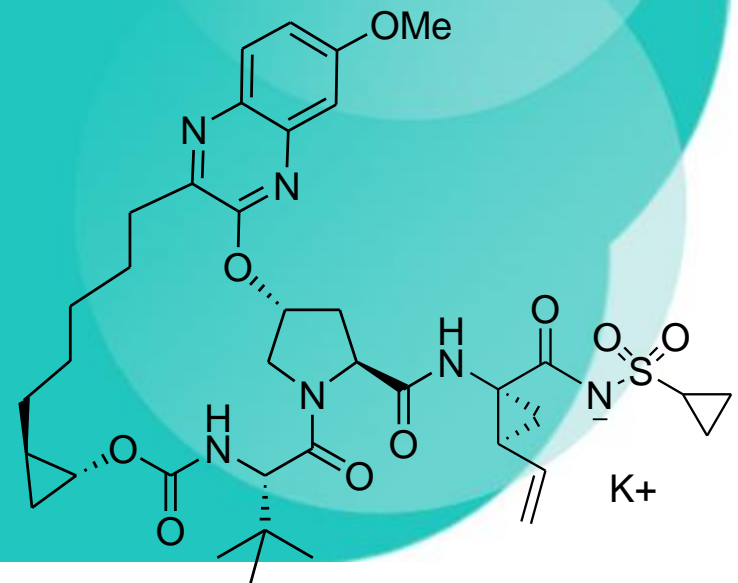


# Safety and Antiviral Activity of MK-5172, a Next Generation HCV NS3/4A Protease Inhibitor with a Broad HCV Genotypic Activity Spectrum and Potent Activity Against Known Resistance Mutants, in genotype-1 and -3 HCV-Infected Patients

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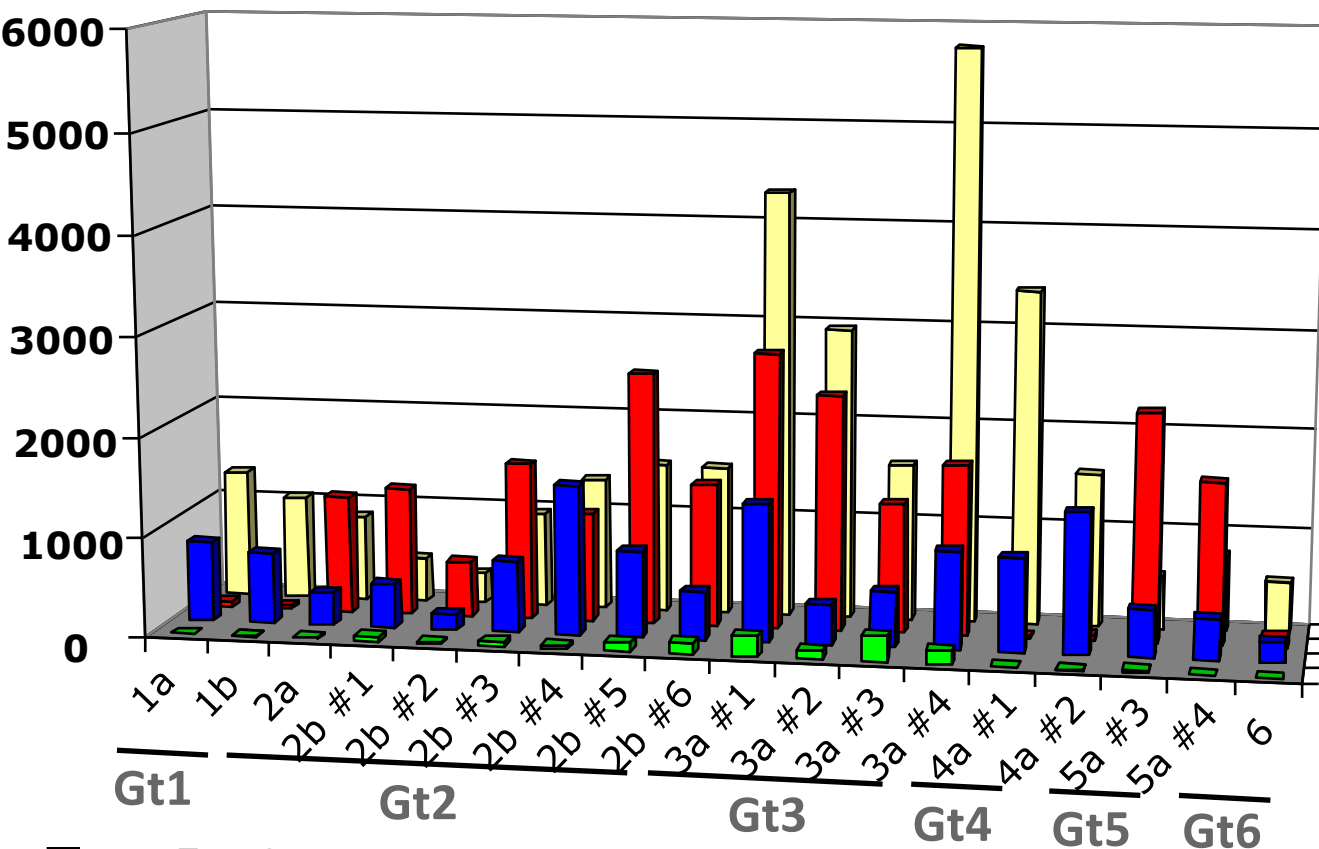
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# Disclosures

