### Supplemental Table. Inhibitors of VWF-mediated platelet adhesion

<table>
<thead>
<tr>
<th>Compound</th>
<th>Antithrombotic mechanism</th>
<th>Development stage</th>
<th>Preclinical and clinical antithrombotic evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>82D6A3</td>
<td>• Moab</td>
<td>preclinical</td>
<td>• Epitope overlaps with collagen-binding region in VWF A3 domain&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>• Targets VWF</td>
<td></td>
<td>• Inhibited in vitro binding of VWF to collagen, with a more pronounced effect with increasing shear stress&lt;sup&gt;1,2&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>• A3 domain</td>
<td></td>
<td>• Abolished thrombus formation in a thrombosis model in baboons without prolongation of bleeding time&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>• Interrupts VWF binding</td>
<td></td>
<td>• Humanized version has been constructed&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>6B4</td>
<td>• Moab (Fab)</td>
<td>preclinical</td>
<td>• Epitope identified as two different regions in GPIb&lt;sub&gt;α&lt;/sub&gt;&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>h6B4</td>
<td>• Targets GPIb&lt;sub&gt;α&lt;/sub&gt;</td>
<td></td>
<td>• Inhibited ex vivo VWF-mediated platelet agglutination and platelet adhesion to collagen&lt;sup&gt;6&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>• Interrupts VWF-GPIb&lt;sub&gt;α&lt;/sub&gt; binding</td>
<td></td>
<td>• Fab fragments inhibited thrombus formation in two thrombosis models in baboons without significant effect on bleeding times&lt;sup&gt;6,7&lt;/sup&gt;</td>
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<td></td>
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<td>• Fab fragments showed a broader safe therapeutic window compared to a</td>
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</tbody>
</table>
**GPIIb/IIIa antagonist in baboons**

- Humanized version was constructed and abolished thrombus formation in baboons\(^8,9\)

<table>
<thead>
<tr>
<th>AJvW2</th>
<th>AJW200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moab</td>
<td>Targets VWF</td>
</tr>
<tr>
<td>Clinical (No active clinical studies)</td>
<td>A1 domain</td>
</tr>
<tr>
<td>Interrupts (ongoing)</td>
<td>Inhibited ex vivo VWF-mediated platelet adhesion and agglutination(^10,11)</td>
</tr>
<tr>
<td>VWF-GPIba binding</td>
<td>Abolished thrombus formation and showed a superior bleeding safety profile in comparison to GPIIb/IIIa antagonism in both guinea pigs and dogs(^11,12)</td>
</tr>
<tr>
<td>Conformation epitope identified in VWF A1 domain(^10)</td>
<td>A humanized version (AJW200) was generated which inhibited thrombus formation in dogs with a safer bleeding profile compared to GPIIb/IIIa antagonism(^13,14)</td>
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<tr>
<td></td>
<td>AJW200 was well tolerated in human volunteers without bleeding complications(^15)</td>
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<tr>
<th>GPG-290</th>
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<tbody>
<tr>
<td>Chimeric recombinant protein containing gain-of-function GPIba fragment</td>
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<td></td>
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</tr>
</tbody>
</table>
• Targets VWF A1 domain
• Interrupts VWF-GPIba binding

**ARC1779**
- **Aptamer**
  - Targets VWF A1 domain
  - Interrupts VWF-GPIba binding
  - Clinical (no active clinical studies ongoing)
  - Inhibited VWF dependent platelet adhesion and agglutination
  - Inhibited thrombus formation in a cynomolgus monkey thrombosis model
  - Well tolerated in human volunteers
  - Inhibited ex vivo VWF activity in blood from patients with acute coronary syndrome
  - Raised platelet counts in patients with TTP
  - Prevented thrombocytopenia in patients with VWD type 2B
  - Reduced cerebral embolization in patients undergoing carotid endarterectomy

**ALX-0081**
- **Nanobody**
  - Targets VWF A1 domain
  - Interrupts VWF-GPIba binding
  - Clinical
  - Abolished thrombus formation in a baboon thrombosis model and showed superior therapeutic window compared to aspirin, clopidogrel and abciximab

**ALX-0681**
- **Nanobody**
  - Targets VWF A1 domain
  - Interrupts VWF-GPIba binding
  - Well tolerated and inhibited ex vivo platelet adhesion in patients having TTP or undergoing PCI
  - Entered a Phase II study in TTP patients

**rADAMTS13**
- **Recombinant protein**
  - Preclinical
  - Delays thrombus formation in a mouse thrombosis model
Cleaves VWF A2 domain
Improves experimental stroke outcome in mice

Supplemental references


