XeriJect™: Enabling subcutaneous delivery of high-concentration monoclonal antibodies

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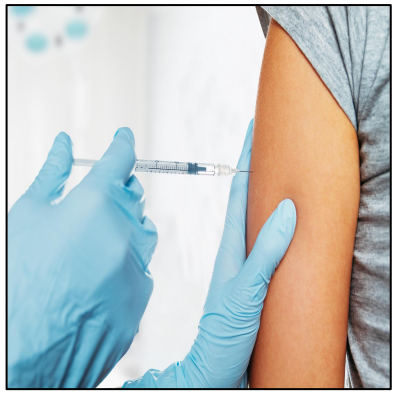
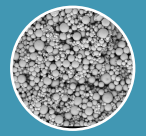
XeriJect™ Enables Subcutaneous Delivery of High Concentration Monoclonal Antibodies

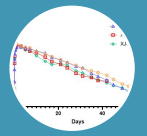
XeriJect™





High-concentration viscoelastic suspensions

Pharmaceutical elegant presentation



Pharmacokinetics comparable to aqueous formulations

Good injection site tolerability

Xeris Pharmaceuticals, Inc.

XERIS

from ancient Greek ξηρός (xērós, meaning "dry")

Corporate Headquarters & Product Development Center
Fulton Market

Founded 2005

2006 – 1st XeriJect™ Patent

2018 – IPO ~$98M NASDAQ: XERS

2019 – Gvoke PFS/ HypoPen® FDA Approved Sep

2021 – Ogluo® EMA Approved Feb

2022 – Xeris acquired StrongBridge Oct; XeriJect™ partnership Oct; FDA Approved Dec

2023 – XeriJect™ partnership Nov; XeriJect™ partnership Mar

171 patents globally issued (34 in US)
111 patent applications pending globally (16 in US)
60 technology patents

Subcutaneous vs. Intravenous Administration of Monoclonal Antibodies

Benefits of SC Administration vs. IV[1]

- Shorter clinic/office visits for the patient
- Optimized use of resources (Cost Savings)
- Self-administration is possible
- Less invasive than IV administration
- IV requires placement of port systems with risk of systemic infections

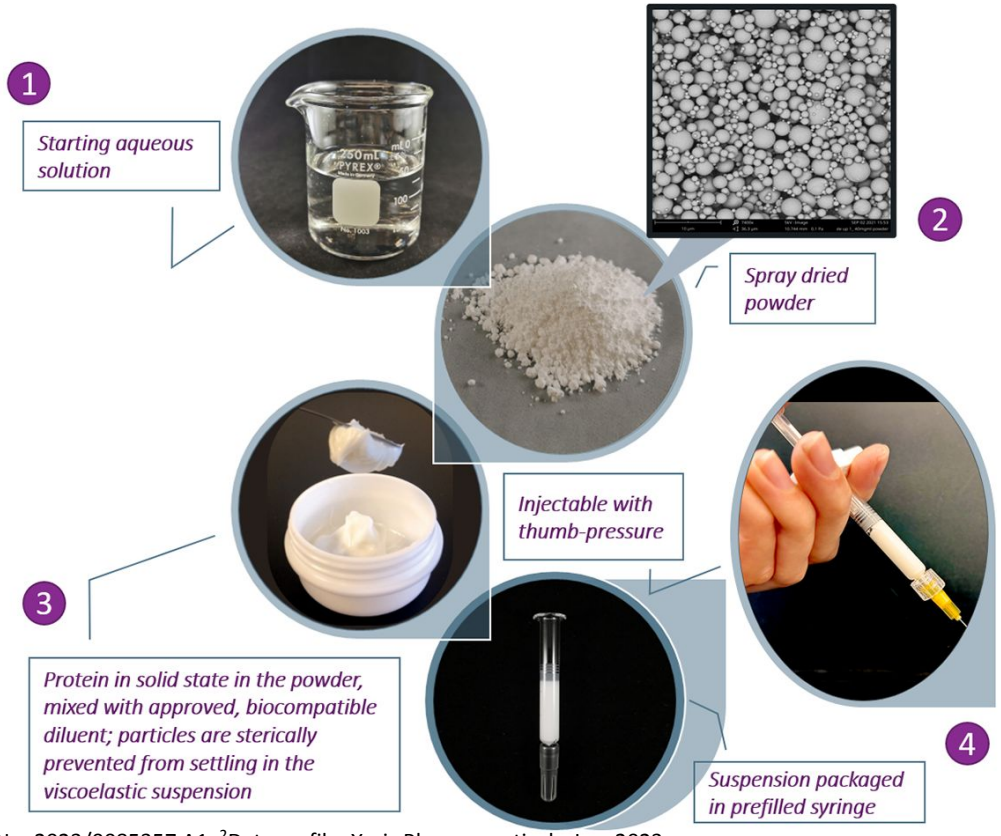
Challenges of SC Administration vs. IV[1]