IP Fraser, A Petry, K Van Dyck, RB Nachbar, I De Lepeleire, M Robberechts, L Han, J Palcza, and JA Wagner are current employees of Merck, Sharp and Dohme and Corp.

# MK-5172 - Background

A next generation, competitive inhibitor of the HCV NS3/4a protease with a broad HCV genotypic activity spectrum



- MK-5172
- Boceprevir
- TMC-435
- Telaprevir

Enzyme	MK-5172 IC <sub>50</sub> (nM)
GT1a	0.02
GT1b	0.01
GT2a	0.09
GT2b	0.15
GT3a	0.98
GT4a	0.07
GT5a	0.07
GT6a	0.04

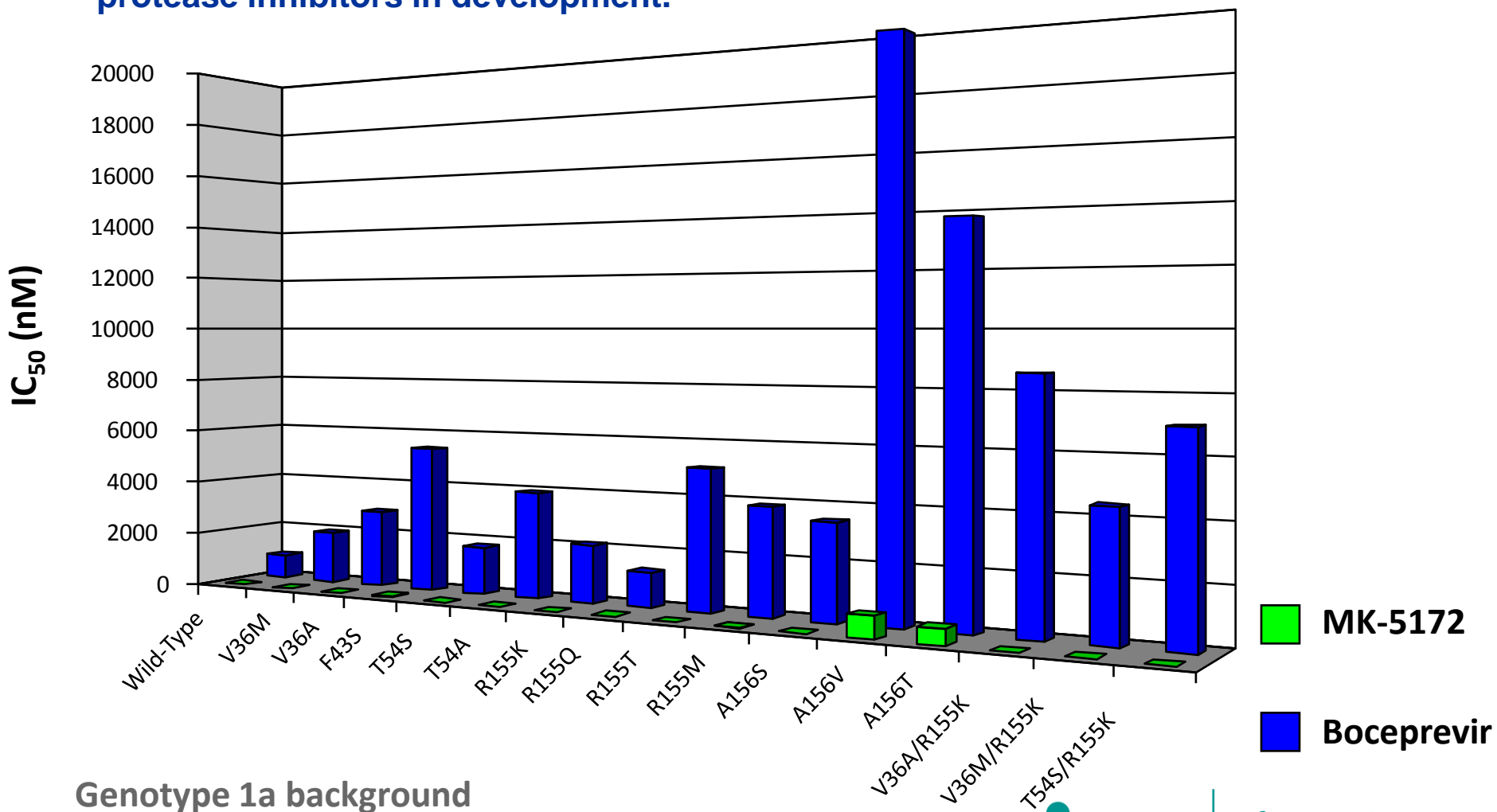


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# MK-5172 - Background

Selective, potent *in vitro* activity against viral variants that are resistant to other protease inhibitors in development.



