<table>
<thead>
<tr>
<th>Angiogenic Stimulator</th>
<th>Functions</th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>VEGF</td>
<td>Inducer of angiogenesis and lymphangiogenesis.</td>
<td>34,35</td>
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<tr>
<td>FGF</td>
<td>Regulates endothelial cells proliferation, migration and differentiation.</td>
<td>35</td>
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<tr>
<td>HGF</td>
<td>Stimulates cell growth. Useful for the treatment of critical limb ischemia.</td>
<td>36</td>
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<tr>
<td>Ang1 and Ang2</td>
<td>Stimulates the matured vessel formation and regulate angiogenesis.</td>
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<tr>
<td>PDGF</td>
<td>Stimulates angiogenesis and regulate cell growth and division.</td>
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<tr>
<td>IGF</td>
<td>Stimulates angiogenesis and myogenesis and induces nerve regeneration.</td>
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<tr>
<td>Endoglin</td>
<td>Stimulates endothelial cell proliferation, extracellular matrix production and TGF-β/ALK1 signal transduction.</td>
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<td>Interleukin 8</td>
<td>Stimulates endothelial cell proliferation, survival and matrix metalloproteinases.</td>
<td>41</td>
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<td>Thyroxin</td>
<td>Stimulates early coronary angiogenesis.</td>
<td>42</td>
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<td>VE-cadherin</td>
<td>Stimulates endothelial junctional molecules.</td>
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<tr>
<td>G-CSF</td>
<td>Helps in endothelial cell proliferation and act as neuro-protective agent.</td>
<td>44</td>
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<tr>
<td>Integrins</td>
<td>Promote cell attachment and stimulates cell migration.</td>
<td>45</td>
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<tr>
<td>Ephrin</td>
<td>Helps in vascular development and angiogenic remodeling also determine the formation of arteries or veins.</td>
<td>46</td>
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<tr>
<td>eNOS</td>
<td>Stimulates angiogenesis via eNOS signaling cascade.</td>
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<tr>
<td>TGFbeta</td>
<td>Induces angiogenesis through VEGF-mediated apoptosis. Plays a dual role as a tumor suppressor in early stages and as tumor promoter in late stages of tumor progression.</td>
<td>48, 49</td>
</tr>
<tr>
<td>YKL40</td>
<td>Angiogenic factor to promote tumor angiogenesis and plays role inradioresistance, and progression of glioblastoma.</td>
<td>50, 51</td>
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<tr>
<td>HIF1α</td>
<td>Regulate tumor angiogenesis and invasion.</td>
<td>52</td>
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</table>
HDGF  Plays vital roles in cancer cell transformation, angiogenesis, apoptosis and metastasis.  

Notch/DLL4  Negative regulator of tumor angiogenesis and upregulated in tumor vasculature in cancer progression.  

Semaphorins  Anti-angiogenic agents, stimulate tumor angiogenesis. 

<table>
<thead>
<tr>
<th>Anti-angiogenic Drugs</th>
<th>Mechanism of action</th>
<th>Cancer types</th>
<th>Ref.</th>
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<td>Avastin</td>
<td>Anti-VEGF monoclonal antibody</td>
<td>Advanced metastatic colorectal cancer and glioblastoma.</td>
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<td>Sunitinib</td>
<td>Act as multi-TKI that targets VEGFR-1–3, PDGFR.</td>
<td>Kidney cancer and neuroendocrine tumors</td>
<td>76,77</td>
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<tr>
<td>Sorafenib</td>
<td>TKI which targets VEGFR-2, -3, Flt-3 PDGFR-b.</td>
<td>Primary kidney cancer, RCC, liver cancer.</td>
<td>77,78</td>
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<tr>
<td>Everolimus</td>
<td>Inhibitor of mammalian target of rapamycin (mTOR)</td>
<td>Kidney cancer and neuroendocrine tumors</td>
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<tr>
<td>Imatinib</td>
<td>(TKI) Selective inhibitor of Bcr/Abl</td>
<td>CML and GIST.</td>
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<tr>
<td>Pazopanib</td>
<td>Act as multi-targeted receptor tyrosine kinase inhibitor</td>
<td>Kidney cancer and soft tissue sarcoma</td>
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<tr>
<td>Axitinib</td>
<td>Second generation inhibitor of VEGF-1, 2, and 3.</td>
<td>Renal cell carcinoma</td>
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<td>Denibulin</td>
<td>Vascular-disrupting agent (VDA) and reversibly inhibits</td>
<td>Solid tumors</td>
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<tr>
<td>Compound</td>
<td>Function</td>
<td>Applications</td>
<td>Notes</td>
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<td>----------------------------------------------------------------</td>
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<td>(MN-029)</td>
<td>microtubule assembly.</td>
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<tr>
<td>ZD6126</td>
<td>Vascular targeting agent and VDA</td>
<td>Metastatic renal cell carcinoma and metastatic colorectal cancer</td>
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<td>ABT-571</td>
<td>VDA and acts as antimitotic agent.</td>
<td>Non-small cell lung cancer</td>
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<td>Ombrabulin (AVE8062)</td>
<td>VDA</td>
<td>Advanced-stage soft-tissue sarcoma and head and neck squamous cell carcinoma</td>
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<tr>
<td>Serial No.</td>
<td>Nature of nanoparticles</td>
<td>Anti-angiogenic activity</td>
<td>Ref.</td>
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<td>Cerium oxide</td>
<td>Ovarian tumor model</td>
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<td>Inhibition of Human Renal Cell Carcinoma Xenografts</td>
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<td>Carbon</td>
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<td>Cuprous oxide</td>
<td>Inhibition of angiogenesis via down regulation of VEGFR2 expression</td>
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<td>Carbon nanomaterials: and its derivative.</td>
<td>Anti-angiogenic activity through the down-regulation of KDR</td>
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<td>Perfluoro carbon</td>
<td>Diagnosis and treatment of atherosclerosis</td>
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<td>Magnetic mesoporous silica-based siRNA</td>
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<td>Anti-neovascular efficacy in the rabbitVx2 cancer model</td>
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