- Administration of larger fluid volumes**
- Minimization of adverse events at the injection site
- Absorption and bioavailability

****XeriJect™ Enables Delivery of Monoclonal Antibodies by Short SC Injection via High Concentration, Low Volume Formulation**

[1]Jackisch C, et.al. Subcutaneous Administration of Monoclonal Antibodies in Oncology. *Geburtshilfe Frauenheilkd*. 2014;74(4):343-349

XeriJect™: Stability of a Solid + Syringeability of a Fluid Common, Scalable Pharmaceutical Processes [1,2]



KEY FEATURES

- **Ready-to-use:**
  No reconstitution or mixing required
- **High drug loading / low injection volume**
  (> 400 mg/mL)
- **Short Injection time**
  (< 30 seconds, up to 2mL)
- **Administered IM and SC through**
  standard PFS syringes and needles
- **Long-term 2-8° C stability**
  Improved CRT stability

[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023

XeriJect™ Formulation Platform

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XeriJect™ Formulation Platform[1,2]

Manufacturing Process

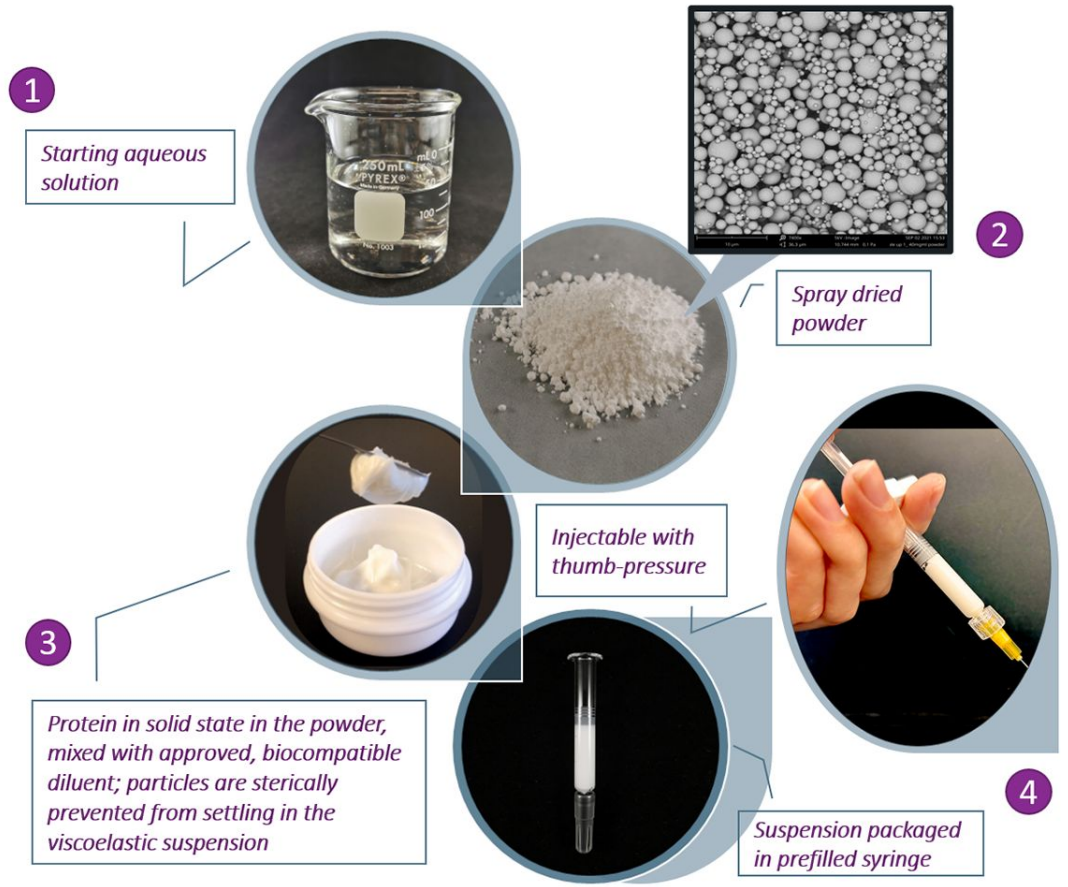
- Formulation Composition/Excipients
- Primary Powder Drying
- Secondary Powder Drying
- Powder Blending with nonaqueous diluent to form Viscoelastic Suspension (VES)

