Population Pharmacokinetic Analysis to Support and Facilitate Switching from Risperidone Formulations to Rykindo in Patients with Schizophrenia

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Table S1. Description of the clinical trials included in the population PK model development.

Trial	Planned Dosing and Sample Size	PK Sampling
CT-1S01	12.5 mg, 25 mg, 37.5 mg, 50 mg of LY03004; 8 patients per dose level	0 (within 30 min prior to dosing), 1, 3, 8 hr on Day 1, Days 2, 5, 8, 11, 15, 18, 22, 25, 29, 36, and 43 post-dose.
CT-USA-104	25 mg LY03004: 8 patients 25 mg Consta: 7 patients 50 mg LY03004: 8 patients 50 mg Consta: 8 patients	0 (within 30 min prior to dosing), 1, 3, 8 hours on Day 1, and Days 2, 5, 8, 11, 15, 18, 22, 25, 29, 32, 36, 39, 43, 50 and 57 post-dose
CT-USA-102	5 Injections of either 25 mg LY03004 or Consta: LY03004: 54 patients Consta: 54 patients	1st injection (Day 1): within 30 min prior to dosing and 3 (±15 min), 8 (±15 min), 24, 96 hr and Day 8 post-dose 2nd injection (Day 15): within 30 min prior to dosing and 3 (±15 min), 24 hr, and Day 22 after dosing; 3rd injection (Day 29): within 30 min prior to dosing and 3 (±15 min), 24 hr, and Day 36 after dosing; 4th injection (Day 43): within 30 min prior to dosing and 3 (±15 min), 24 hr, and Day 50 after dosing; 5th injection (Day 57): within 30 min prior to dosing and 3 (±15 min), 8 (±15 min), 24, and 72 hours after dosing, as well as on Days 62, 64, 67, 69, 71, 74, 78, 85, 92, 99, and 113. One PK sample was collected from 8 to 10 am (±15 min) on those days listed above.

Table S2. Exposure comparability test of active moiety of Rykindo and Consta at steady state

Parameters	Ratio% (Rykindo/Consta)	90% CI-Lower	90% CI-Upper
C_{maxss}	93.02	90.62	95.49
$AUC_{\tau ss}$	94.43	92.00	96.92
C_{minss}	121.75	115.91	127.88
PTF%	93.1	/	/

Steady state concentrations were taken following 6^{th} dose (day 70 to day 84)

C_{maxss}: Maximum simulated drug concentration at steady state;

$AUC_{\tau ss}$, Area under the concentration-time curve of one dosing interval at steady-state;

C_{minss}, Minimum simulated drug concentration at steady state;

C_{avess} - average concentration over time of one dosing interval=AUC_{ss}/14;

PTF%, concentration fluctuation =100*(C_{maxss}-C_{minss})/C_{avess}.

