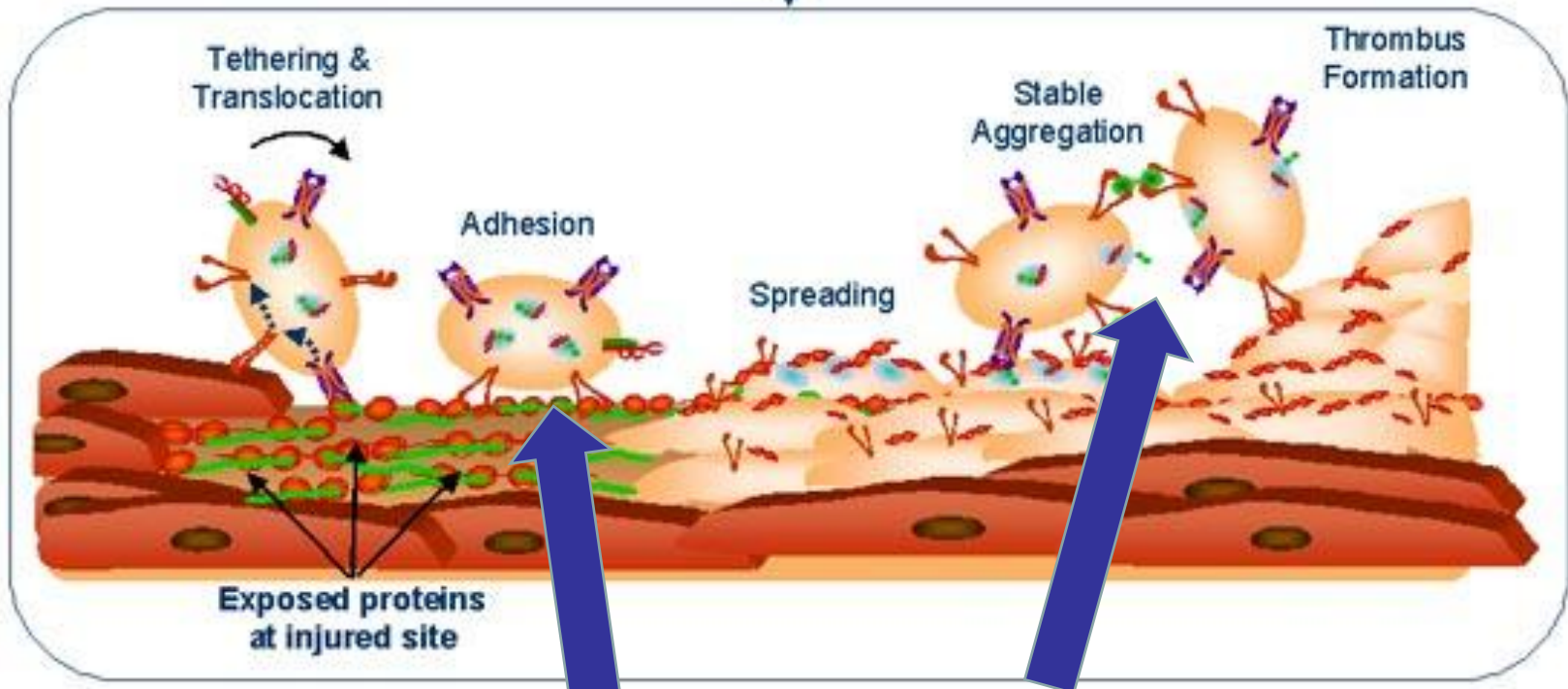
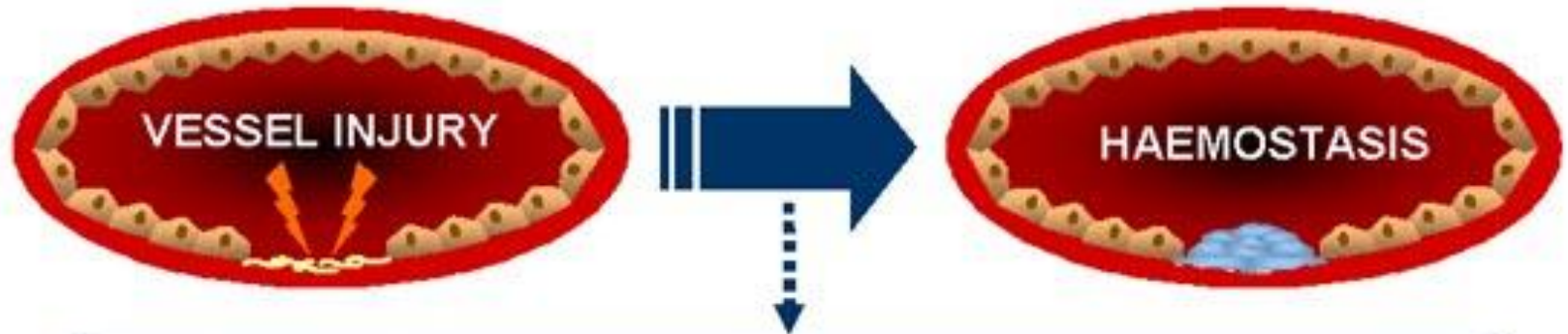


