



# ProCrysta

Refined Purification, Formulation and Effective  
Delivery of Biopharmaceuticals

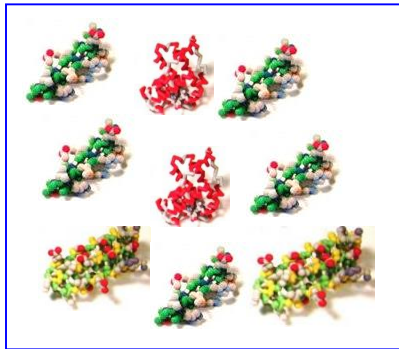
Dedicated Team |  
| Quality Work

# ProCrysta Biologix Inc.

- Founded in December 2009
- Private company, located in Natick MA (5000 sq. ft. lab space)
- Business model
  - A Strategic Collaborative Partnership for Pharmaceutical Companies
    - Enter into select collaborative partnerships on patent protected products for enriched drug delivery

# Translating Proteins to Efficacious Products

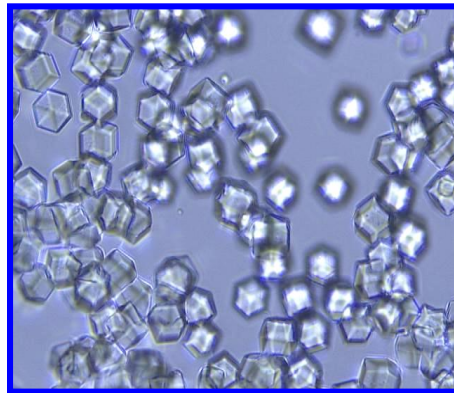
## Protein solution



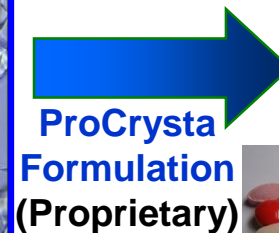
Impure  
Unstable



## Protein Crystals



Higher Purity  
Stable  
Concentrated  
More active



## Protein products

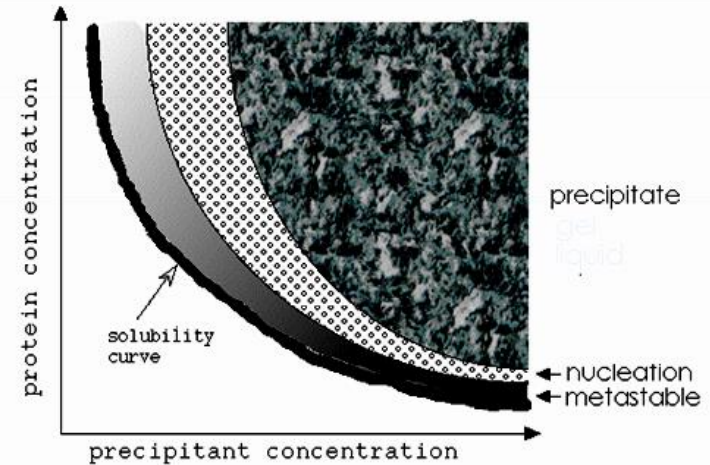


Improved shelf-life  
Lower dosage  
Higher potency  
Multiple delivery options

**Demonstrating Strategy**

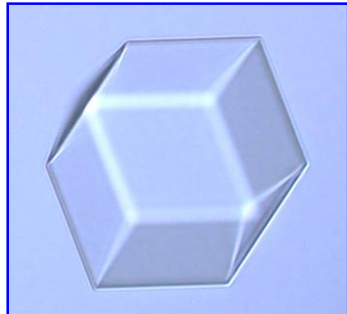
# Protein Crystallization

- Crystallization conditions can be manipulated by changing
  - Crystallization parameters
  - Achieve desired crystal
    - Size
    - Shape
    - yield



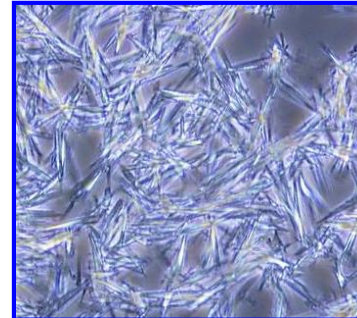
Solubility curve indicates the state of saturation. Various super-saturated states are shown above the curve.