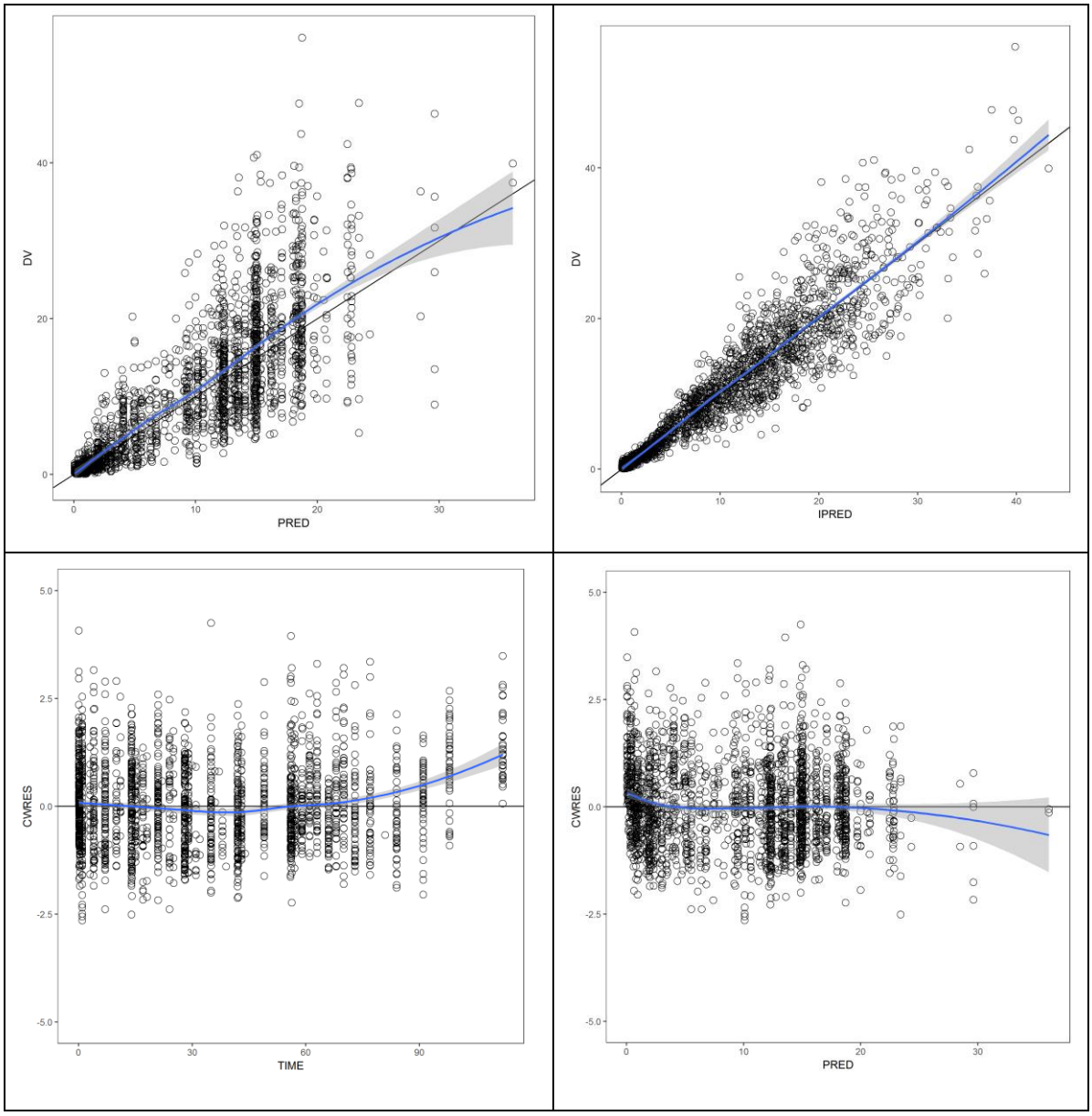

Fig. S1. Diagnostic plots of the final model of Rykindo Goodness-of-fit plots for final model of active moiety (risperidone + 9-OH-risperidone) from three phase I data of Rykindo. Panels in the upper left column display observed values of active moiety versus population predicted concentrations, the upper right column display observed values versus individual predicted concentrations, the lower left panels depict conditional weighted residuals versus time since the first dose (day), and the lower right panels depict conditional weighted residuals versus population predicted concentrations.

