

Discovery of a novel small-molecule drug candidate targeting IL-33

Azcuris Co., Ltd.

Disease Area	Immunology
Product Type	Small molecule (NCE)
Indication	Asthma/Atopic dermatitis
Target	Interleukin-33 (IL-33)
Mechanism of Action	Azcuris’ novel synthetic compound is a first-in-class small-molecule PPI inhibitor that binds to IL-33, thus inhibiting its interaction with ST2 (IL-33 receptor), thereby downregulating the allergic IL-33 signaling pathway.
Competitiveness	Small molecule cytokine inhibitors are more competitive than injectable antibodies in terms of ease of administration and cost. In addition, since its MOA is different from that of conventional small-molecule allergy treatment, it is expected to be a blockbuster allergy therapeutics as it can replace or co-administer conventional treatments.
Development Stage	Discovery
Route of Administration	Oral & Topical
Key Data	<div><div>■HDM induced chronic asthma model : AL 5628 vs. Surrogate dupilumab (IL-4R mAb)</div><div><div><div><div><div><div>▼</div><div>▼</div><div>▼</div><div>▼</div><div>▼</div></div><div><div>0</div><div>1</div><div>2</div><div>3</div><div>4</div><div>5</div><div>6</div><div>7</div><div>8</div><div>9</div><div>10</div><div>11</div><div>12</div><div>13</div><div>14</div><div>15</div><div>16</div><div>17</div><div>18</div><div>19</div><div>20</div><div>21</div><div>22</div><div>23</div><div>24</div><div>25</div><div>26</div><div>27</div><div>28</div></div><div><div>WT BALB/c</div><div>▼ Intranasal exposure with HDM (<i>D. farinase</i> 25 µg and <i>D. pteronyssinus</i> 25 µg)</div><div>↑ AL 5628 (30 mg/kg, qd, p.o.)</div><div>↑ Surrogate dupilumab (100 mg/kg, total, s.c.)</div><div>↑ Dexamethasone (High, H, qd, p.o.)</div><div>↑ Dexamethasone (Low, L, qd, p.o.)</div><div>Sacrifice</div><div>• EOS/NEU counts in BALF</div><div>• IgE ELISA in Serum</div><div>• Cytokine RT-PCR in Lung</div></div></div><div><div><div>Eosinophils in BALF</div><div>Numbers (10<sup>4</sup> cells)</div><div>Con Veh AL 5628 Dexa (L) Asthma</div><div>***</div></div><div><div>Neutrophils in BALF</div><div>Numbers (10<sup>4</sup> cells)</div><div>Con Veh AL 5628 Dexa (L) Asthma</div><div>*</div></div><div><div>AHR</div><div>Rrs (% of saline control)</div><div>Con Veh AL 5628 Dexa (L) Methacholine at 50 mg/ml</div><div>***</div></div></div><div><div><div>Eosinophils in BALF</div><div>Numbers (10<sup>5</sup> cells)</div><div>Con Veh AL 5628 mAb Dexa (H) Asthma</div><div>***</div></div><div><div>Neutrophils in BALF</div><div>Numbers (10<sup>5</sup> cells)</div><div>Con Veh AL 5628 mAb Dexa (H) Asthma</div><div>*</div></div><div><div>IgE in Serum</div><div>Serum total IgE (ng/mL)</div><div>Con Veh AL 5628 mAb Dexa (H) Asthma</div><div>**</div></div></div><div><div><div>IL-4 in Lung</div><div>Relative mRNA expression</div><div>Con Veh AL 5628 Dexa (L) Asthma</div><div>n.s</div></div><div><div>IL-13 in Lung</div><div>Relative mRNA expression</div><div>Con Veh AL 5628 Dexa (L) Asthma</div><div>n.s</div></div><div><div>iNOS in Lung</div><div>Relative mRNA expression</div><div>Con Veh AL 5628 Dexa (L) Asthma</div><div>**</div></div></div></div></div></div></div>
IP	Patent pending toward Republic of Korea and PCT Patent pending toward 10 major markets