Powder Characterization

- Morphology
- Particle Size and Size Distribution

XeriJect™ Characterization

- Trastuzumab Concentration
- Injection Force
- Stability



[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023

XeriJect™ Formulation Platform[1,2]

Spray drying

- Standard spray drying process with custom designed proprietary equipment
- Highly scalable

Suspension mixing

- Planetary-centrifugation mixer to create viscoelastic suspensions

Syringe filling/piston placement

- Commercial suspension filling and piston placement instruments

[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023

Formulation Components[1,2]

Aqueous mAb solution is processed to a powder

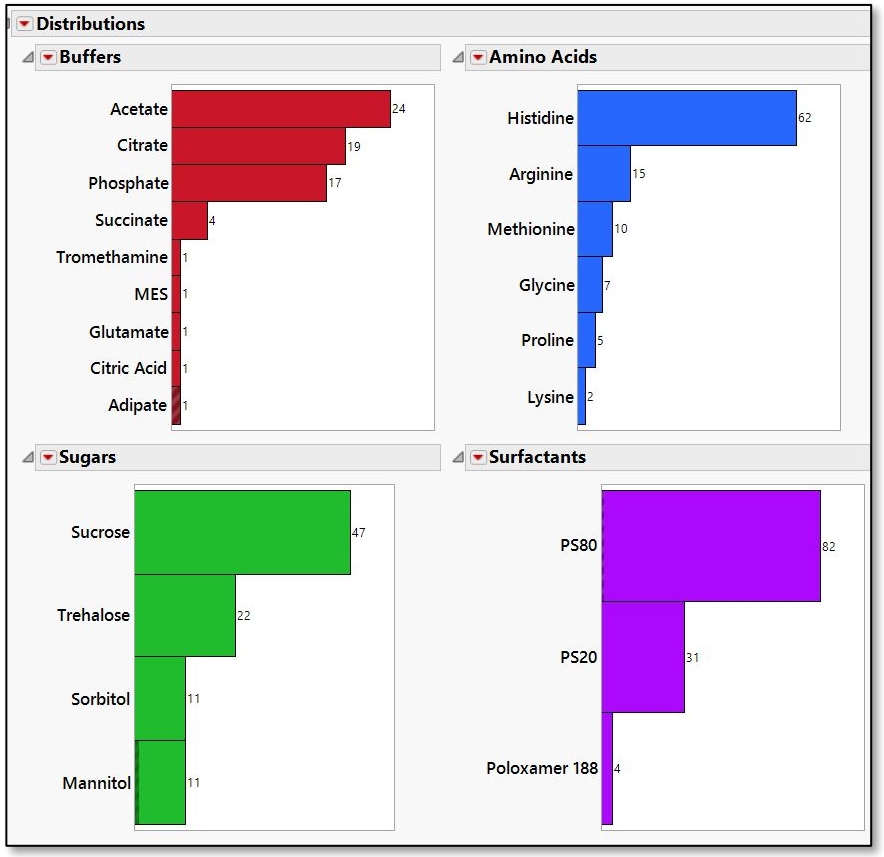
- Spray drying in a common approach

Spray dryer feed solution contains mAb and common excipients found in commercial mAb drug products selected from:

- Buffers
- Amino Acids
- Sugars
- Surfactants

Powders are secondary dried to reduce moisture content to < 2% (w/w) before blending into VES formulation

Formulation Excipients found in <u>124</u> Commercial mAb Drug Products[2,3]



[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023
[3]FDA Purple Book. Updated July 11, 2023. Accessed July 1, 2023. https://purplebooksearch.fda.gov/

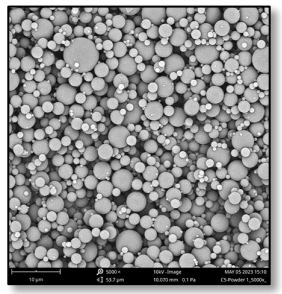
XeriJect™ Viscoelastic Suspension (VES)

Spray dried powder is blended with diluent to yield viscoelastic suspension[1,2]

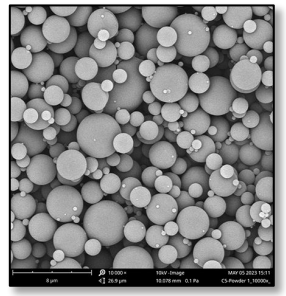
- Powder concentration in the VES exceeds > 600 mg/mL
- Blending process does not impact particle size and morphology

