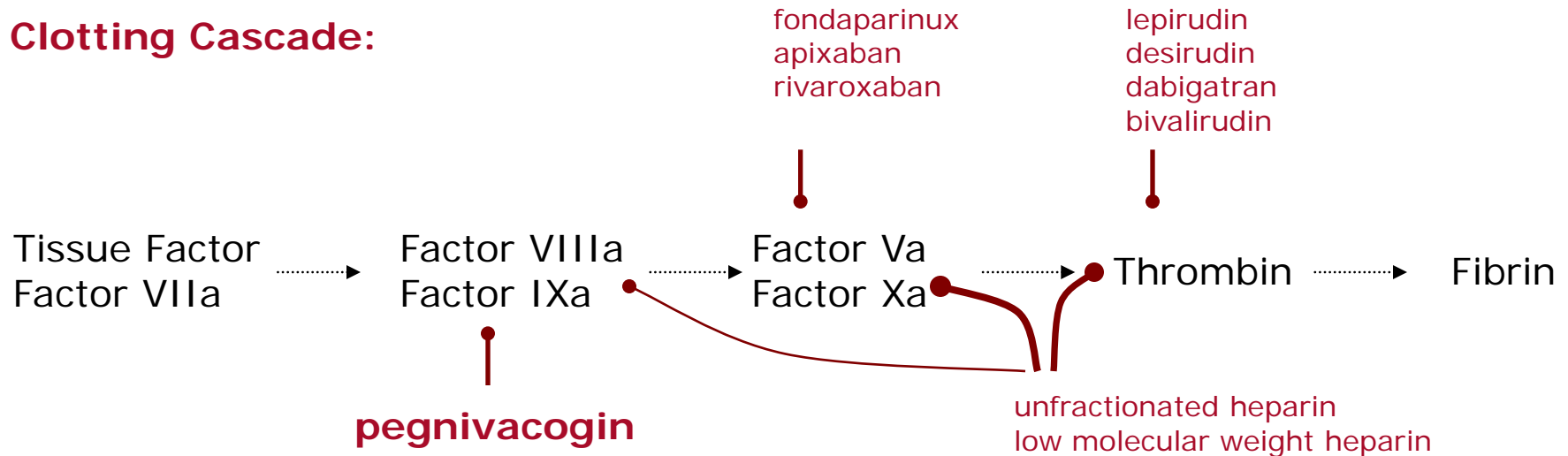
anivamersen Active control agent

- Specific affinity for RB006
- 15 nucleotides
- Very short half life (<5min)



Factor IXa: An innovative and advantageous target

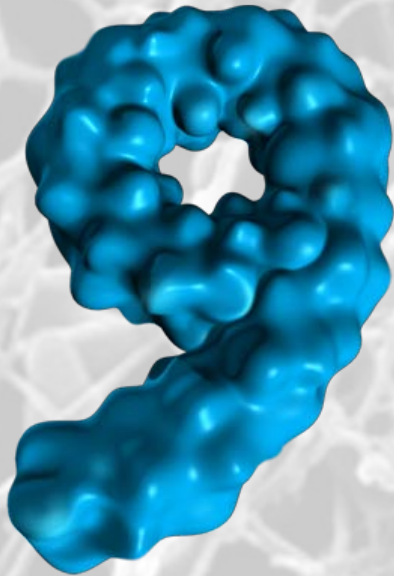
Clotting Cascade:



- FIXa is the proximal driver of clot propagation and is far enough upstream to be part of the integrated system of intrinsic and extrinsic coagulation
- FIXa concentration is lower than Xa and thrombin; thus, high levels of target inhibition are more readily achievable
- High FIX levels are associated with an increase in Acute Coronary Syndrome (ACS) and venous thromboembolism
- FIX is directly activated by foreign materials (e.g., catheters and guidewires)
- FIX infusion in animals leads to clot formation