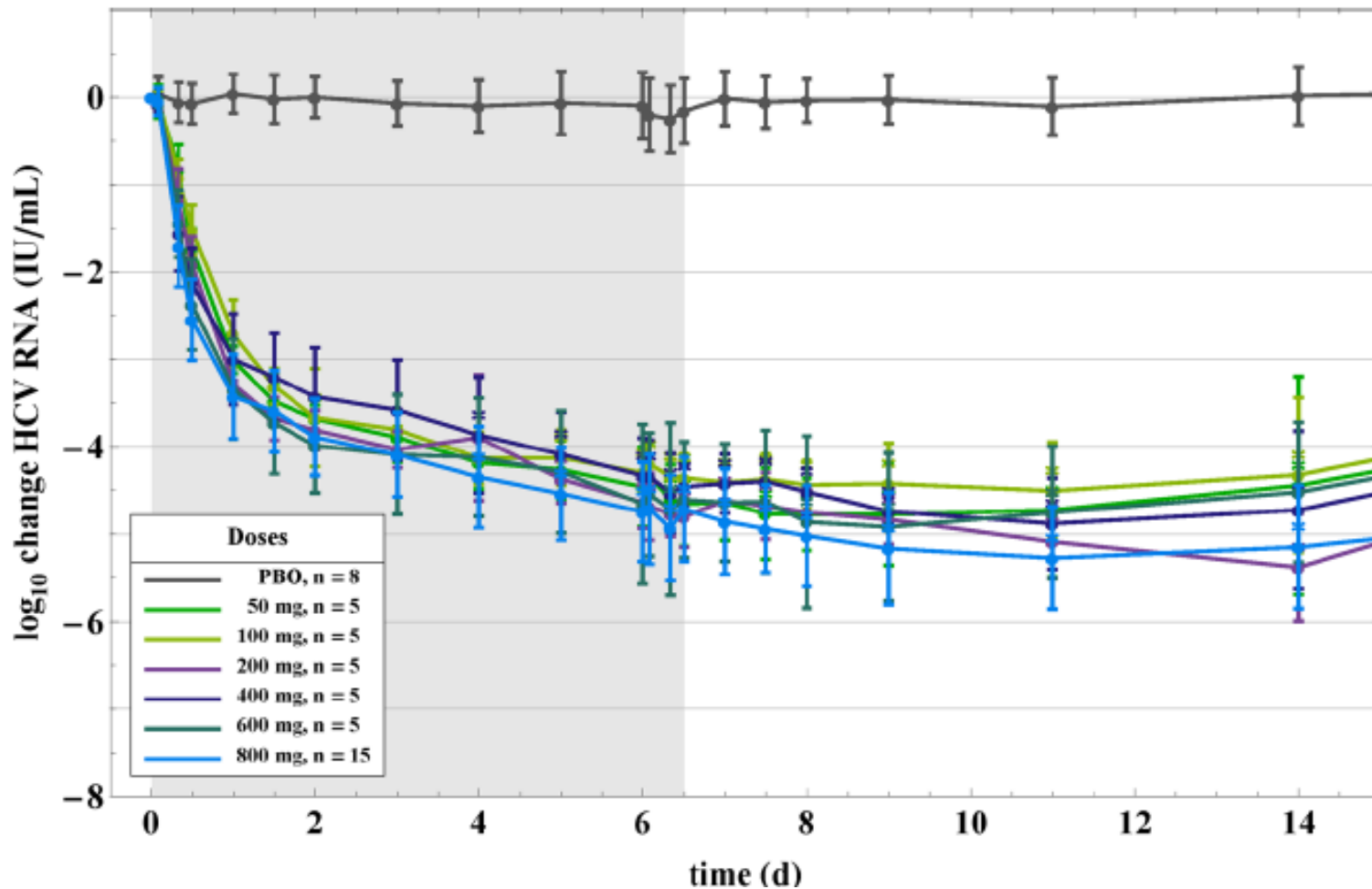
Genotype 1a background

# MK-5172 Monotherapy Phase 1b Study

- ▶ Double-blind, randomized, placebo-controlled.
- ▶ Male patients, 18-65 years of age with HCV RNA > 10<sup>5</sup> IU/mL and GT-1 or -3 chronic HCV infection without clinical evidence of cirrhosis.
- ▶ Oral doses of 50 mg (GT-1) or 100 mg (GT-3) to 800 mg of MK-5172 or placebo administered once daily (qd) fasted, for 7 consecutive days
  - 6 Patients per Panel (except GT-1, 800 mg = 18 Patients)
  - Active:Placebo = 5:1
  - Daily doses of MK-5172 <50 in GT-1 patients ongoing
- ▶ Plasma HCV RNA viral load assay: Roche Cobas TaqMAN<sup>®</sup> 2.0 assay (LLOQ = 25 IU/mL).
- ▶ Completed Patients:
  - GT-1, n = 48
  - GT-3, n = 29

Treatment Panels						
<b>GT1 Patients</b>	50 mg QD	100 mg QD	200 mg QD	400 mg QD	600 mg QD	800 mg QD
<b>GT3 Patients</b>	---	100 mg QD	200 mg QD	400 mg QD	600 mg QD	800 mg QD

