

# Hit optimization and lead generation activating PROKR1 to prevent and treat sarcopenia

<b>Disease Area</b>	<i>Muscular dystrophy</i>
<b>Product Type</b>	Small molecule
<b>Indication</b>	Sarcopenia, sarcopenic obesity
<b>Target</b>	Prokineticin receptor 1 (PROKR1/GPR73)
<b>Mechanism of Action</b>	<ul style="list-style-type: none"> <li>① PROKR1 agonist</li> <li>② Activation of PROKR1-CREB-NR4A2 to increase muscle mass, strength, and basal metabolic rate</li> </ul>
<b>Competitiveness</b>	<ul style="list-style-type: none"> <li>① A novel therapeutic target and mechanism differentiated from androgens and myostatin, which have failed to demonstrate clinical efficacy</li> <li>② Unlike BYM338 (Bimagrumab, Versanis/Eli Lilly), which is a myostatin-neutralizing antibody that inhibits muscle catabolism, it is a small molecule that can be administered orally</li> </ul>
<b>Development Stage</b>	<i>Hit</i>
<b>Route of Administration</b>	Oral
<b>Key Data</b>	<div style="display: flex; justify-content: space-between;"> <div style="width: 65%;"> <p><b>A</b> Bodyweight (g), %Lean mass, %Fat mass, AUC<sub>ITT</sub> (mg/dL*min), Insulin (ng/mL), HOMA-IR</p> <p><b>B</b> AUC<sub>ITT</sub> (mg/dL*min), Insulin (ng/mL), HOMA-IR</p> <p><b>C</b> RER (VCO<sub>2</sub>/VO<sub>2</sub>), EE (kcal/hr/kg), Ambulatory activities (counts/12-hr), Grip strength (g/g bw)</p> <p><b>D</b> Ambulatory activities (counts/12-hr), Grip strength (g/g bw)</p> <p><b>E</b> Immunostaining, Fiber type (%), Fiber size (μm<sup>2</sup>), Mitochondria (per nuclei)</p> <p><b>F</b> Protein level (Male/Female) for Prokr1, pCreb / Creb, Nr4a2, Pgc1a, Tiam, Myh7, Myh4, Myh2</p> </div> <div style="width: 30%; font-size: 0.9em;"> <p><b>Improved muscle phenotype in mouse offspring by SP73C1001 exposure</b></p> <p>A. Dose-dependent decreased body weight and fat mass, and increased muscle mass in male and female offspring by SP73C1001. B. SP73C1001-induced improvement in insulin resistance. C. Increased energy expenditure by SP73C1001. D. Increased ambulatory activities and grip strength by SP73C1001. E. Increased Myh7(+) oxidative muscle fiber composition, decreased muscle fiber size, and increased mitochondria mass by SP73C1001. F. Activation of the Prokr1-Creb-Nr4a2 signaling pathway in muscle tissue by SP73C1001. PPM: particles per million diet (PPM/10 = mg/kg bodyweight, e.g. 700 PPM = 70 mg/kg bodyweight)</p> </div> </div>
<b>IP</b>	