Mechanism of action

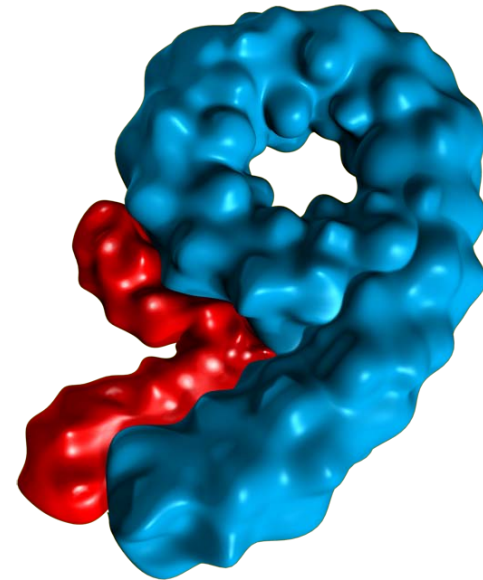
Activated



Factor IXa

Coagulation proceeds unimpeded; clots form

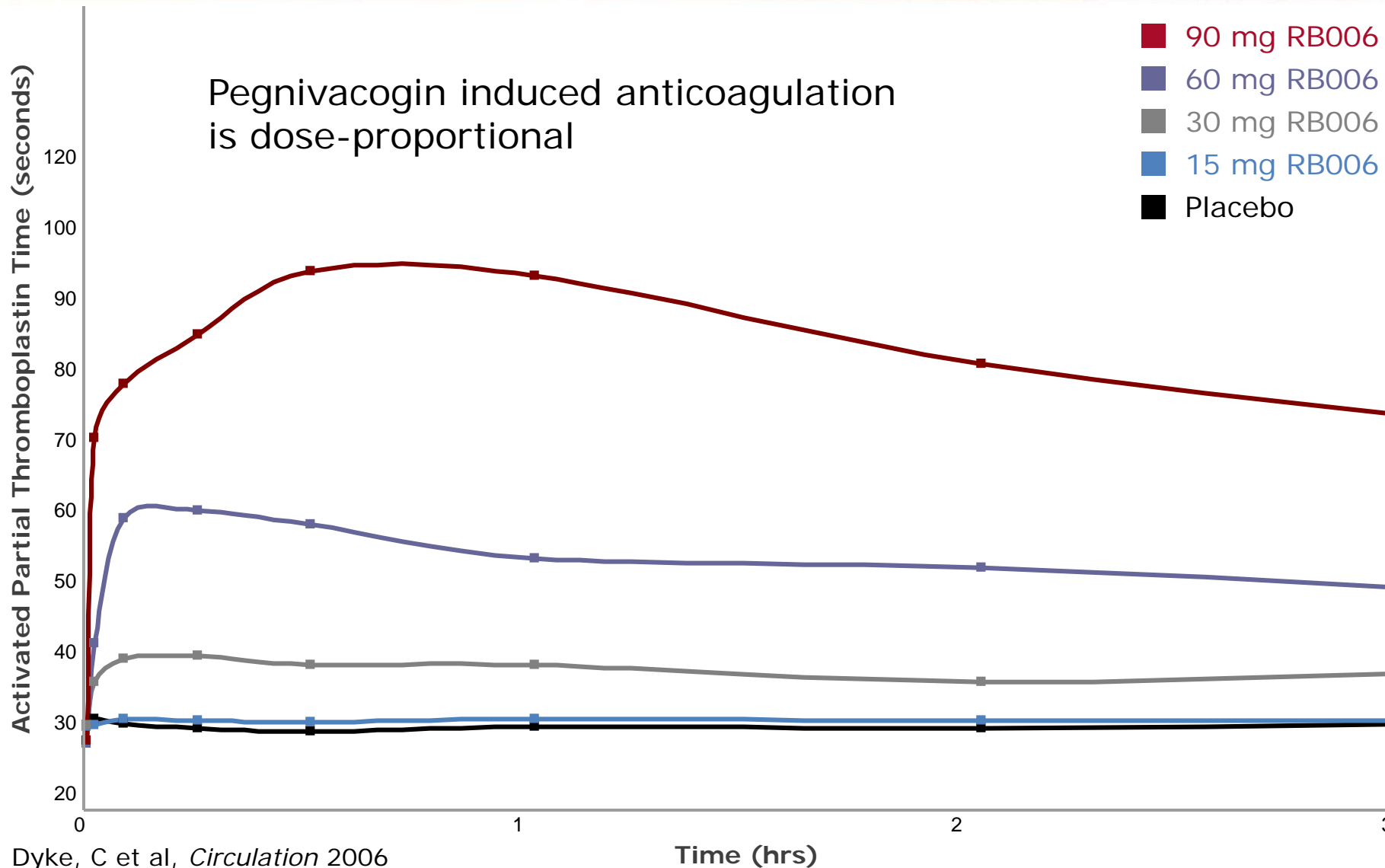
Inactivated



pegnivacogin: Factor IXa complex

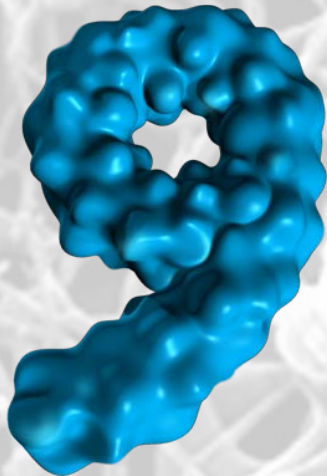
Pegnivacogin selectively inhibits Factor IXa; clotting cannot proceed

