Surgical bleeding: a novel antifibrinolytic strategy

- **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) after early (1h, Figure A) and late (3h) administration
  - 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 (p<0.001).
- CM-352: Optimal profile for acute systemic administration (i.v.) with short half-life, ideal for short-term control of bleeding.

**Intellectual Property**
- New antifibrinolytic compounds. WO2014012964 (novel chemical series of proprietary compounds and drug repositioning).

**Papers**

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