# MK-5172 Monotherapy Efficacy – GT1



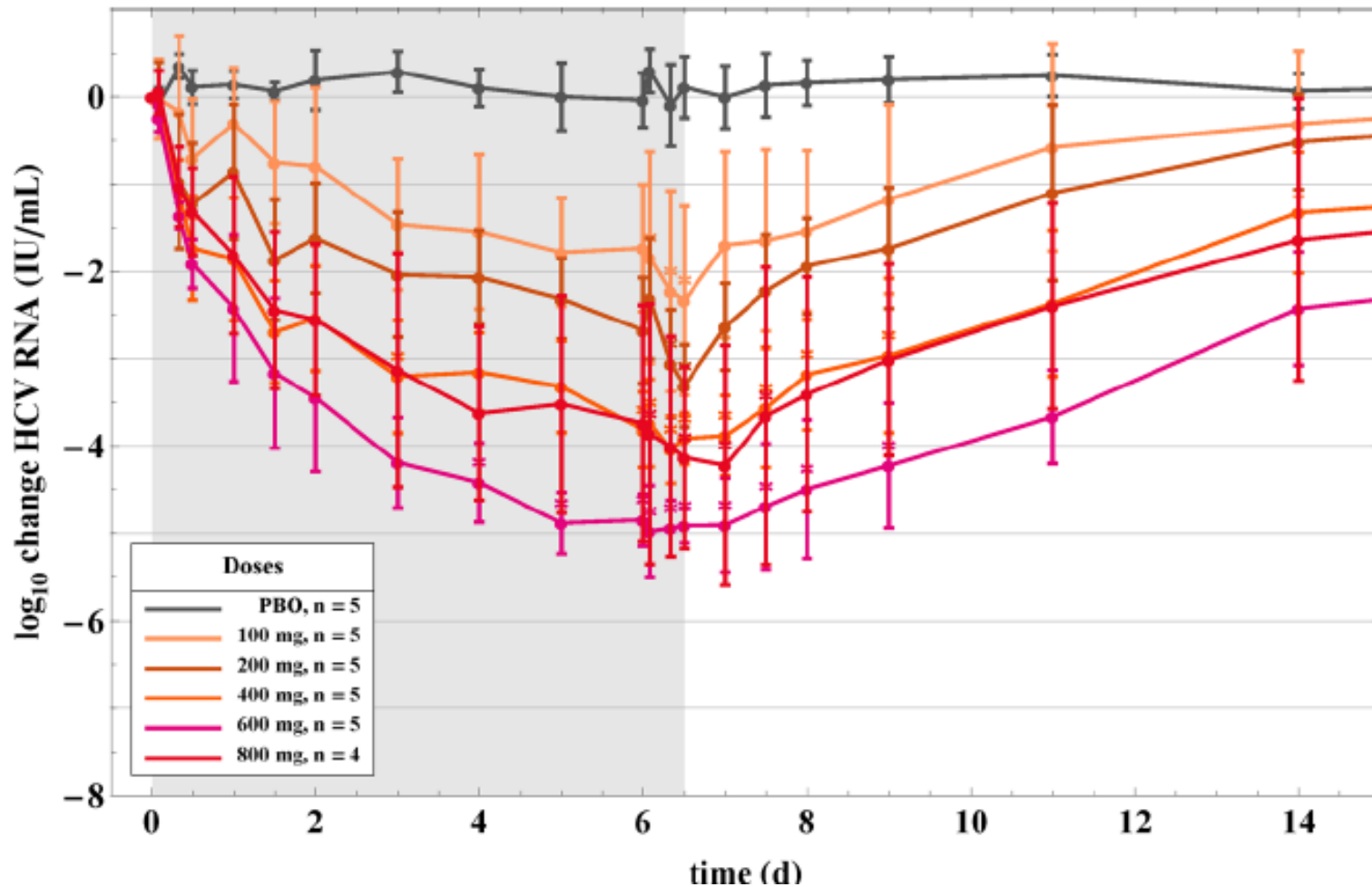
LLOQ/2 used to impute BLOQ observations to compute means

