How the rise of oral peptides like Icotrokinra triggers the revival of LPPS

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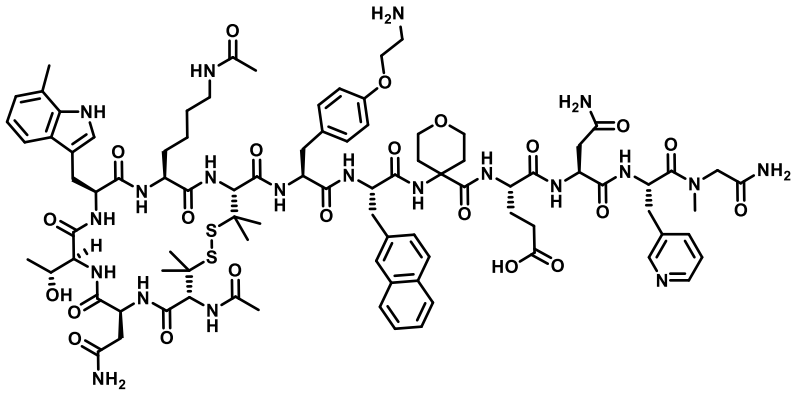
Icotrokinra[1] is a first-in-class oral peptide *IL*-23-receptor inhibitor under FDA and EMA review for plaque psoriasis, with planned evaluation in other *IL*-23-mediated disorders. Co-developed by Johnson & Johnson and Protagonist, the 13-residue cyclic peptide incorporates seven non-natural amino acids and can be isolated as crystalline material.



The molecule is fully GI-resistant and exhibits antibody-comparable binding, while clinical reports indicate superior skin-clearance versus marketed oral small molecules, demonstrating that oral peptides can bridge biologics' selectivity and small molecules' distribution advantages. Scaling oral peptides to therapeutic volumes, however, creates new manufacturing imperatives: the high API demand and low target cost-of-goods favor liquid-phase and fragment-based strategies over traditional *SPPS* workflows. This presentation will also compare *SPPS* and *LPPS* approaches with respect to scalability, cost drivers, and regulatory considerations for commercial supply.

[1] Fourie, A.M., Cheng, X., Chang, L. *et al*. *Sci Rep,* **2024**, 14, 17515.
https://doi.org/10.1038/s41598-024-67371-5