Spray Dried Powder

Powder (5kx)

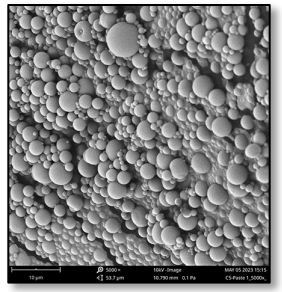


Powder (10kx)

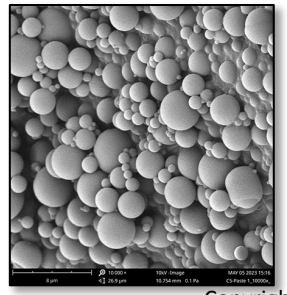


Blended VES

VES (5kx)



VES (10kx)



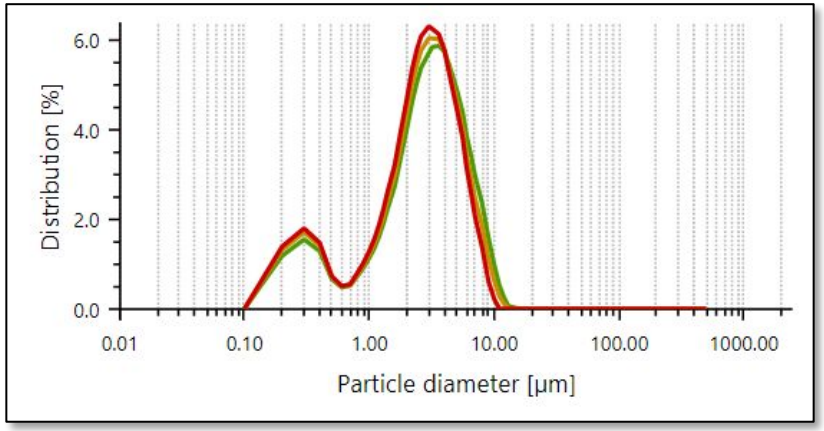
[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023

Powder Particle Size Distribution[1,2]

- The spray drying process parameters yield small particle populations (D_{90} < 10 µm) having distinct fines population
- Smaller particles fill in the void volumes between larger particles and maximize powder loading

Particle size distribution requirements	D_{10}	D_{50}	D_{90}	Span $(D_{90} – D_{10}) / D_{50}$
	< 0.8 µm	2.0 – 4.0 µm	< 10 µm	1.5 – 2.5

Typical Particle Size Distribution



[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023

XeriJect™ Syringe Filling[1,2]

- XeriJect™ formulations are filled into standard 1 mL and 2.25 mL syringes

Lab-Scale
Syringe Filler

Syringes Filled
and Stoppered

XeriJect™ Filled
1-mL Long PFS

[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023

XeriJect™ Monoclonal Antibody Stability[1,2]

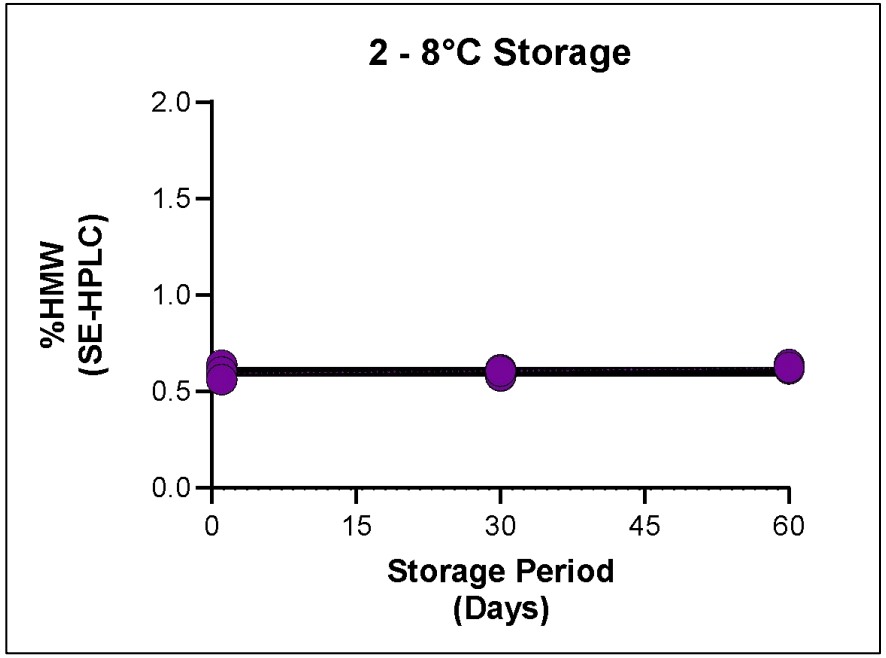
XeriJect™ Trastuzumab formulations supporting non-clinical studies exhibited excellent short-term stability

