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(54) Title: BISPECIFIC BINDING MOLECULES FOR ANTI-ANGIOGENESIS THERAPY

(57) Abstract: Bispecific binding molecules, in particular immunoglobulin single variable domains such as VHHs and domain antibodies, comprising a VEGF-binding component and a Dll4-binding component in one molecule. Pharmaceutical compositions containing same and their use in the treatment of diseases that are associated with VEGF- and Dll4-mediated effects on angiogenesis. Nucleic acids encoding the bispecific binding molecules, host cells and methods for preparing same.

Fig. 48

| VHH ID | Format | description |
|---|---|---|
| A1 |  | VEGFBII038-*35gs,cys15*-DLLBII018 |
| A2 |  | VEGFBII038-*9gs*-ALB8-*9gs*-DLLBII018 |
| A3 |  | VEGFBII038-*35gs,cys15*-VEGFBII032-*35gs*-DLLBII018 |
| HSA1 |  | VEGFBII038-*35gs*-DLLBII018-HSA |
| HSA2 |  | VEGFBII038-*9gs*-VEGFBII032-*35gs*-DLLBII018-HSA |
| HSA3 |  | DLLBII039-*35gs*-VEGFBII038-*9gs*-VEGFBII032-HSA |
| HSA4 |  | VEGFBII038-*35gs*-DLLBII018-*35gs*-HSA |
| HSA5 |  | VEGFBII038-*9gs*-VEGFBII032-*35gs*-DLLBII018-*35gs*-HSA |
| HSA6 |  | DLLBII039-*35gs*-VEGFBII038-*9gs*-VEGFBII032-*35gs*-HSA |

Legend:

| Nanobody, linker or HSA | description |
|---|---|
| ■ | DLLBII018 |
| △ | DLLBII039 |
| ◍ | VEGFBII038 |
| ▩ | VEGFBII032 |
| ◇ | HSA |
| ◌ | ALB8 |
| ⌒ | *9gs* linker |
| ∿ | *35gs* linker |
| ∿• | PEGylated *35gs,cys15* linker |

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