Error bars: ± 1 Standard Deviation



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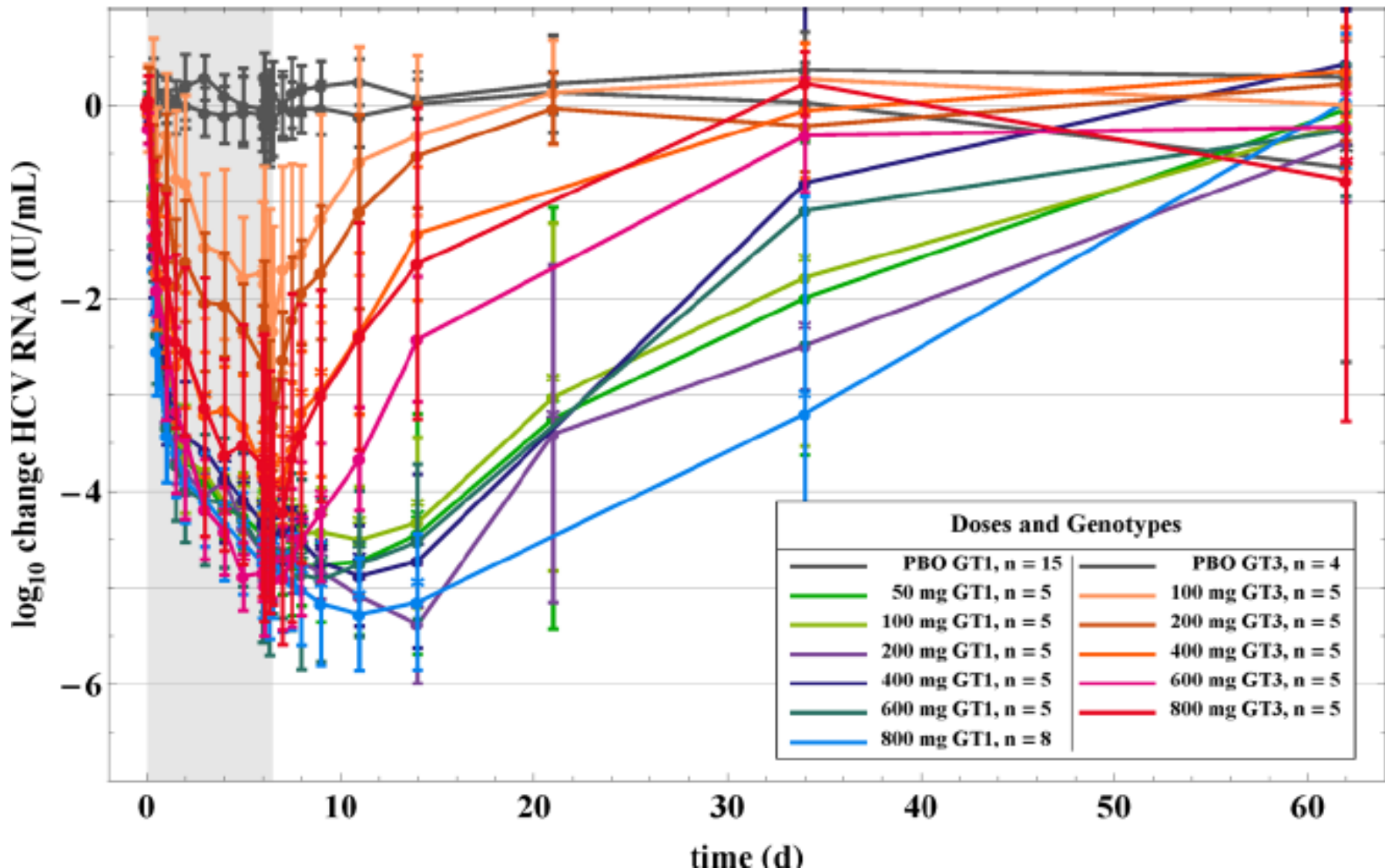
# MK-5172 Monotherapy