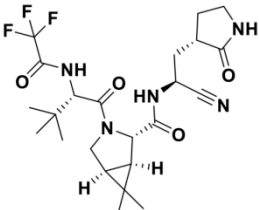
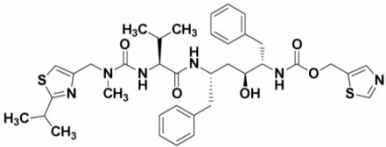








Supplementary Material:

The development of an oral solution containing nirmatrelvir and ritonavir and assessment of its pharmacokinetics and stability

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Table S1. The basic physical and chemical properties of NRV and RTV [1–3].

Generic Name	NRV	RTV
Chemical name	(1R,2S,5S)-N-((1S)-1-Cyano-2-((3S)-2-oxopyrrolidin-3-yl) ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo [3.1.0] hexane-2-carboxamide	10-Hydroxy-2-methyl-5-(1-methylethyl)-1-[2-(1methylethyl)-4-thiazolyl]-3,6-dioxo-8,11-bis(phenylmethyl)-2,4,7,12-tetraazatridecan-13-oic acid, 5-thiazolylmethyl ester, [5S-(5R*,8R*,10R*,11R*)]
CAS	2628280-40-8	155213-67-5
Chemical Formula	C ₂₃ H ₃₂ F ₃ N ₅ O ₄	C ₃₇ H ₄₈ N ₆ O ₅ S ₂
Molecular Weight	499.54	720.95
State	A non-hygroscopic, white to pale-colored crystalline powder	A non-hygroscopic, a white to light tan powder
Structure		
Solubility	It has low solubility in water and buffered aqueous media.	It is almost insoluble in water.
pKa	–	2.01 and 2.51
Melting point	about 192 °C	about 123 °C
Logp	0.845(predictive)	The partition coefficient in the n-octanol-phosphate buffer (0.05 mol/L, pH = 7.4) system was 4.7×10^4
BCS classification	BCS II / IV	BCS II

	Shape			Description	Manufacture
	front	back	side		
Paxovid®				A pink film-coated tablet	Dry granulation
	length 17.5 mm	width 8.5 mm	thickness 5.7 mm		
Paxovid®				A white to off-white, film-coated tablet	Hot melt extrusion, amorphous solid dispersion
	length 17.1 mm	width 9.1 mm	thickness 6 mm		

Figure



BCS: biopharmaceutical classification system; NRV: nirmatrelvir; RTV: ritonavir; -: no data.

Table S2. Selected marketed products containing cosolvent-based systems [4].

Drug substance	BCS	Trade name	Indication	Company	Formulation
Ritonavir	II	Norvir®	HIV infections	AbbVie	ethanol, water, polyoxyl 35 castor oil, propylene glycol
Lopinavir / Ritonavir	II / II	Kaletra®	HIV infections	AbbVie	ethanol, propylene glycol, polyoxyl 40 hydrogenated castor oil, povidone
Tipranavir	II	Aptivus®	HIV antiviral	Boehringer Ingelheim	polyethylene glycol, vitamin E polyethylene glycol succinate, water, propylene glycol
Cyclosporine	II	Neoral®	Anti-immune	Novartis	alcohol, propylene glycol, corn oil-mono-di-triglycerides, polyoxyl 40 hydrogenated castor oil, DL- α -tocopherol
Amprenavir	II	Agenerase®	HIV antiviral	GSK	polyethylene glycol 400, propylene glycol, vitamin E polyethylene glycol succinate
Nimodipine	II	Nymalize®	Hypotensive	Azurity	ethanol, glycerin, methylparaben, polyethylene glycol 400

BCS: biopharmaceutical classification system.

Table S3. Solubility of NRV and RTV in different organic solvents.

	Concentration of NRV (mg/mL) *	Concentration of RTV (mg/mL) [1].
Ethanol	16.5<S<33	165
Ethyl acetate	>57	1.5
Propylene glycol	<1.6	>200

* Crude concentration.

References

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