Factor IXa inhibitor pegnivacogin (aka RB006) effectively prevents clotting



Anivamersen as a control agent for pegnivacogin

Activated

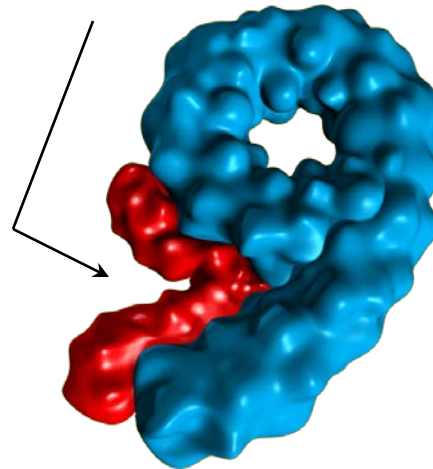


Coagulating

Coagulation proceeds unimpeded and clots form

Inactivated

pegnivacogin

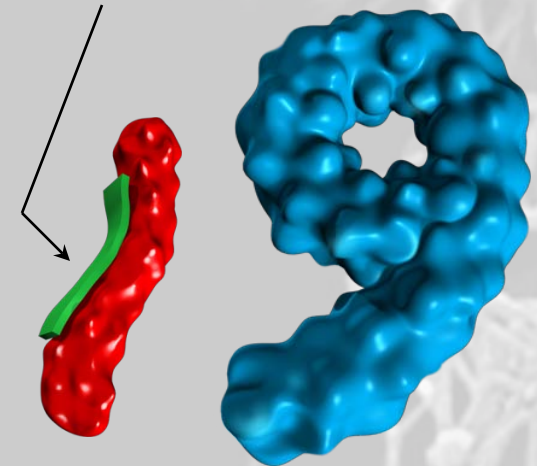


Anticoagulated

Pegnivacogin selectively inhibits Factor IXa and clotting cannot proceed

Activated

anivamersen

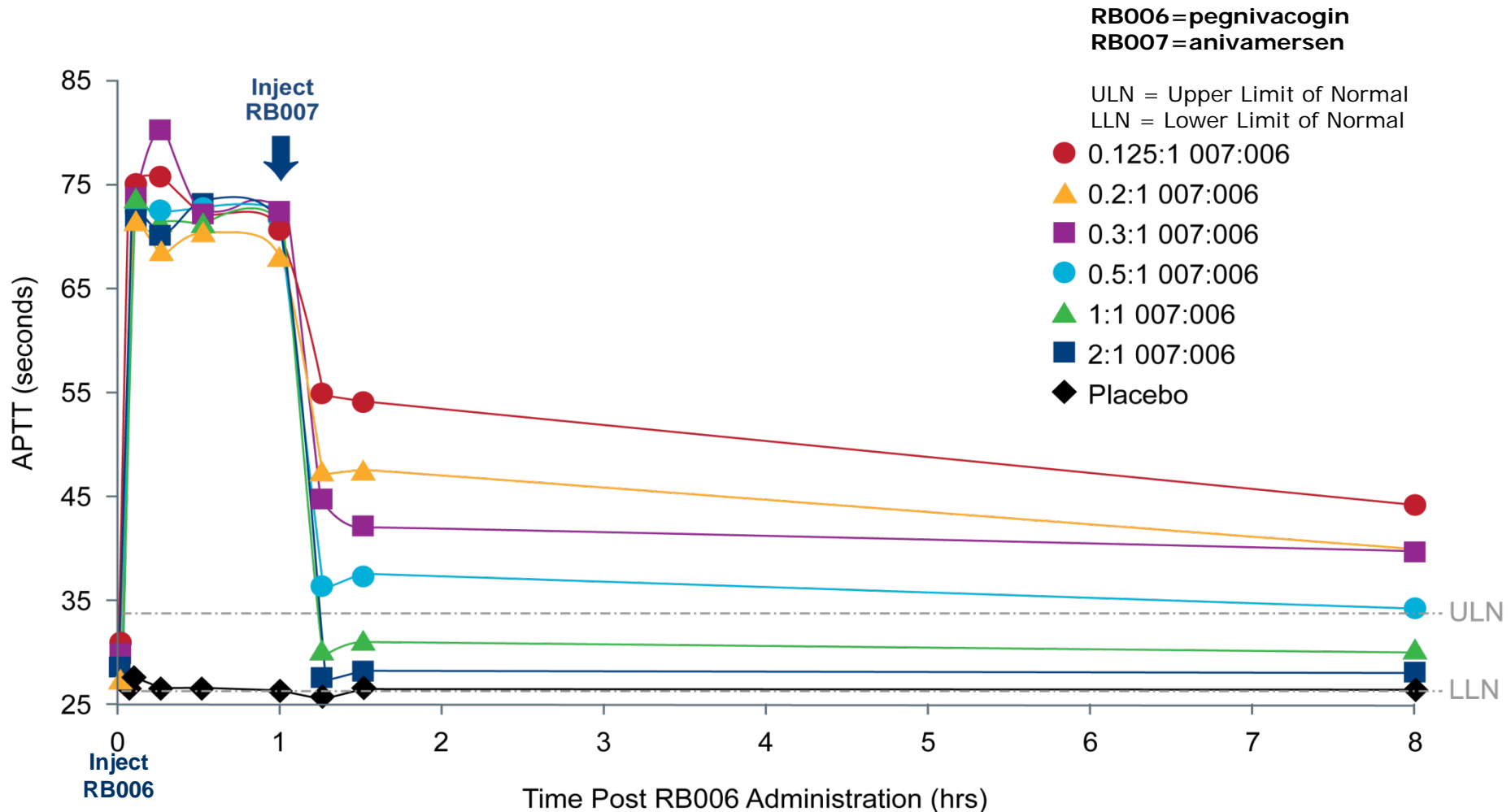


Coagulating

Anivamersen binds to pegnivacogin; the resulting complex is incapable of inhibiting Factor IXa and clotting cascade resumes

