

## Pharmaceutical Business

### Clinical Development as of August 1, 2018

<In-house development>

Code (Generic Name)	Potential Indication/Dosage form	Mechanism		Phase	Note
JTZ-951 (enarodustat)	Anemia associated with chronic kidney disease /Oral	HIF-PH inhibitor	Increases red blood cells by stimulating production of erythropoietin, an erythropoiesis- stimulating hormone, via inhibition of HIF-PHD.	Phase3 (Japan) Phase1 (Overseas)	In-house Co-development with Torii
JTE-052 (delgocitinib)	Autoimmune/allergic diseases /Oral, Topical *Atopic dermatitis/Topical	JAK inhibitor	Suppresses overactive immune response via inhibition of Janus kinase (JAK) related to immune signal.	Phase3 (Japan)	In-house *Co-development with Torii
JTE-051	Autoimmune/allergic diseases /Oral	Interleukin-2 inducible T cell kinase inhibitor	Suppresses overactive immune response via inhibition of the signal to activate T cells related to immune response.	Phase2 (Overseas)	In-house
JTT-251	Type 2 diabetes mellitus /Oral	PDHK inhibitor	Decreases blood glucose by activation of pyruvate dehydrogenase (PDH) related to carbohydrate metabolism.	Phase1 (Overseas)	In-house
JTE-451	Autoimmune/allergic diseases /Oral	ROR $\gamma$ antagonist	Suppresses overactive immune response via inhibition of ROR $\gamma$ related to Th 17 activation.	Phase1 (Overseas)	In-house
JTT-751 (ferric citrate)	Iron-deficiency anemia/Oral	Oral iron replacement	Corrects iron-deficiency anemia by using absorbed iron for synthesis of hemoglobin.	Phase3 (Japan)	In-license (Keryx Biopharmaceuticals) Co-development with Torii Additional indication

Clinical trial phase presented above is based on the first dose.

<Licensed compounds>

Compound (JT's code)	Licensee	Mechanism		Note
trametinib	Novartis	MEK inhibitor	Inhibits cellular growth by specifically inhibiting the activity of MAPK/ERK pathway.	Marketing application submitted (trametinib+dabrafenib) for melanoma (adjuvant) with BRAF V600 mutation in EU
Anti-ICOS monoclonal antibody	MedImmune	ICOS antagonist	Suppresses overactive immune response via inhibition of ICOS which regulates activation of T cells.	
JTE-052	LEO Pharma ROHTO Pharmaceutical	JAK inhibitor	Suppresses overactive immune response via inhibition of Janus kinase (JAK) related to immune signal.	
JTZ-951	JW Pharmaceutical	HIF-PH inhibitor	Increases red blood cells by stimulating production of erythropoietin, an erythropoiesis- stimulating hormone, via inhibition of HIF-PHD.	

Updates since the previous announcement on May 1, 2018:

<In-house development>

- JTK-351: terminated
- JTS-661: terminated
- JTT-751: advanced to Phase3 in Japan

<Licensed compounds>

- trametinib: Novartis announced that Mekinist® (trametinib) has approved in U.S,  
in combination with Tafinlar® (dabrafenib), for the treatment of BRAF V600E/K mutant melanoma(adjuvant) on April 30, 2018.\*additional indication

(Reference)

- trametinib  
Novartis announced that Mekinist® (trametinib) has approved in U.S,  
in combination with Tafinlar® (dabrafenib), for the treatment of BRAF V600E mutant anaplastic thyroid cancer. (May 4, 2018) \*additional indication.
- Novartis Pharma K.K. announced that Mekinist® (trametinib) has approved in Japan,  
in combination with Tafinlar® (dabrafenib), for the treatment of BRAF V600 mutant melanoma(adjuvant). (July 2, 2018) \*additional indication