## X-ray crystallography grade



- >500 $\mu$ m size
- Good quality crystals
- Slow growth rate
- Single crystals preferred

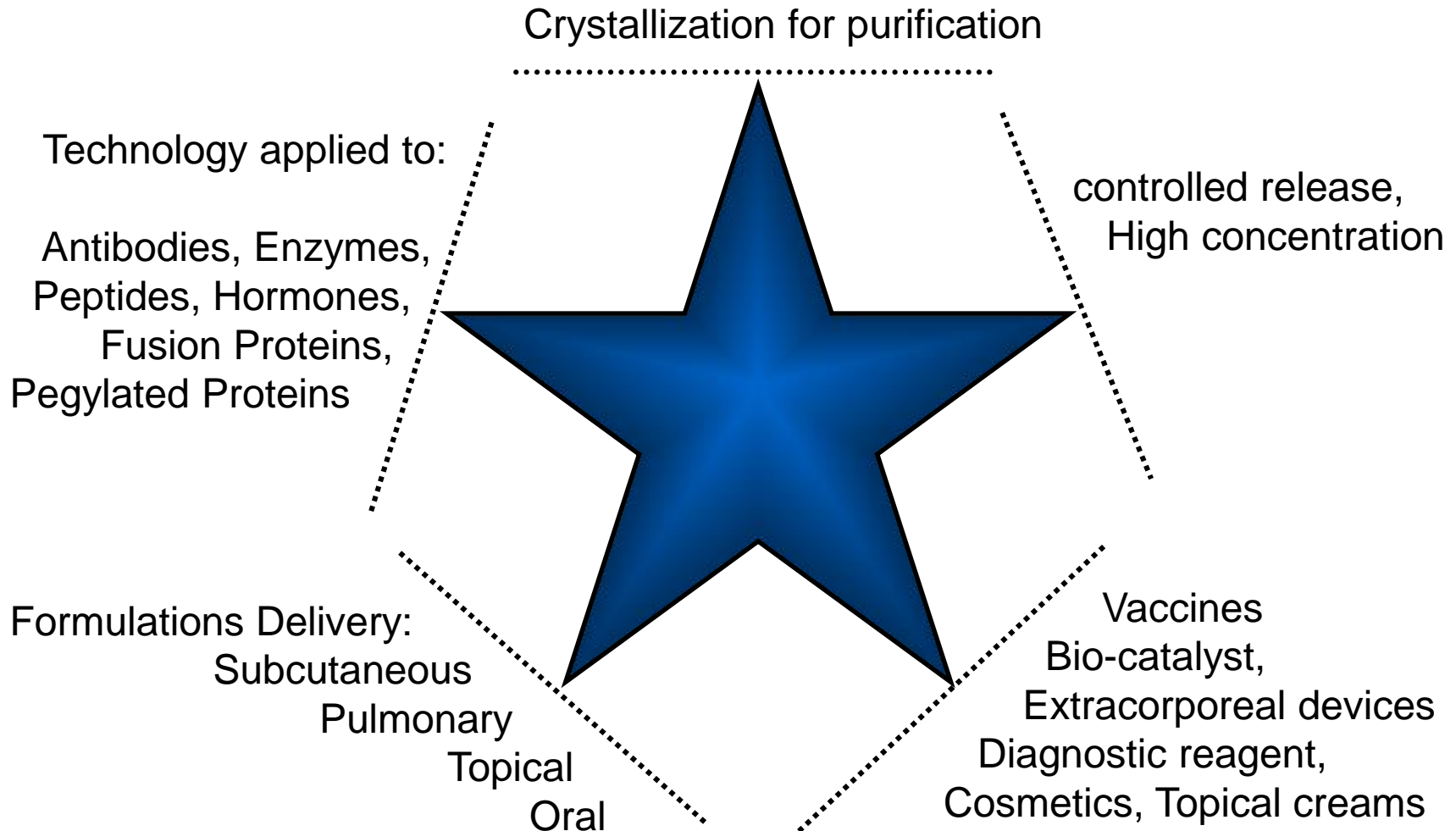
## ProCrysta standard



- 0.1-100 $\mu$ m size
- Faster growth rate
- High yield very important
- Cost effectiveness
- Scalable
- Reproducible
- Facilitates regulatory compliance