- ~ 0.2% increase in High Molecular Weight (HMW) products over 2mo. (2 – 8°C)

Longer-term (6 month) storage stability with other XeriJect™ monoclonal antibody formulations showed similar profiles

- Refrigerated (2 – 8°C): < 0.50% increase in HMW products
- Controlled Room Temperature (25°C): < 2.0% increase in HMW products

XeriJect™ Trastuzumab Formulation Short-term Stability

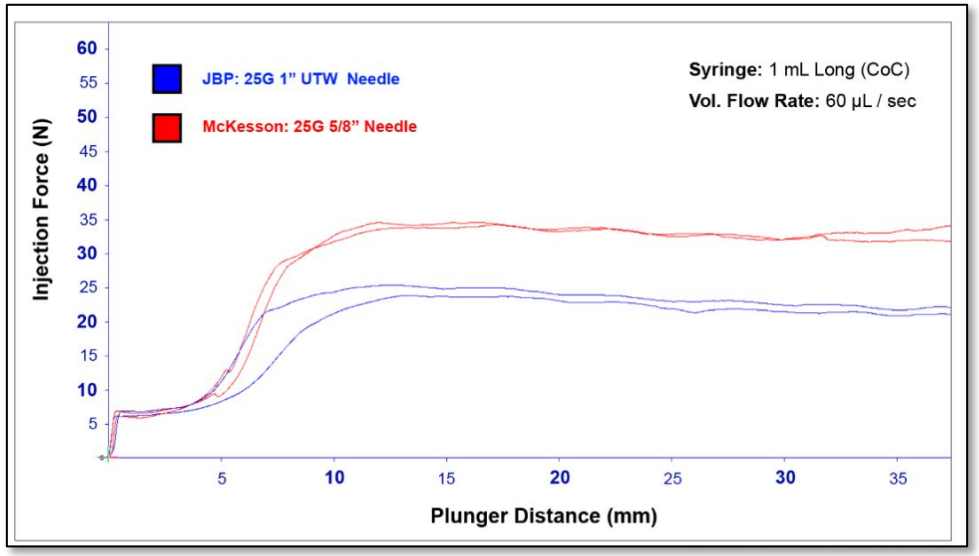


[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023

XeriJect™ Injectability[1,2]

- XeriJect™ formulations are Non-Newtonian fluids with shear-thinning behavior
- XeriJect™ formulations are viscous but can be delivered through standard syringes and needles with suitable injection forces
- Multiple XeriJect™ trastuzumab formulations prepared during development have antibody contents > 400 mg/mL with injection forces < 30 N

Injection Force of 1 mL Syringe with 25G Needles



% Solids Content (w/w)	Trastuzumab Content (mg/mL)	Break-Loose Force (N)	Mean Glide Force (N)
60	477	5.0	21.4
60	429	5.4	21.3
64	522	4.0	26.1
62	451	6.8	19.9

[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023

XeriJect™ Preclinical Results

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Nonclinical Evaluation of XeriJect™ Formulated Monoclonal Antibodies for Subcutaneous Injection

- **Pharmacokinetics in Minipigs**
  - XeriJect™ Trastuzumab SC vs. Herceptin® IV and Herceptin Hylecta® SC [1,2,3,5]
  - XeriJect™ Bevacizumab vs. Avastin® administered IV and SC [1,2,4,6]

- **Local Tolerance[2]**
  - XeriJect™ Vehicle local tolerance in minipigs
  - XeriJect™ Trastuzumab vs. Herceptin Hylecta® local tolerance in rabbits

[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023 [3]MED-US-0TH-23-00008 [4]MED-US-0TH-23-00012 [5]Fitch R, et al. AACR; Cancer Res 2023;83(8_Suppl):Abstract nr LB024. [6]Fitch R, et al. CRS 2023: Abstract nr 357

XeriJect™ Trastuzumab Pharmacokinetics[1-4]

