

# Development of LCN2 inhibitor for multiple sclerosis

<b>Disease Area</b>	<b>Autoimmune</b>																					
<b>Product Type</b>	Small molecule																					
<b>Indication</b>	Multiple sclerosis																					
<b>Target</b>	Lipocalin-2 (LCN2)																					
<b>Mechanism of Action</b>	Inhibition of immune cell infiltration by LCN2 inhibition																					
<b>Competitiveness</b>	<ol style="list-style-type: none"> <li>1. Differentiated MOA : LCN2-LCN2R interaction inhibition</li> <li>2. Potential to by-pass BTK-related adverse effects</li> </ol>																					
<b>Development Stage</b>	<b>H2L</b>																					
<b>Route of Administration</b>	Oral																					
<b>Key Data</b>	<p><b>1. Proposed mechanism : Inhibition of LCN2-induced neuroinflammation</b></p> <p><b>2. Hit profile compared to Tecfidera</b></p> <table border="1"> <thead> <tr> <th>Items</th> <th>Tecfidera</th> <th>LCN2 inhibitor (DN301950)</th> </tr> </thead> <tbody> <tr> <td>in vitro chemokine inhibition (ELISA, IC<sub>50</sub>, μM)</td> <td>8.8 μM (CCL2)* , 30.0 μM (CXCL9)**</td> <td>up to 6.2 (CXCL10, astrocyte)</td> </tr> <tr> <td>in vitro cytokine inhibition (ELISA, IC<sub>50</sub>, μM)</td> <td>12.2 μM (IL6)*</td> <td>n/a</td> </tr> <tr> <td>LPS-induced neuroinflammation mouse</td> <td>clinical score ~50% decrease (30 mpk, i.p.)***</td> <td>Reduced inflamm. (20 mpk, i.c.v.), Tnf mRNA ~50%, Il1b mRNA ~75% decrease</td> </tr> <tr> <td>EAE mouse</td> <td>clinical score ~62% decrease (100 mpk, i.p.)****</td> <td>clinical score ~20% decrease (5 mpk, i.p.)</td> </tr> <tr> <td>MOA</td> <td>- Oxidative stress induced Nrf2 activation - Nrf2 independent immune system control - Multi-target mechanism (NF-kB, GSH, etc.) *****</td> <td>- Inhibition of neuroinflammation by LCN2-LCN2R interaction</td> </tr> <tr> <td>Toxicity, side effect</td> <td>Kidney, liver, stomach tox. / brain infection</td> <td>No target related toxicities reported</td> </tr> </tbody> </table> <p><small>*Arthritis. Res. Ther. 2016, 18, 139; **WO2020169054; ***Front. Immunol. 2021, 12, 737065; ****Brain, 2021, 144, 3126-3141; *****Autoimmunity Rev. 2021, 144, 3126.</small></p>	Items	Tecfidera	LCN2 inhibitor (DN301950)	in vitro chemokine inhibition (ELISA, IC <sub>50</sub> , μM)	8.8 μM (CCL2)* , 30.0 μM (CXCL9)**	up to 6.2 (CXCL10, astrocyte)	in vitro cytokine inhibition (ELISA, IC <sub>50</sub> , μM)	12.2 μM (IL6)*	n/a	LPS-induced neuroinflammation mouse	clinical score ~50% decrease (30 mpk, i.p.)***	Reduced inflamm. (20 mpk, i.c.v.), Tnf mRNA ~50%, Il1b mRNA ~75% decrease	EAE mouse	clinical score ~62% decrease (100 mpk, i.p.)****	clinical score ~20% decrease (5 mpk, i.p.)	MOA	- Oxidative stress induced Nrf2 activation - Nrf2 independent immune system control - Multi-target mechanism (NF-kB, GSH, etc.) *****	- Inhibition of neuroinflammation by LCN2-LCN2R interaction	Toxicity, side effect	Kidney, liver, stomach tox. / brain infection	No target related toxicities reported
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<b>ID</b>	To be filed (Patentability confirmed)																					