Efficacy – GT3



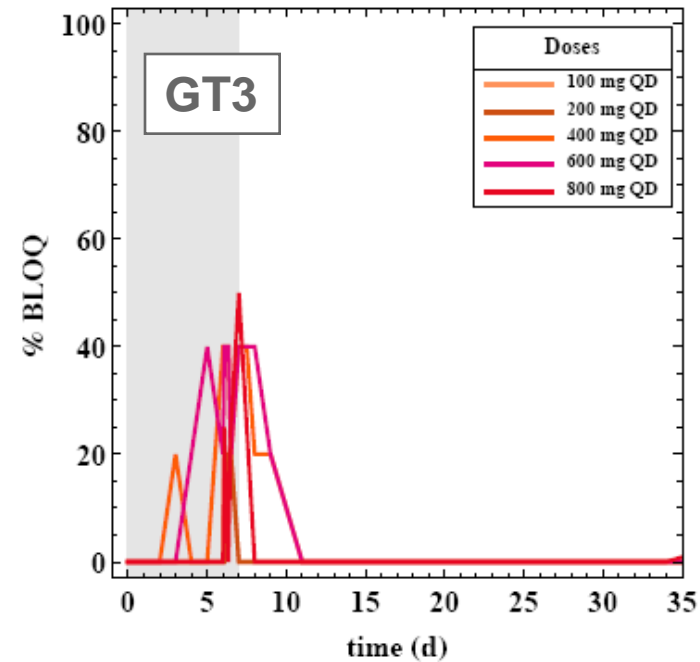
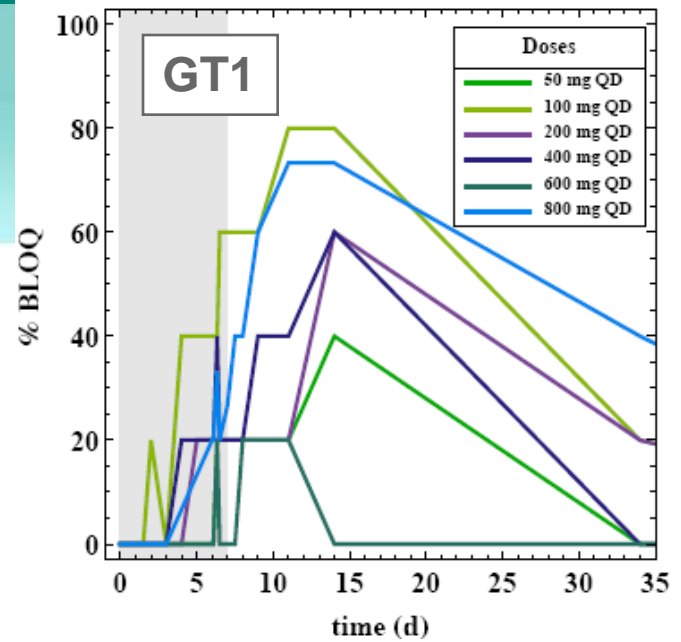
LLOQ/2 used to impute BLOQ observations to compute means