Pharmacokinetic Study Design

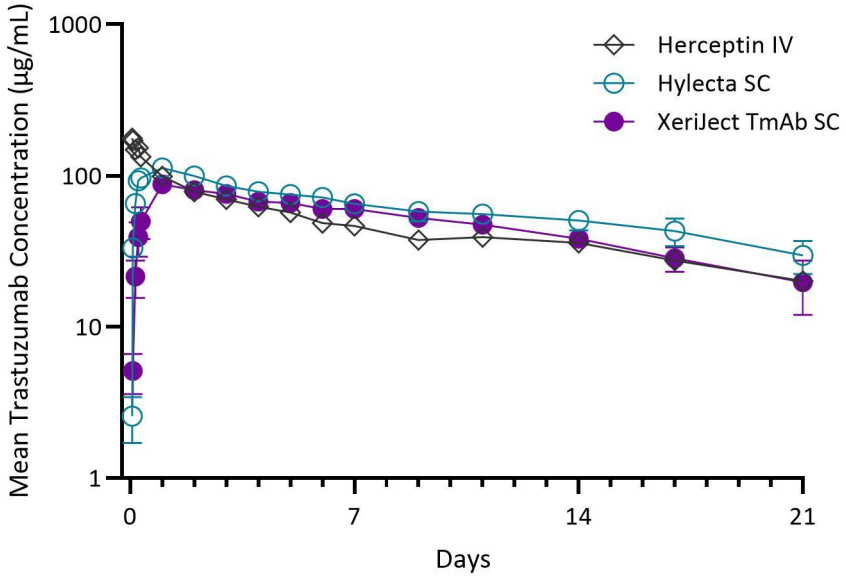
- 12 Female Göttingen Minipigs
- Single dose (IV or SC)
- Plasma samples over 21 days

Groups

Formulation	Dose	N	Body Weight	Dose Conc (mg/mL)	Dose (mL)
Herceptin®	10 mg/kg IV (90 min)	4	11.4 kg	21 mg/mL	5.3 mL
Herceptin Hylecta®	120 mg SC	4	10.6 kg	120 mg/mL	1 mL
XeriJect™ Trastuzumab	120 mg SC	4	10.9 kg	432 mg/mL	0.28 mL

[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023 [3]MED-US-0TH-23-00008 [4]Fitch R, et al. AACR; Cancer Res 2023;83(8_Suppl):Abstract nr LB024.

XeriJect™ Trastuzumab Pharmacokinetics[1-4]



Absorption

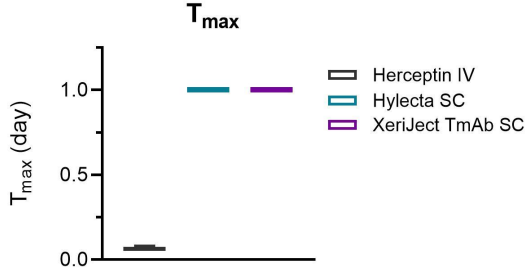
XeriJect™ group demonstrates similar absorption to reference drug administered SC

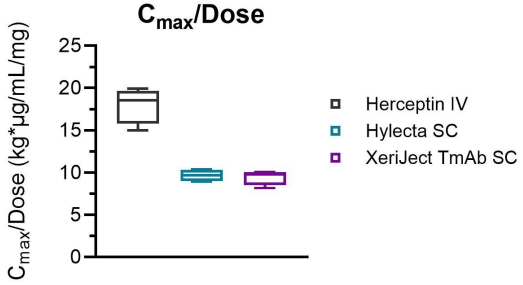
Exposure

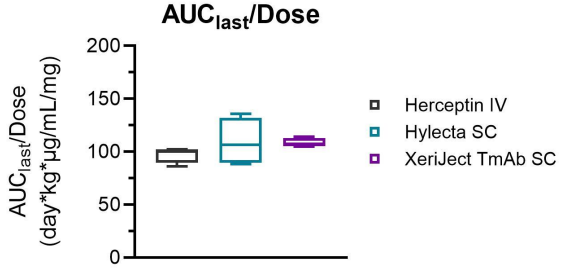
XeriJect™ group demonstrates similar exposure to reference drug administered SC

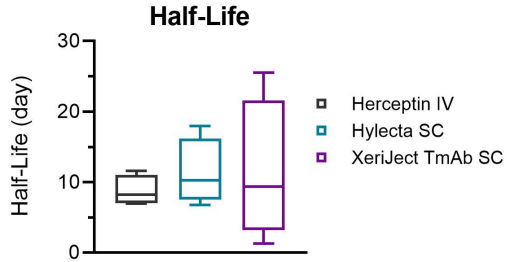
Elimination

XeriJect™ group demonstrates similar elimination curve to reference drugs administered IV and SC









[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023 [3]MED-US-0TH-23-00008 [4]Fitch R, et al. AACR; Cancer Res 2023;83(8_Suppl):Abstract nr LB024.