**A humanised monoclonal antibody
inhibiting the platelet receptor for
von Willebrand Factor, glycoprotein Ib,
as an effective and safe antithrombotic**

Summary

- Target: platelet glycoprotein (GP) Ib α
- Drug candidate: humanised anti-GPIb α (6B4) Fab
- Disease opportunities
 - Initial focus: ischemic stroke
 - Additional indications:
 - acute thrombotic events (PTCA, thrombolysis...),
 - thrombotic thrombocytopenic purpura (TTP)
 - xenotransplantation (porcine into human)

Description of the technology



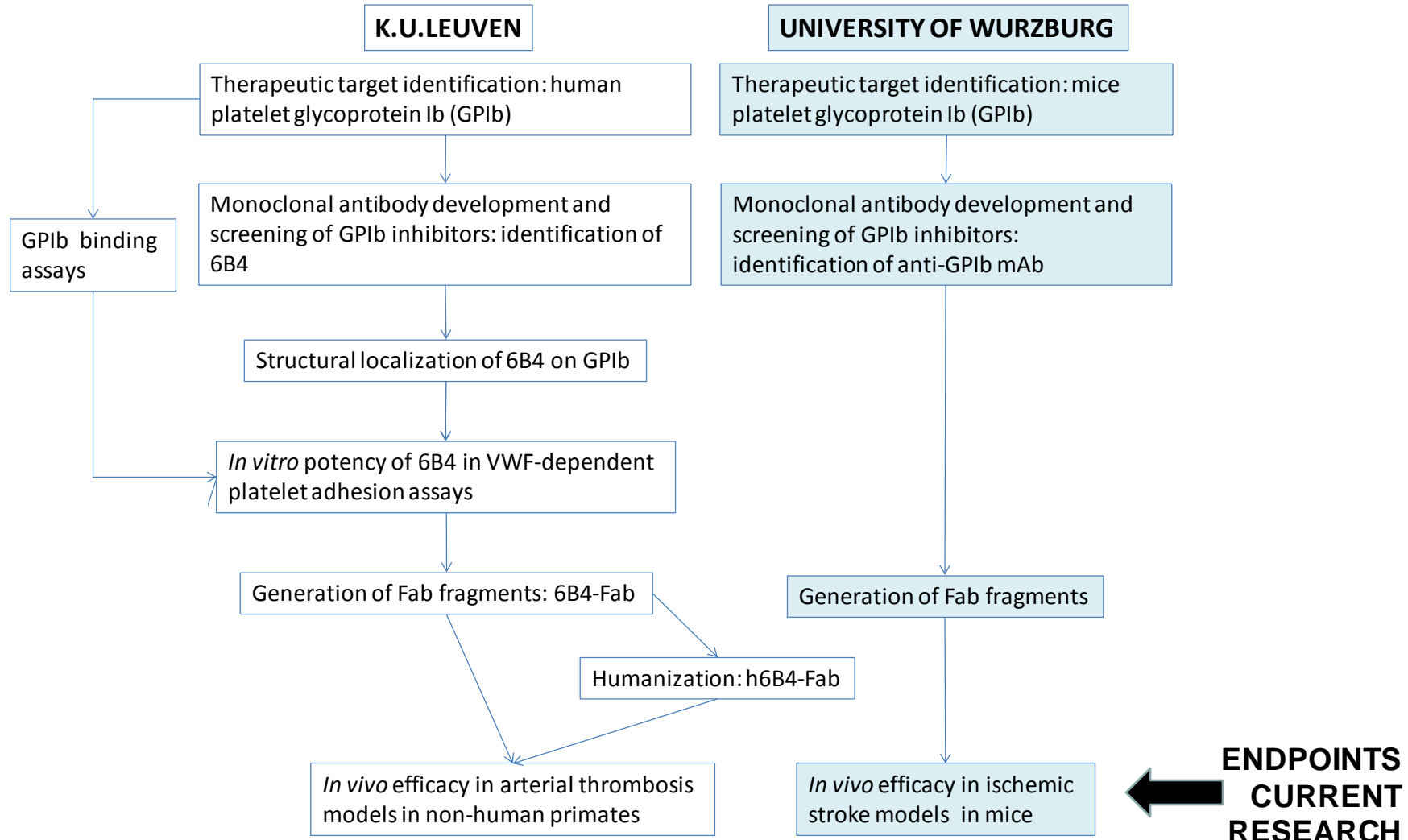
Description of the technology

Inhibition of platelet receptor GPIIb

- Non-redundant receptor (= no “escape”)
- Only on platelets (= low risk for unexpected side effects)
- Needed for platelet adhesion (= first step in thrombosis)
- Works essentially in fast flowing blood
(little effect in veins = lower bleeding risk)