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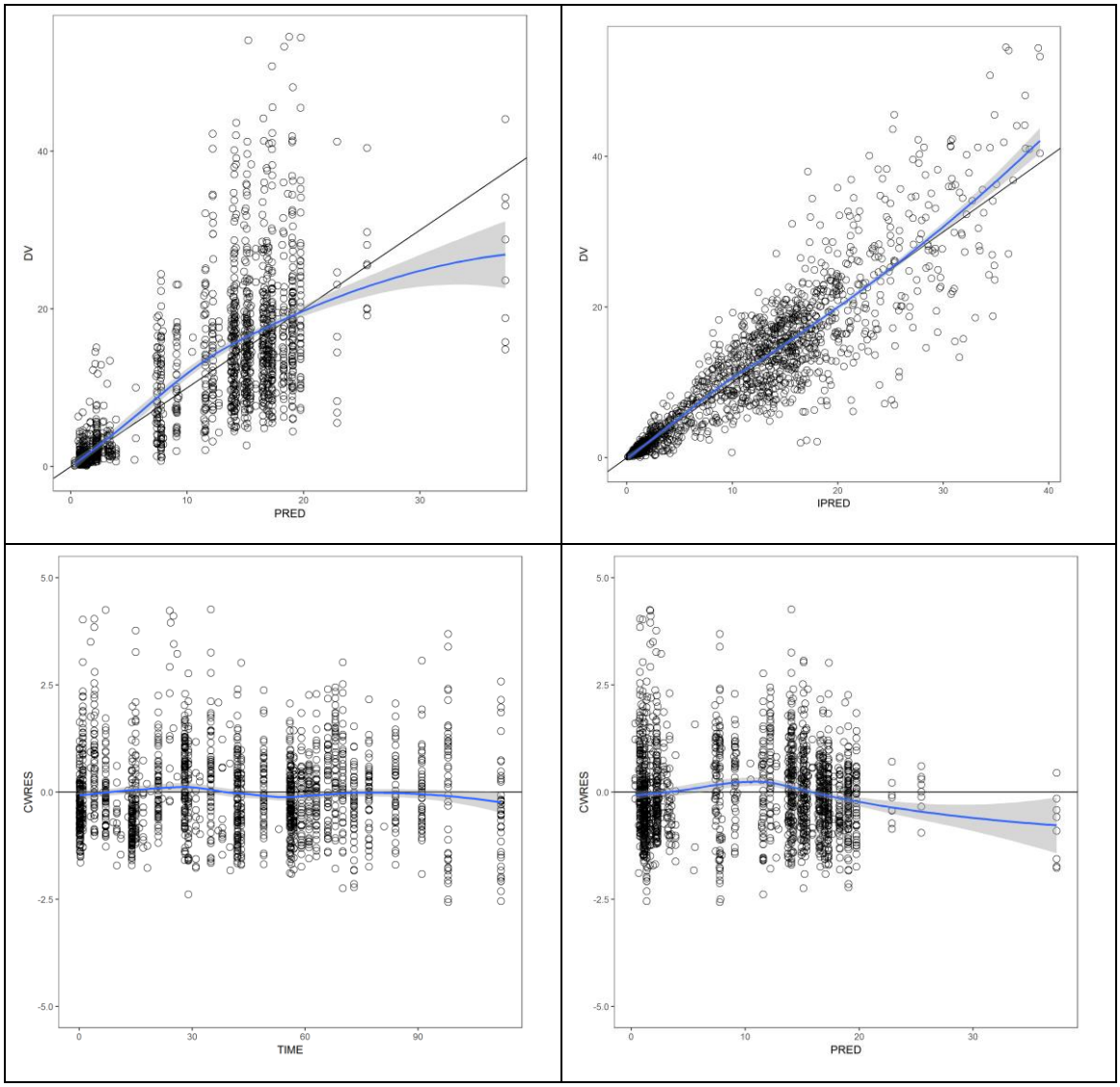

Fig. S2. Diagnostic plots of the final model of Rykindo Goodness-of-fit plots for final model of active moiety (risperidone + 9-OH-risperidone) from two phase I data of Consta. Panels in the upper left column display observed values of active moiety versus population predicted concentrations, the upper right column display observed values versus individual predicted concentrations, the lower left panels depict conditional weighted residuals versus time since the first dose (day), and the lower right panels depict conditional weighted residuals versus population predicted concentrations.

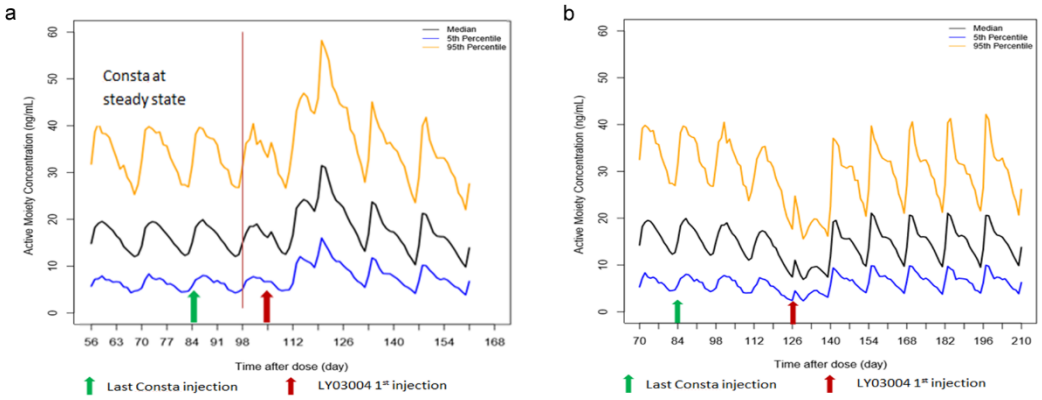

Fig. S3. Simulated PK profiles of the active moiety for the switch to Rykindo (LY03004, 25 mg every 2 weeks) 3 weeks (a) and 6 weeks (b) after the last Consta (25 mg every 2 weeks) injection.

Acknowledgments to the principal investigators

The authors thank the study investigators (listed in Table S3) for their contributions to the study.

Table S3. List of Study Investigators.

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