XeriJect™ Bevacizumab Pharmacokinetics[1-4]

Pharmacokinetic Study Design

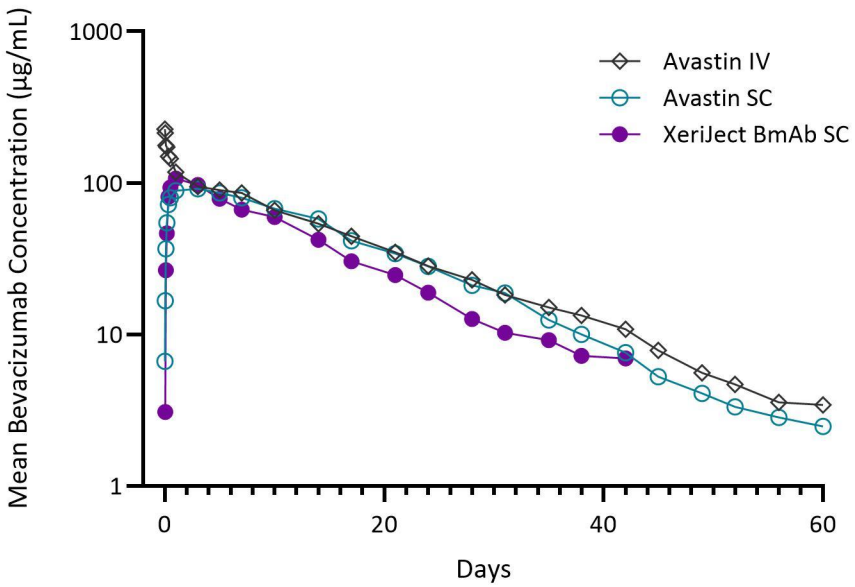
- 12 Female Göttingen Minipigs
- Single dose (IV or SC)
- Plasma samples over 60 days

Groups

Formulation	Dose	N	Body Weight	Dose Conc (mg/mL)	Dose (mL)
Avastin®	100 mg IV	4	11 kg	26 mg/mL	4.1 mL
Avastin®	100 mg SC	4	11 kg	26 mg/mL	4.1 mL
XeriJect™ Bevacizumab	100 mg SC	4	11 kg	439 mg/mL	0.21 mL

[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023 [3]MED-US-0TH-23-00012 [4]Fitch R, et al. CRS 2023: Abstract nr 357

XeriJect™ Bevacizumab Pharmacokinetics[1-4]



Absorption

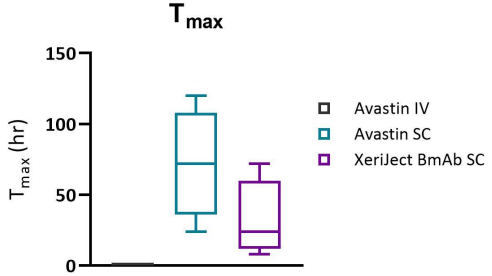
XeriJect™ group demonstrates similar absorption to reference drug administered SC

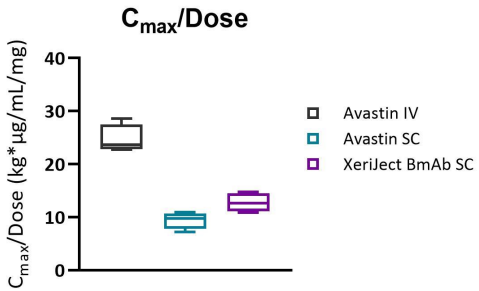
Exposure

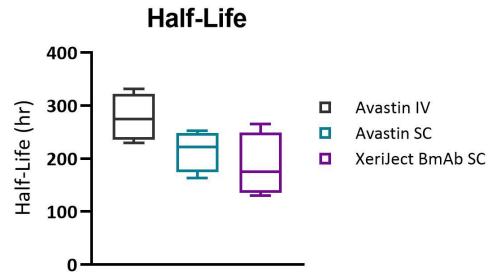
XeriJect™ group demonstrates similar exposure to reference drug administered SC

Elimination

XeriJect™ group demonstrates similar elimination curve to reference drugs administered SC







[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023 [3]MED-US-0TH-23-00012 [4]Fitch R, et al. CRS 2023: Abstract nr 357

XeriJect™ Vehicle Local Tolerance in Minipigs[1]

Local Tolerance Study Design

- 6 Female Göttingen Minipigs
- Single injection SC
- Monitor daily for 14 days (Draize)