REG1 phase 1 results: well tolerated active control

3 studies, 174 patients, placebo controlled, randomized, double-blinded
Dose-dependent, predictable relationship RB007:RB006



REVERSAL-PCI (phase 2a) results

Conclusion: REG1 enables safe and effective PCI

Pegnivacogin (RB006)

Inhibition of Factor IXa using peginvacogin provided for rapid, reproducible, stable and effective anticoagulation

Anivamersen (RB007)

Partial or complete reversal control using anivamersen was predictable, rapid, effective and reproducible

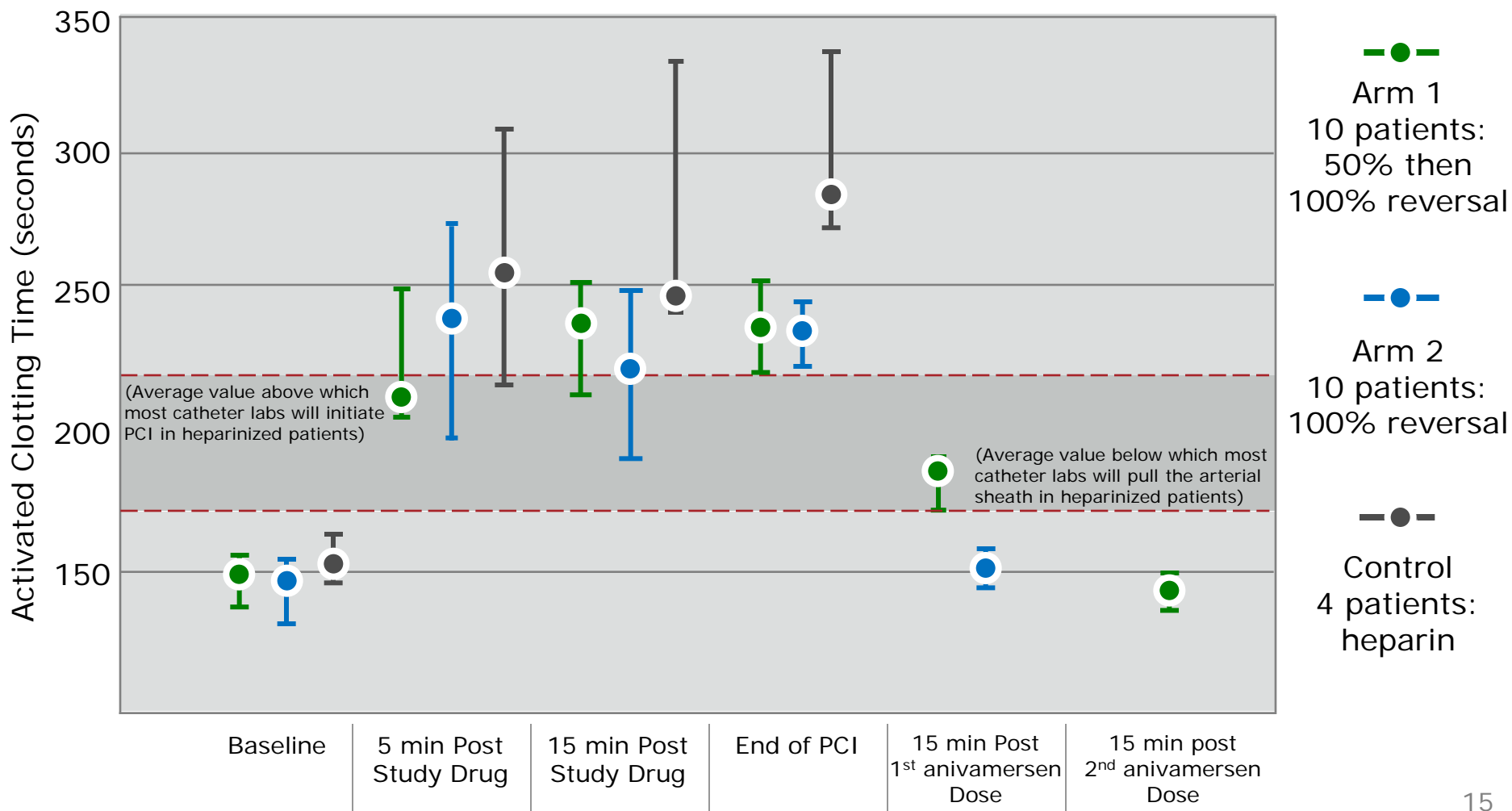
REG1 (pegnivacogin and anivamersen) was well tolerated