**Quality by Design**

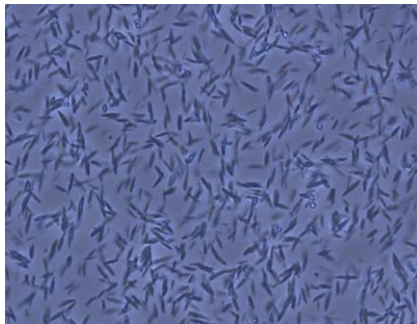
# Broadly Applicable Technology



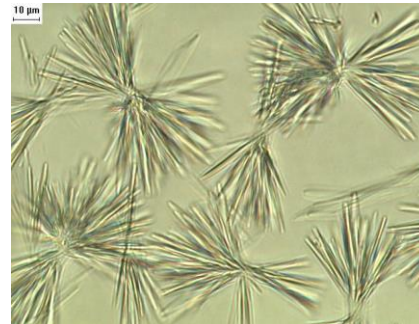


# Crystallization Applications

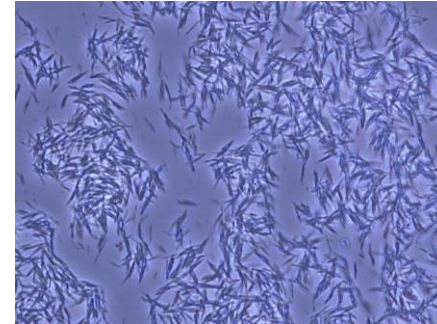
- Applicable to most therapeutic protein classes
- Our team has crystallized >30 proteins from different sources
  - Bacterial, Fungal, Cell culture, and Transgenic sources



**Monoclonal Antibody**



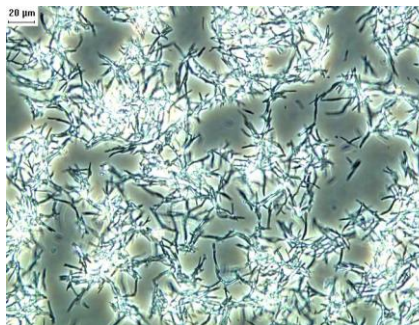
**Fusion protein**



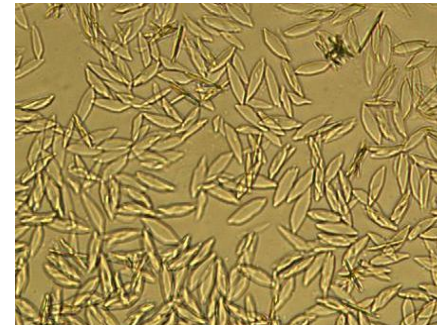
**Hormone**



**Enzyme**



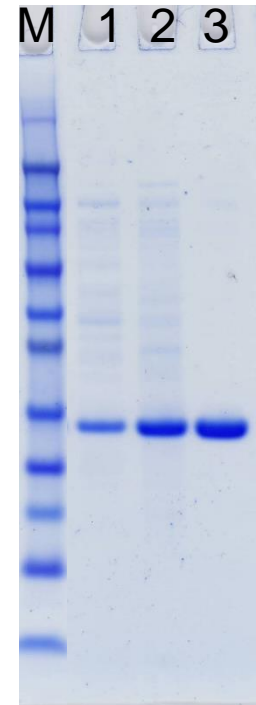
**Polyclonal antibody**



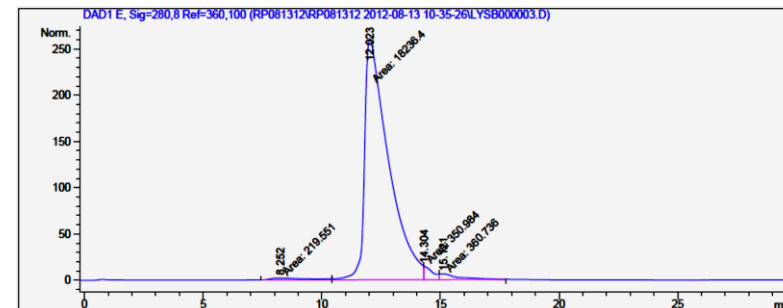
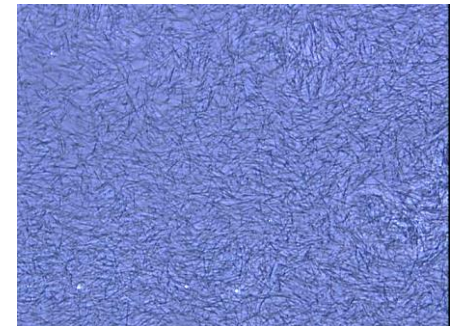
**Pegylated protein**

