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Ultrahigh-Concentration Subcutaneous Delivery of Biotherapeutics Enabled by a High Glass Transition Temperature Excipient

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Introduction

- High dose protein therapeutics are central to modern drug pipelines, yet many remain limited to intravenous administration.
- While subcutaneous delivery offers greater patient convenience, it is limited by protein instability at high concentrations and elevated formulation viscosity that compromises injectability.
- We present a novel formulation platform, using a proprietary high glass transition temperature (Tg) excipient, that stabilizes proteins during spray drying and enables ultra-high concentration subcutaneous delivery of biotherapeutics such as monoclonal antibodies.

Methods

- Protein microparticles comprising a clinically relevant antibody biotherapeutic and a proprietary excipient were spray dried and suspended in a non-aqueous carrier (**Figure 2**).
- The high-Tg excipient enhanced protein stability and promoted spherical particle morphology.
- Injectability and stability, as well as pharmacokinetics and efficacy following subcutaneous administration in preclinical models, was evaluated after the biotherapeutics were reformulated as ultra-high-concentration suspensions.

Results

- Smooth, glassy particles, enabled by protective excipient spray drying, drive syringeability (**Figure 3**, **Figure 4**).
- Demonstrated across >10 modalities (<1 kDa to ~160 kDa), Manufactured using industry-standard spray drying and commercially available equipment, positioning aseptic spray drying as a scalable next-generation capability
- High-concentration formulations reduced required injection volumes relative to dose-matched aqueous controls while maintaining comparable pharmacokinetics and efficacy.

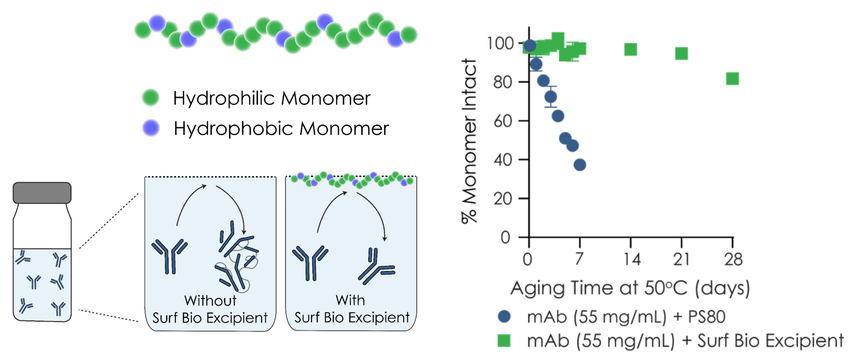
Technology Background

- Proprietary excipient designed to stabilize biotherapeutics across formulation, spray drying, storage, and injection (**Table 1**).
- Excipient demonstrates improved stability of aqueous mAb after stressed aging (**Figure 1**).

Table 1. Comparison of novel excipient to common surfactant

Surf Bio Protective Excipient	Common Surfactants
Prevents interfacial aggregation (no micelles)	Micelle formation can destabilize proteins
Robust excipient engineered for biotherapeutic stability	Chemically and enzymatically degradable
High glass transition temperature (glassy)	Low glass transition temperature (sticky/tacky)

Figure 1. Excipient enabled stabilization of aqueous mAb



Data on File.
Klich JH, *et al. Adv Ther.* 2023; 6:2200102.