Error bars:  $\pm 1$  Standard Deviation

# MK-5172 Monotherapy – Postdose Effect



# MK-5172 Monotherapy – Reaching BLOQ



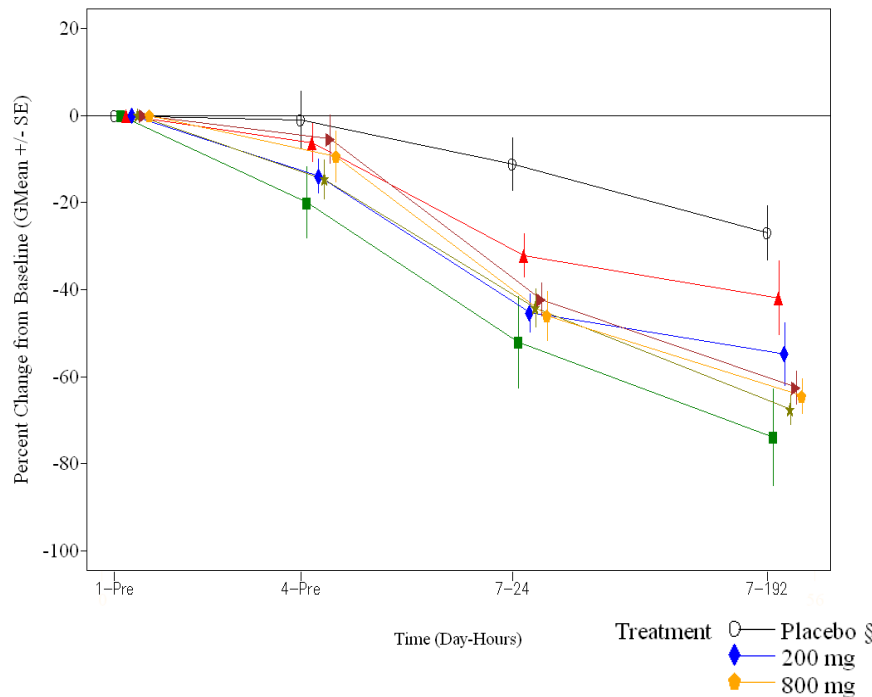
Group	Dose (mg)	N	Mean	Standard Error	n BLOQ <sup>†</sup>
GT-1	Placebo	8	-1.05	1.83	1
	50	5	-5.11	0.61	2
	100	5	-4.61	0.43	4
	200	5	-5.39	0.61	3
	400	5	-5.20	0.46	5
	600	5	-5.36	0.85	3
	800	15	-5.37	0.55	13
GT-3	Placebo	5	-0.39	0.19	0
	100	5	-2.48	0.88	1
	200	5	-3.34	0.43	1
	400	5	-4.08	0.30	2
	600	5	-5.22	0.36	3
	800	4	-4.41	1.06	2

<sup>†</sup> Number of patients with at least one value below the limit of quantification (LOQ, 25 IU/mL)