Partial or complete anticoagulation reversal allowed for planned early sheath removal (~4 times sooner than with heparin) with no bleeding or ischemic complications

PD response to REG1 during PCI consistent with current PCI practice standards and comparable to that observed in all subject populations in phase 1 studies

REVERSAL-PCI (phase 2a) results

REG1 effectively anticoagulates and provides predictable, real time partial or total reversal control



REG1 is differentiated from the current injectable anticoagulant landscape

Agent Characteristics	Unfractionated heparin	Low molecular weight heparin	Bivalirudin	REG1
Rapid onset of action	+	-	+++	+++
Low patient variability; Reduced monitoring	-	+	+	+++
Applicability in renally impaired patients	+	+	+	+++
Non-immunogenic	-	-	+++	+++
Reduced bleeding rates	-	-	+	+++
Predictable, active & rapid reversibility	+	-	-	+++
	(non-specific; protamine)			
Patient and setting specific modulation	-	-	-	+++

RADAR (phase 2b) design

Randomized, Partially-Blinded, Multi-Center, **A**ctive-Controlled, **D**ose-Ranging Study **A**ssessing the Safety, Efficacy, and Pharmacodynamics of the **R**EG1 Anticoagulation System Compared to Unfractionated Heparin or Low Molecular Heparin in Subjects with Acute Coronary Syndrome

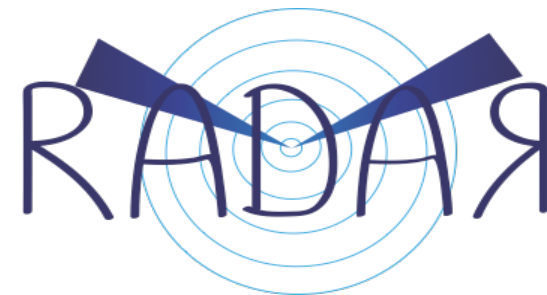
Study Population:

Subjects admitted for Acute Coronary Syndrome, unstable angina and myocardial infarction without ST-segment elevation - UA/NSTEMI - intended for cardiac catheterization within 24 hours

Sites: >90 centers

USA, Canada, Poland, France, Germany, Netherlands, Belgium

Treatment Arms	Number of Subjects
pegnivacogin (1 mg/kg) + anivamersen (100% reversal)	200
pegnivacogin (1 mg/kg) + anivamersen (75% reversal)	100
pegnivacogin (1 mg/kg) + anivamersen (50% reversal)	100
pegnivacogin (1 mg/kg) + anivamersen (25% reversal)	200
Heparin (UFH or LMWH + GPIIb/IIIa inhibitor)	200
Total patients	800



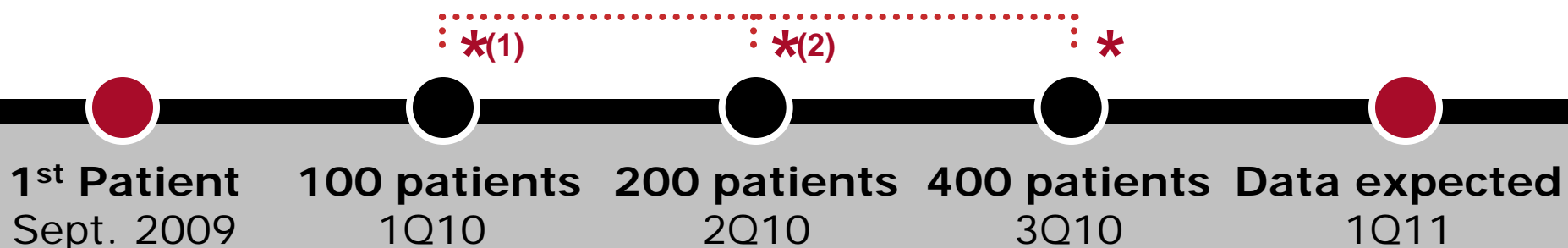
Cost: ~\$15 million

RADAR (phase 2b) design and milestones

Recruitment: **15 months**

Follow-up: **30 days**

DSMB: **3 planned reviews (adaptive design)**



(1) DSMB: April 19, 2010

Study continues as designed; no safety concerns relative to ischemic endpoints and no study arms discontinued (bleeding safety “triggers” not achieved in any arm)

(1) DSMB: June 2, 2010

Based on adjudicated data from first 100 subjects, one REG1 arm discontinued; study continues as planned

(2) DSMB: August 6, 2010

Based data from first 200 subjects, study continues without further modification

*** General safety review and any RB007 arm with a bleeding rate in excess of heparin will be discontinued and remaining subjects intended for that arm will be re-randomized to retained RB007 arms**

RADAR (phase 2b) endpoints

Primary Endpoint: The composite incidence of major and minor bleeding (not related to CABG) through Day 30 [anivamersen dose selection]

Secondary Endpoints:

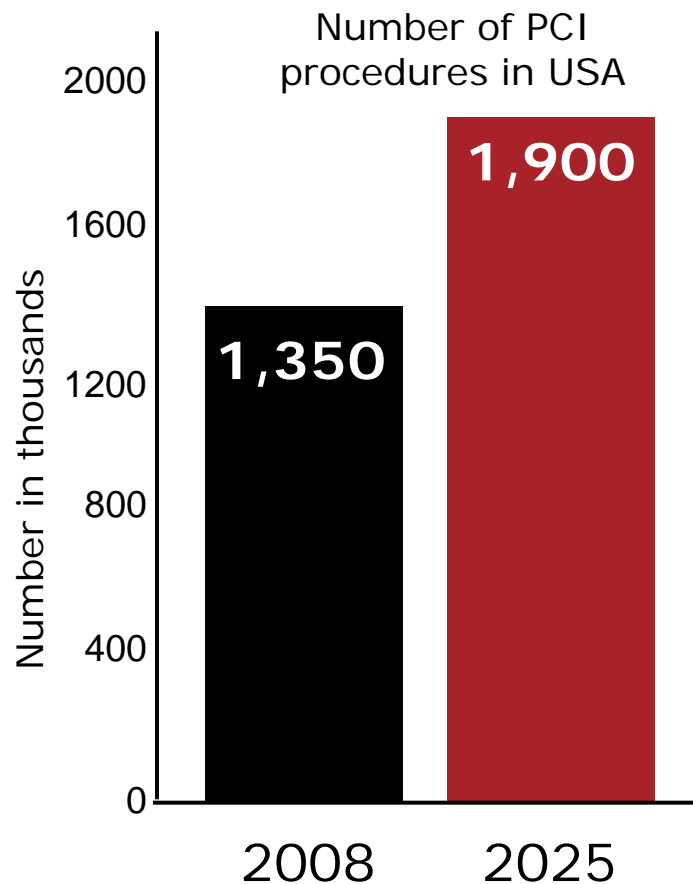
The proportion of subjects with a composite of ischemic events as defined as death, nonfatal myocardial infarction (MI), or urgent target vessel revascularization (TVR) through Day 30 [Estimate anticoagulant efficacy]

Additional Secondary Endpoints

- Correlation of the predicted pharmacodynamic responses of RB007 to the observed responses
- Correlation of bleeding and ischemic events by Activated Clotting Time (ACT) < 225 and > 225 seconds for REG1 and heparin
- Full PK/PD profile for the first 20 subjects receiving pegnivacogin [confirm consistency of drug properties and profile in this study population]
- Collection of a variety of pharmacoeconomic indicators

REG1 U.S. market opportunity in PCI

1.9% CAGR expected in U.S. PCI market



U.S. Peak Revenues:

~ **\$955M**

~ \$1250/treatment
~ 30% penetration

REG2 – venous thrombosis



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**VTE prophylaxis
in abdominal surgery**

REG2 (subcutaneous pegnivacogin + IV bolus anivamersen) phase 1

Design

- Single-center, double-blind, randomized, placebo-controlled, single ascending dose study
- 36 healthy volunteers between 18 and 45 years
- Five treatment cohorts (30 subjects)
- Four dose cohorts; 0.5, 1.0, 3.0 mg/kg
- 2.0 mg/kg cohort (8 subjects) receives anivamersen (1.0 mg/kg) at predefined time intervals
- Endpoints: Safety, PD/PK

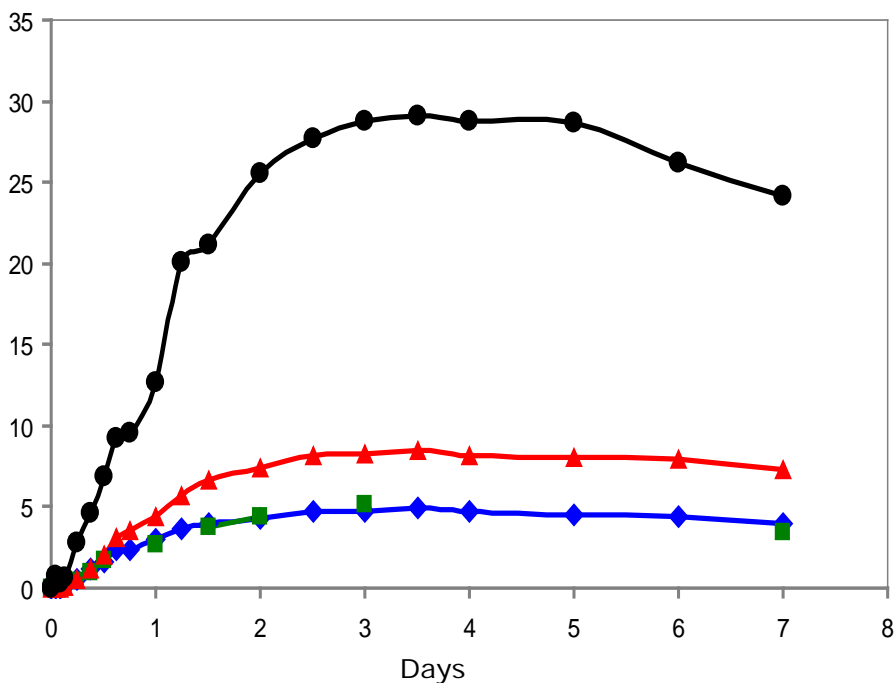
Results

- No SAEs
- All subjects completed study
- All injections well tolerated
- No injection difficulties
- All injection site reactions minor and transient
- No difference in bleeding events from placebo
- No dose related AEs