Figure 2. Particle-based, ultra high concentration suspension formulations

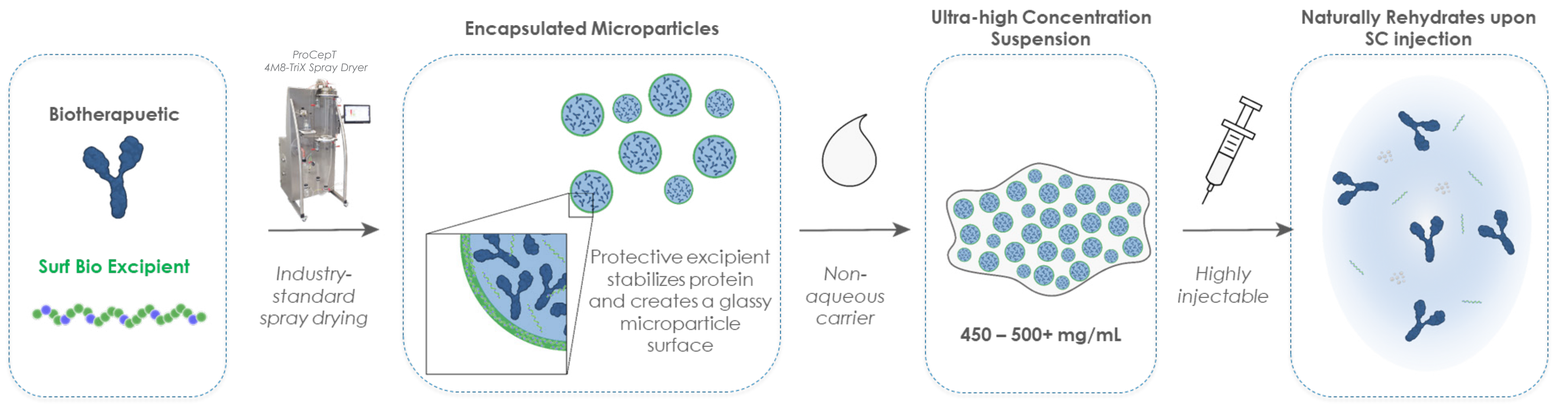


Figure 3. SEM of spray dried mAb particles

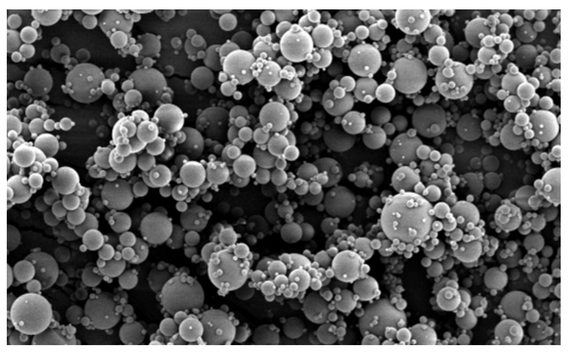


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Figure 4. Injectability of high concentration suspension formulations

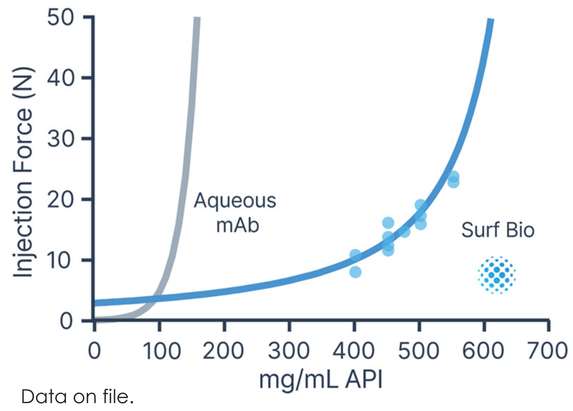

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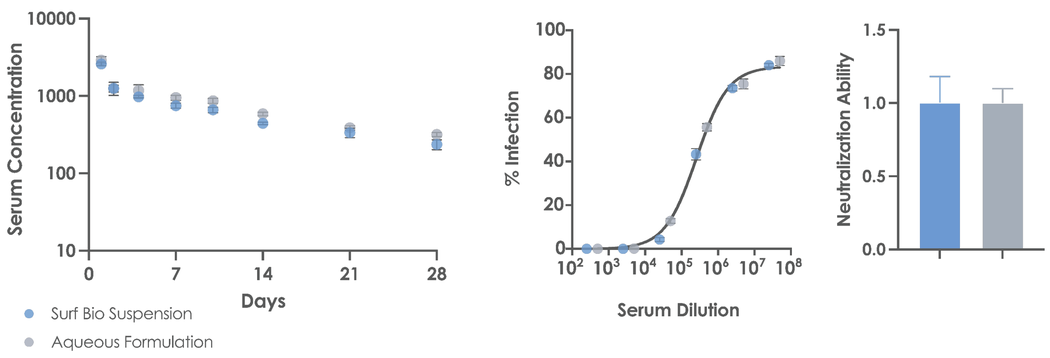
Figure 5. Rodent PK equivalence and neutralization potency is maintained at ultra-high concentration for an anti-Covid mAb



SC dosing in rodents; Surf Bio suspension ~400 mg/mL vs aqueous formulation ~20 mg/mL, dose-normalized. PK profiles are statistically insignificant. Data on file.
Jons CJ, *et al. Sci. Transl. Med.* 2025; 17(812), eadv6427.

Conclusions

- **Excipient-enabled spray drying produced protein microparticles that were suspended in a non-aqueous carrier, enabling high-concentration formulations with maintained injectability, stability, and exposure comparable to aqueous formulations while reducing injection volume.**
- **This platform uses spray-drying to unlock a broader design space for high-concentration subcutaneous biologics, advancing patient-centric, at-home therapies.**

References

1.Mann JL, *et.al. Sci Transl. Med. 2020*; 12(550), eaba6676.
2.Klich JH, et al. Adv Ther. 2023; 6:2200102.
3.Jons CJ, *et al. Sci. Transl. Med.* 2025; 17(812), eadv6427.

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