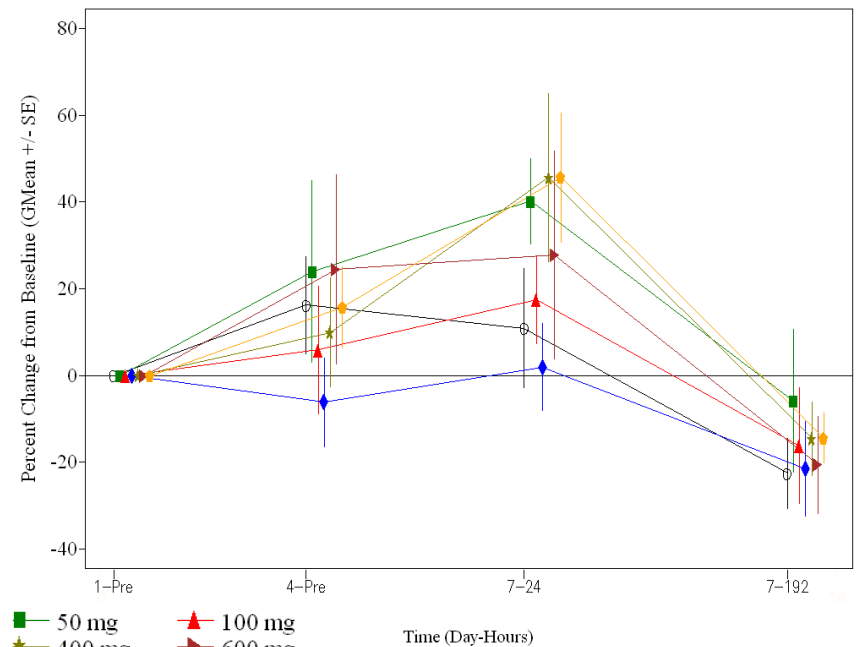
# MK-5172 – Safety Summary

- ▶ No SAEs, generally well-tolerated
- ▶ Most common AEs (reported by  $\geq 2$  patients): headache, tiredness, nausea, loose stools, and pruritus.
- ▶ No consistent treatment-related changes in vital signs or ECG safety parameters.

## ALT



## Total Bilirubin



§ Placebo is pooled over panels

# Conclusions

- ▶ MK-5172 demonstrated potent and rapid viral load reductions with 7 days of monotherapy
  - 75% (30/40) of patients with chronic GT1 infection achieved reductions in plasma HCV RNA to BLOQ.
- ▶ Antiviral activity persisted for several days beyond the treatment period in GT-1 patients.
- ▶ MK-5172 was generally well-tolerated with no SAEs, and no discontinuations due to AEs or safety laboratory abnormalities.
  - The current study is ongoing (GT1, daily doses <50mg)
- ▶ These findings support further clinical investigation of MK-5172 for the treatment of chronic HCV-infection.



# Discussion

- ▶ Multiple oral doses of MK-5172 monotherapy up to 800 mg daily for 7 days were generally well-tolerated in HCV-infected patients.
- ▶ HCV viral RNA declined rapidly after the first dose of MK-5172.
  - Mean maximum reductions from baseline of HCV viral RNA (SEs) were **5.4** (0.38) and **5.22** (0.16)  $\log_{10}$  IU/mL for GT-1 and -3, respectively.
- ▶ No on-treatment viral load rebound was observed in any patient.
- ▶ Mean viral load reductions with 7 days of MK-5172 monotherapy in GT-1 patients were similar among all dose groups from 50- to 800-mg qd. However, more patients achieved viral load suppression to below the limit of quantitation at higher doses, with a greater proportion of patients with plasma HCV RNA persisting below the limit of quantitation at higher doses.
  - 75% (30/40) of GT- 1, and 38% (9/24) of GT- 3 HCV-infected patients achieved HCV RNA levels below the limit of quantitation\_ with a 7 day monotherapy course of MK-5172
  - 87% (13/15) of GT-1 HCV-infected patients treated with 800 mg MK-5172 qd monotherapy achieved undetectable plasma HCV RNA below the limit of quantitation.
- ▶ Mean time to viral load nadir > 2 days after last dose.
- ▶ By the 1 month follow-up visit, mean plasma levels of HCV RNA were still below baseline for all dose levels in GT-1 patients, and for the highest dose levels in GT-3 patients



# Acknowledgements

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- Clinical Research Unit staff
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