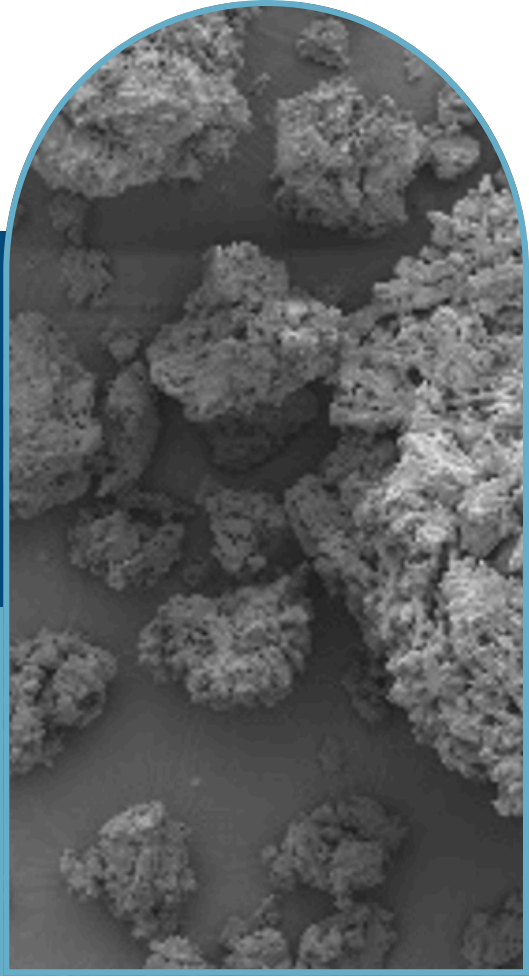
solvias

IMPROVING THE SOLID-STATE PROPERTIES OF A PEPTIDOMIMETIC THERAPEUTIC

Combining salt screening and crystallization optimization to improve purity and developability



A pharmaceutical company was developing a peptidomimetic therapeutic with a molecular weight of approximately 1,550 Da and a combination of natural and unnatural amino acids. The compound was available as an amorphous acetate salt, but the drug developer had concerns about its hygroscopicity and wanted to improve its purity. In addition, the team was interested in searching for alternative salt forms that could offer superior properties. To identify a crystalline salt with an improved overall developability profile and establish suitable crystallization conditions, the company partnered with Solvias.

THE CHALLENGES

Poor Physico-Chemical Properties of the Amorphous Salt
The initial amorphous acetate salt was hygroscopic, and the customer was concerned about potential deliquescence and physical instability of an amorphous form in the drug product.

Suboptimal Purity
Although the amorphous acetate salt had a reasonably high purity, the company wanted a purity that exceeded 99.0 area-%.

OUR COLLABORATIVE APPROACH

Screening for Crystalline Versions of the Acetate Salt
Solvias performed 32 high-throughput screening experiments were performed on 1/3 of a 96-well microtiter plate to search for crystalline forms of the acetate salt. Several promising crystallization conditions were discovered.

Screening for Other Salts of the Peptide
64 high-throughput screening experiments were performed on the other 2/3 of the 96-well microtiter plate to search for crystalline forms other salts. The amorphous acetate salt was equilibrated with 8 other potential salt formers in 8 solvent systems each. Potential leads were found with 2 other salt formers.

Scale-Up of the Crystalline Acetate Salt
Several scale-up experiments were carried out, and while one solvent system led to a crystalline form of the acetate sale with >99.0 area-% purity, the yield was suboptimal. Further solvent systems were subsequently explored on a laboratory scale and successfully improved the yield.

Scale-Up of Other Salt Leads
Salt leads with 2 other salt formers (adipic acid and hydrochloric acid) were also scaled up and characterized by a variety of physicochemical methods to provide potential back-up alternatives to the acetate salt.

Purity Testing and Comparison of Properties
The crystalline acetate salts showed superior purity compared to the amorphous form with 3 different crystallization conditions leading to > 99.0 area-% purity. The crystalline adipate salts and the crystalline hydrochloride salts also led to improved purity but were inferior to the acetate salts in terms of their physicochemical properties.

THE RESULTS

- The amorphous acetate salt could successfully be crystallized with a purity of > 99.0 area-%.
- Two new alternative salt formers were also identified in the screening and demonstrated to lead to crystalline salts that could serve as backup candidates.
- The crystalline acetate salt was selected as the solid form with the best combination of properties for development.
- Optimization of the solvents used in the crystallization process improved the yield of the acetate salt further.

CONCLUSION

A combined salt and crystallization screening led to multiple improved solid forms of a peptidomimetic therapeutic that were crystalline and highly pure. A crystalline salt candidate that was suitable for further development was selected.

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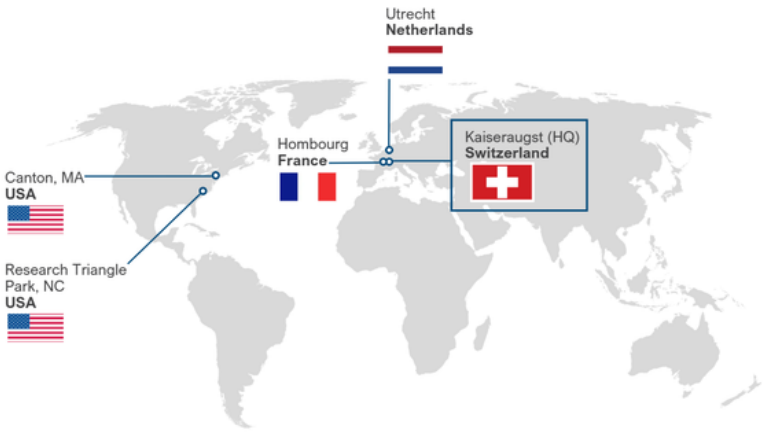
- 5 centers of excellence



Contact us to speak with an expert: info@solvias.com

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