# Crystallization for Purification

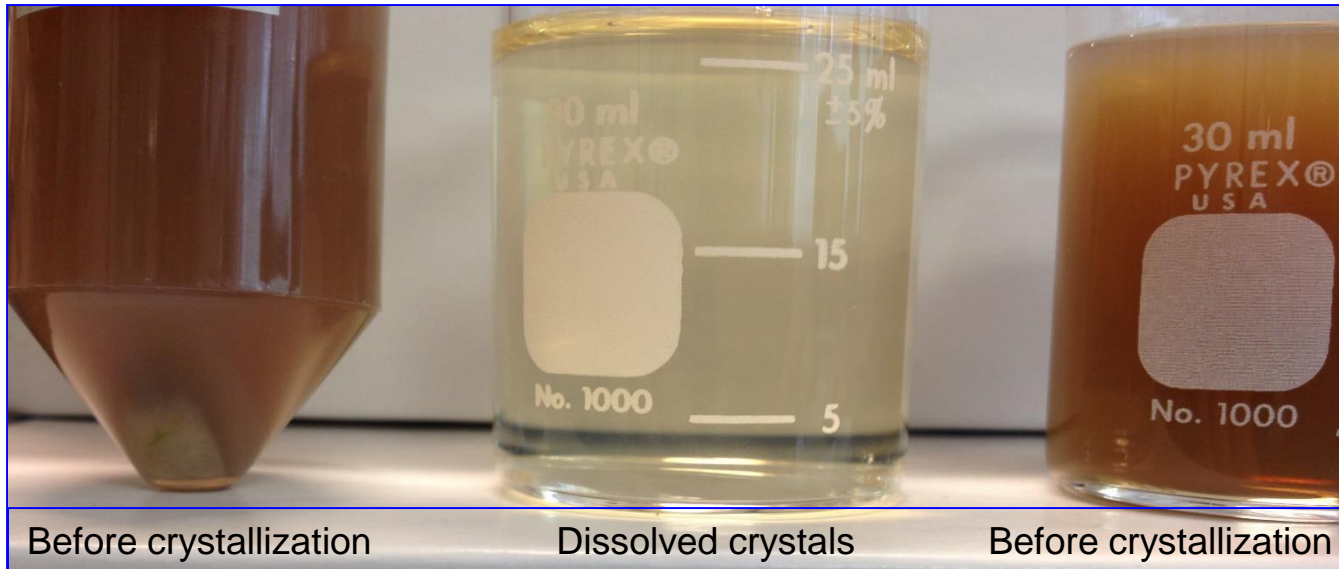
- Advantages of Crystallization for purification
  - Applicable to many classes of proteins such as
    - Enzymes, hormones, antibodies, Pegylated proteins, fusion proteins
  - Higher purity in fewer steps
  - Crystallized from crude sources like fermentation or cell culture broth
  - High protein recovery: >90% yield
  - Cost effective
    - Savings from columns, buffers, eluents, and processing time
  - Scalable and reproducible for manufacturing
  - Removes endotoxins
  - Reduces viral load (>3 to 5log)
  - Protein retains its structural integrity and activity
  - Crystal shape and size can be controlled for formulation needs



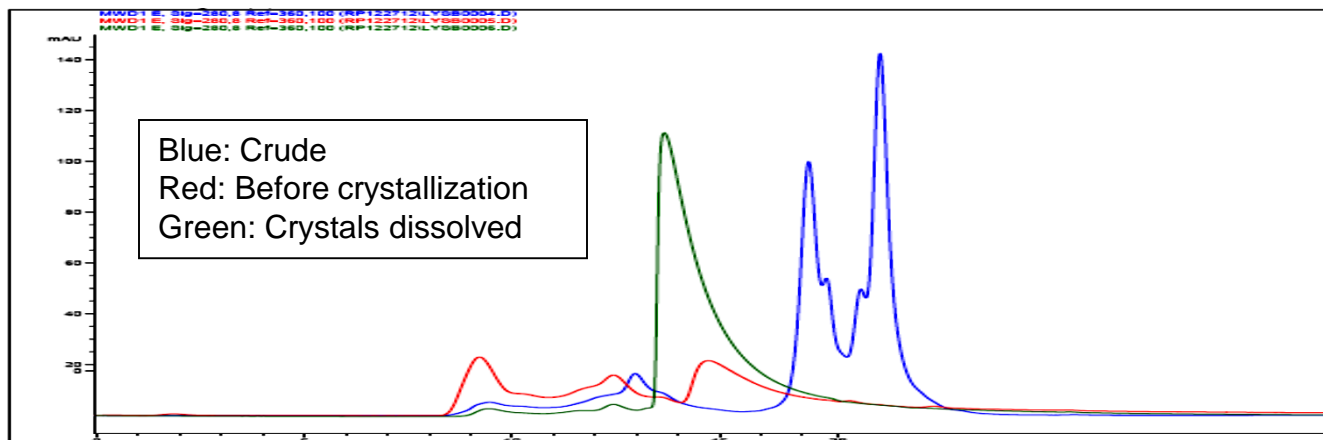
- 4-12% Bis Tris SDS PAGE
- MES Running buffer
- Reduced gel
- Lane M: Marker
- Lane 1: Cell lysate
- Lane 2: Ammonium sulfate precipitates
- Lane 3: Crystals