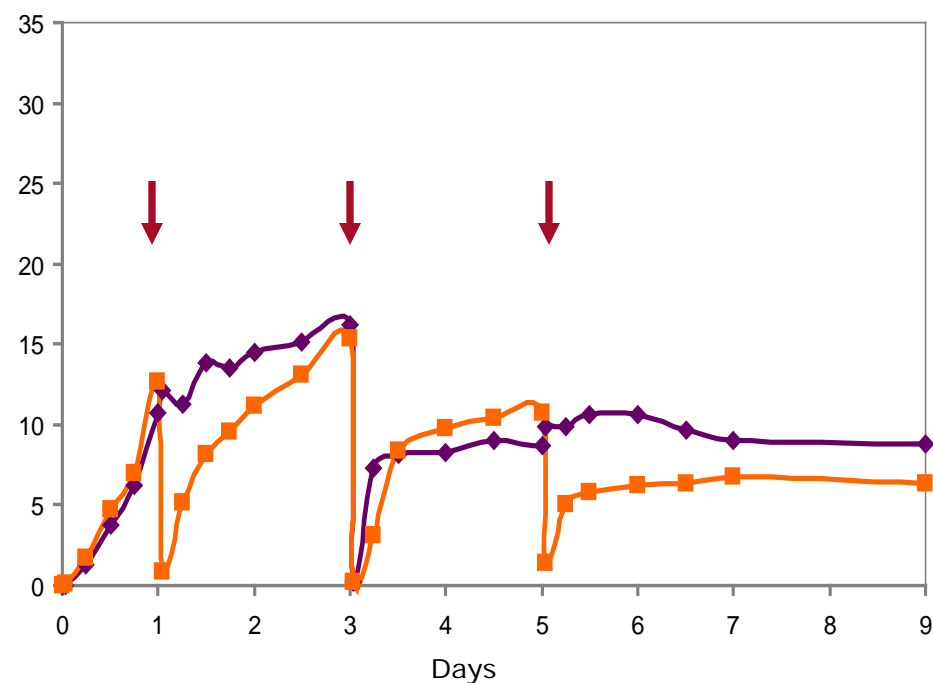
First successful subcutaneous administration of an aptamer in humans

REG2 pharmacokinetics (phase 1) results

Pegnivacogin Mean Plasma Concentration ($\mu\text{g/mL}$) $T_{1/2} > 7$ days



- ◆ 0.5 mg/kg
- ▲ 1.0 mg/kg
- 0.5 mg/kg
- 3.0 mg/kg



- ◆ 2.0 mg/kg pegnivacogin; anivamersen at 72 hrs
- 2.0 mg/kg pegnivacogin; anivamersen at 24, 72, 120 hrs
- ⋮ 1.0 mg/kg anivamersen injected

REG2 phase I conclusions

Safety

- Well tolerated – no SAEs
- SC formulation easy to administer
- No significant site reactions, even with higher volumes
- No dose related adverse events
- No difference in bleeding complications to placebo
- Reversal possible with anivamersen

Efficacy

- Plasma levels comparable to IV
- Drug activity confined to plasma compartment – behavior should be predictable based on REG1
- Achieved appropriate PTT for target indications
- Long half life with single injection

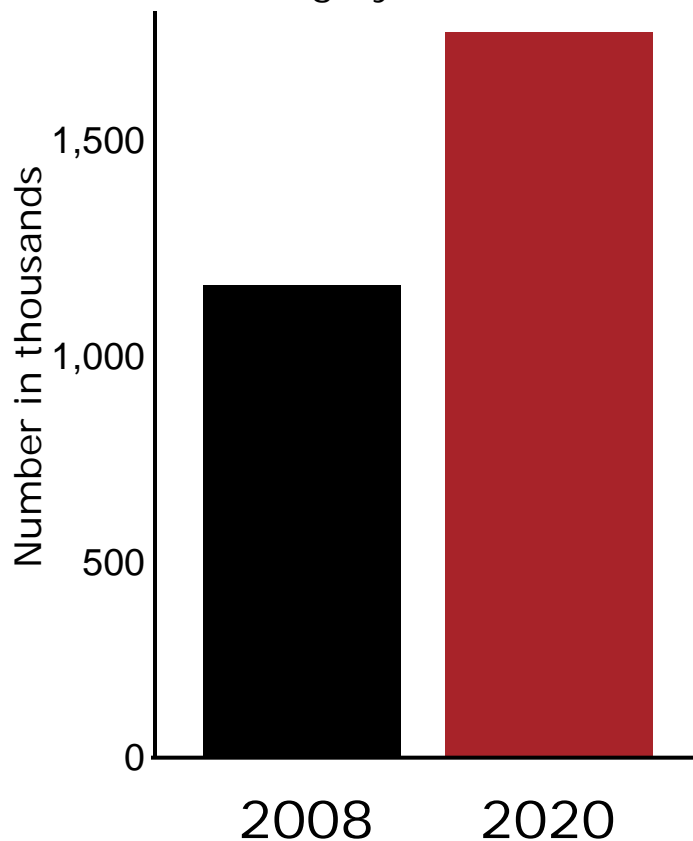
Next steps:

4Q10/1Q11 - initiation of multiple ascending dose trial

REG2 U.S. market opportunity in VTE prophylaxis in abdominal surgery

3.6% CAGR expected in U.S. market

Number of DVT in abdominal surgery count in USA



U.S. Peak Revenues:

~ \$750M

~ \$300/dose twice weekly*
 ~ 35% penetration

* 2x/week was an estimate based on monkey data; actual ~2x/month will provide significant upside in value

REG-AP: Antiplatelet discovery program

- Unmet medical needs in ACS, PCI, ischemic stroke, atrial fibrillation cardioversion
- Wide range of validated antiplatelet targets (P2Y₁₂, PAR-1, GPVI, GPIb, etc.)
- Regado leverages demonstrated expertise in aptamer drug discovery and development
- Lead optimization of potent antiplatelet aptamers essentially completed (GPVI program; RB571)
 - Specific, complementary control agent identified (RB515)
- **REG3** (RB571 + RB515) targeted for initiation of clinical study in early 2011

Comprehensive antithrombotic pipeline

	Preclinical	Phase 1	Phase 2a	Phase 2b	Phase 3
<p>REG1: pegnivacogin (IV bolus) + anivamersen (IV bolus)</p>			<p>ACS – PCI Open Heart Surgery (incl. CABG)</p>		
<p>REG2: pegnivacogin (SC inj.) + anivamersen (IV bolus)</p>			<p>VTE Prophylaxis</p>		
<p>REG3: RB571 (IV) + RB515 (IV)</p>			<p>Antiplatelet Therapy</p>		

Antithrombotics: A multi-billion dollar market

Heparin

Low mol. wt. heparins
(enoxaparin)

Bivalirudin

Antiplatelet agents
(clopidogrel, prasugrel,
GPIIb/IIIa inhibitors)

Factor Xa inhibitors
(fondaparinux + orals)

> \$20B
global market

**REG1, REG2, REG3 and the
Regado antithrombotic platform
have potential application
throughout this market**

PCI
Catheter ablation
Coronary ischemia
Peripheral
arterial disease
VTE prophylaxis
DVT indications
Hemodialysis
Atherosclerosis
NSTEMI & STEMI
Stroke
CABG

Strong Regado platform patent estate

Protection through 2025 and beyond

17 Issued or allowed U.S. and foreign patents related to:

- Anti-Factor IXa aptamers
- Oligonucleotide modulators of aptamers
- REG1 and REG2 product claims
 - Composition of matter for pegnivacogin and anivamersen

Other U.S. and foreign applications pending:

- Methods of use for Anti-Factor IXa aptamers and their modulators
- REG1 and REG2 product administration
- Aptamers and modulators thereof for antiplatelet targets (REG3)
- Additional molecular classes of modulators
- Anti-FX/Xa, VII/VIIa, thrombin and ANG2 aptamers and methods

Experienced management team

David J. Mazzo, Ph.D., **President and Chief Executive Officer**

(CEO of Aeterna Zentaris; CEO of Chugai Pharma USA; Sr. VP, Dev Ops, Schering-Plough)*

Chris Rusconi, Ph.D., **Sr. VP and Chief Scientific Officer (Co-Founder)**

(Director of Research, Combinatorial Therapeutics, Duke University)*

Steven Zelenkofske, D.O., F.A.C.C., **Sr. VP and Chief Medical Officer**

(VP Cardiovascular/Thrombosis Medical Unit-US, Sanofi-Aventis)*

Ellen McDonald, M.B.A., **Sr. VP and Chief Business Officer**

(CBO of Aeterna Zentaris; CBO of Chugai Pharma USA;

Sr. VP Cardiovascular Marketing and Medical, Bristol-Meyers Squibb)*

Alexander R. Giaquinto, Ph.D., **Sr. VP Reg. Affairs/Quality Assurance**

(Sr. VP Worldwide Regulatory Affairs, Schering-Plough)* **and Chief Compliance Officer**

Chris Courts, C.P.A., M.B.A., **VP Finance**

(Director, Finance, ITC Deltacom)*

High quality investors

Noteworthy,
respected investors
with a history
of identifying
biotech winners

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P. Sherrill Neff, J.D.
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Taking Science to Heart™

Pioneering innovative
antithrombotic treatments