Groups

Formulation	N	Body Weight	Dose (mL)
XeriJect™ Vehicle – 1	3	17-23 kg	0.3 mL
XeriJect™ Vehicle - 3	3	17-23 kg	0.3 mL

Injection Site Reactions

No adverse injection site reactions

Highest score = 1: slight erythema/very slight edema

- 5 animals score = 0
- 1 animal score = 1

Draize Score Key

Erythema		Edema	
0	None	0	None
1	Slight	1	Very Slight
2	Well-defined	2	Slight (well-defined edges)
3	Moderate or severe	3	Moderate (raised> 1 mm)
4	Severe or slight eschar formation (injuries in depth)	4	Severe (raised> 1 mm and extending beyond the area of exposure)

[1] Data on file, Xeris Pharmaceuticals, Inc. 2023

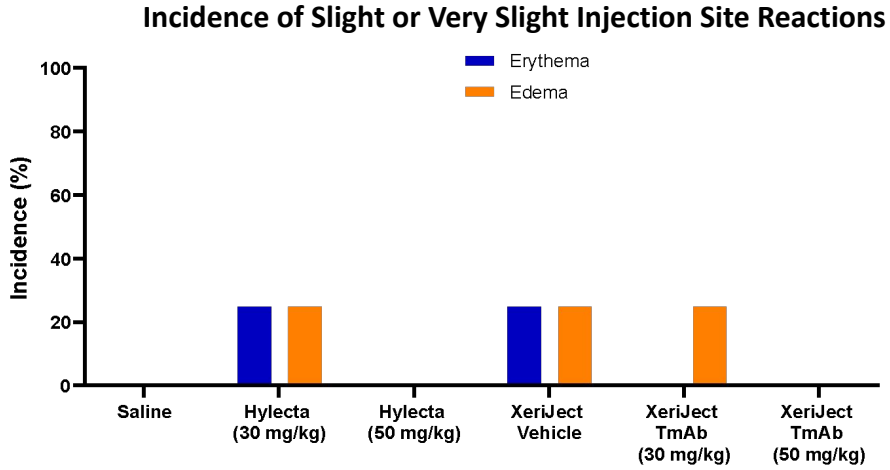
XeriJect™ Trastuzumab Local Tolerance in Rabbits[1]

Local Tolerance Study Design

- 24 Female NZW Rabbits
- Single injection SC
- Monitor daily for 14 days (Draize)

Groups

Formulation	Dose	N	Body Weight	Dose Conc (mg/mL)	Max Dose Vol (mL)
Saline	0 mg/kg SC	4	3 kg	-	1.3 mL
Herceptin Hylecta®	30 mg/kg SC	4	3 kg	120 mg/mL	0.8 mL
Herceptin Hylecta®	50 mg/kg SC	4	3 kg	120 mg/mL	1.3 mL
XeriJect™ Vehicle	0 mg/kg SC	4	3 kg	-	0.4 mL
XeriJect™ Trastuzumab	30 mg/kg SC	4	3 kg	376 mg/mL	0.24 mL
XeriJect™ Trastuzumab	50 mg/kg SC	4	3 kg	376 mg/mL	0.4 mL



Injection Site Reactions

No adverse injection site reactions

Highest score = 1: (slight erythema/very slight edema)

- Low incidence (1 out of 4)
- Not observed in every XeriJect™ group

[1]Data on file, Xeris Pharmaceuticals, Inc. 2023

XeriJect™ Formulation Technology[1,2]

XeriJect™ viscoelastic suspension enables delivery of high concentration monoclonal antibodies in a low SC injection

- Standard pharmaceutical operations and excipients (proprietary parameters)
- Delivered by standard syringes and needles SC with suitable injection forces
- Long term stability at 2-8° C, with potential for CRT stability
- Preclinical validation in pharmacokinetic model, no adverse injection site reactions

[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023

XeriJect™ is rapidly progressing to GMP manufacturing and clinical studies

☑ Routine formulation development at lab scale	• 3 processing suites
☑ In-house production for GLP toxicology studies	• Very low bioburden, endotoxin
☑ 3 Internal research and development projects	• 2 mAbs, 1 recombinant protein
☑ Preclinical validation in large animal model GLP Toxicology Study in progress	• Favorable PK/Tolerance results
☑ Active collaborations with top biopharma companies	• Several in late-stage negotiations
☐ Demonstrate Clinical trial material production (est 2024)	• Next step: First-in-Human study with XeriJect mAb Formulation

[1] US Patent Publ. No. 2023/0085357 A1 [2]Data on file, Xeris Pharmaceuticals, Inc. 2023

Xeris Contact Information

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