

- **Hemorrhage** is a leading cause of death and cost associated with blood transfusion.
- There is a **need** for the improvement of current treatments of bleeding associated with **surgery, trauma, intracerebral hemorrhage (ICH)** or other tissue damages.
- A **novel target** involved in fibrinolysis has been identified.
- **Proprietary novel compounds** to prevent major bleeding have been developed:
 - Small molecule entity (SME).
 - Efficacy: 30,000 times more effective than the currently available therapies.
 - Safety: No thrombus formation and no impact on coagulation.
- **Primary Indication: prophylaxis and acute treatment of bleeding in cardiac surgery.**
- **Life plan**
 - ↓ intravenous: cardiac surgery → other major surgeries → trauma and first-aid → ICH
 - ↓ topical: trauma and first-aid → OTC → veterinary uses

Scope of the problem

- Coronary arteries bypass surgery: 470,000 procedures/year in the 7 Major Markets. Aprotinin withdrawal (\$600M market niche) has generated demand and opportunity for new antifibrinolytics that could significantly reduce the number of blood transfusions.
- **Major surgeries:** 100-120 million procedures every year in the 7 Major Markets, 2.5-3.5% with significant blood loss. Tranexamic acid (TXA) is used in 35-45% of surgeries.
- Annual expenditures on blood transfusion: \$1.62M-\$6.03M per hospital.
- Hemorrhage is responsible for 50% deaths occurring within 24 h of **traumatic injury**.
- **Intracerebral hemorrhage (ICH;** 15% of all strokes), is associated with high mortality (40%) and there is **no proven medical** or surgical **treatment**.

Patient needs addressed

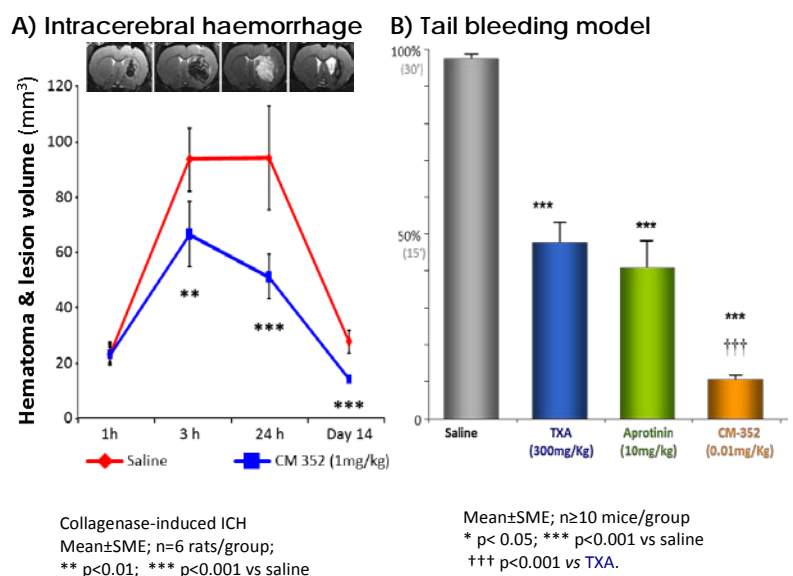
Prophylaxis and treatment of major bleeding in patients undergoing cardiac surgery
Major bleeding (Guidelines ISTH) in trauma and other clinical and surgical settings.

Current Standard of Care & Competitive Landscape

- Antifibrinolytics are the Standard of Care for hemorrhage in surgery and trauma.
- TXA is the only commercially available agent, partially effective at high doses with significant side-effects. Current products in development are restricted to sealants (topical) and clotting factors (plasma derived compounds with higher risk of viral transmissions and thromboembolic complications).

Product Profile

- A new mechanism of action that impacts on fibrinolytic function and not on haemostasis and coagulation.
- Multifactorial process led to optimized compound **CM-352**, safe and efficacious in 4 different *in-vivo* models:
 - Intracerebral hemorrhage (ICH). *Figure A*
 - Tail bleeding associated with tPA. *Figure B*
 - Hepatectomy (*severe bleeding*) blood lost reduced by CM-352 ($p < 0.05$) but not by TXA.
 - Anticoagulant (3 mg/kg Rivaroxaban) associated tail bleeding reduced by 40% ($p < 0.001$; $n = 10$).
- **CM-352:** Optimal profile for acute systemic administration (i.v.) with short half-life, ideal for short term control of bleeding.



Intellectual Property

Strong IP position, 3 patents: WO2014012964, WO2015104343 and WO2015107139 (novel chemical series of proprietary compounds and drug repositioning). Licensed to Digna Biotech.

Papers

Orbe J et al. *J Med Chem.* 2015;58(7):2941-57.
Orbe J et al. *J Med Chem.* 2015;58(5):2465-88.