Strong antithrombotic with safe profile

Current stage of development: stroke



Current stage of development: arterial thrombosis

- 2 studies in baboons with murine 6B4
- 1 study in baboons with humanised 6B4
 - good antithrombotic effect
 - little effect on bleeding time or on blood loss
 - larger therapeutic window as compared to currently available antithrombotics
- with University of the Free State, Bloemfontein, SA

Current stage of development: TTP

- rare, deadly disease (orphan status possible)
- due to ADAMTS13 deficiency overactive UL-VWF
- spontaneous binding VWF to GPIb causes thrombosis
- no animal models
 - inhibitory ab against human ADAMTS13
 - induces TTP in baboons: only model
 - study with 6B4 planned october-november 2010

with University of the Free State, Bloemfontein, SA

Current stage of development: xenotransplantation

- porcine organs for human transplantation
 - porcine VWF binds spontaneously to human GPIb
 - causes occlusion of pig blood vessels when perfused with human blood
 - 6B4 inhibits porcine VWF binding to GPIb
 - 6B4 prolongs patency of porcine lung perfused with human blood
 - study with 6B4 on porcine lung/liver/heart transplanted in baboons planned may-september 2010
- with - University of Baltimore, MD: R Pierson III, A Amzizadeh
- Revivicor
 - NIH

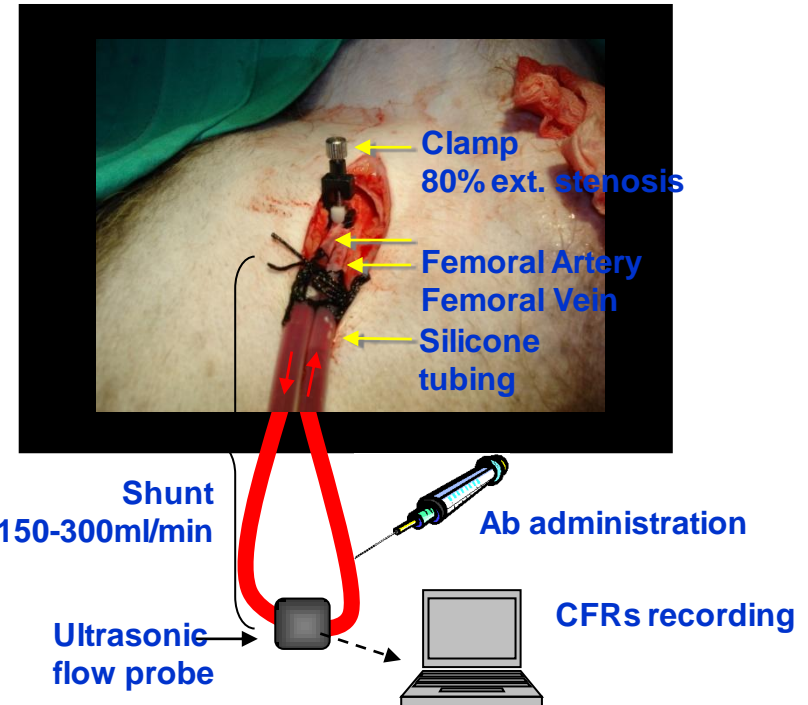
Competitive advantage of the technology

Relative to “gold standards”

(ReoPro & Plavix)

Arterial Thrombosis Model

- Higher Efficacy
- Better safety profile
(lower bleeding risk)
- Larger therapeutic window



Ischemic Stroke Model: **Analogous Ab**

- Higher efficacy (lower bleeding risk, better neurological outcome)
- Larger therapeutic window



Status of patents

- The first patent family concerns humanized antibody inhibition of the VWF-GPIb/V/IX interaction via the GPIb target for platelet adhesion formation disorders such as vascular thrombosis, cerebral thrombosis and metastasis.
The patent family comprises **a granted patent** of Deckmyn et al. US7332162 B1, granted patent EP1200562B1

- A second patent family concerns anti GPIb antibodies for use in the treatment and prevention of stroke. It comprises the **US continuation in part** of Deckmyn et al. US61/124,293 in april 2009.

Competitors

- Ablynx with a cameloid antibody against the VWF-A1 domain
- Glenmark Pharmaceuticals with a monoclonal antibody against the VWF-A1 domain.

➔ In mice KO-models, a more powerful antithrombotic effect was seen in GPIb-KO than in VWF-KO mice (Bergmeier et al., 2006), likely because GPIb in addition binds ligands other than VWF, but also involved in thrombosis.

This clearly indicates that the role of platelet adhesion receptor GPIb far exceeds that of its main ligand VWF in arterial thrombosis.

Research and Management team

- Prof. Hans Deckmyn (K.U.Leuven)
- Dr. Ivo Roelants (IP Officer, K.U.Leuven R&D)
- Dr. Nick Geukens (PharmAbs)
- Collaborators: Prof. G. Stoll (University of Würzburg, Germany),
Prof. G. del Zoppo (University of Seattle, Wa)
Prof. P.N. Badenhorst (University Free State, SA)
Prof. R. Pierson III (University Baltimore, MD)