# Crystallization for Purification



Crystallization can purify all the non protein impurities making the solution clear from colored brown starting material



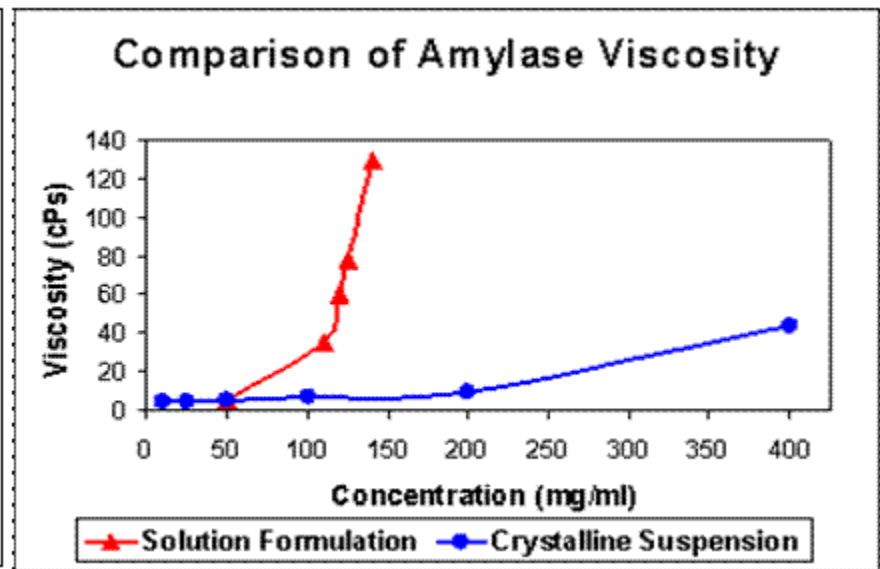
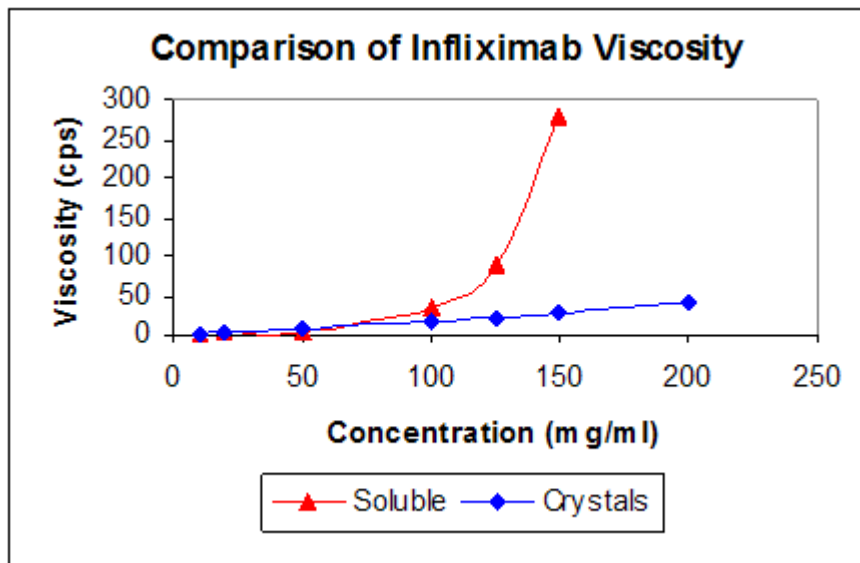
Crystallization enriched the protein as shown in the chromatogram in 3 steps;

- Ammonium sulfate precipitation
- Desalting
- Crystallization



# Proven Formulation Benefit: Higher Concentration with Lower Viscosity

Crystalline forms of proteins show significantly lower viscosity at high concentrations. Viscosity measurements of soluble vs. crystalline forms Infliximab and amylase at different concentrations measured with a Cannon-Fenske viscometer.



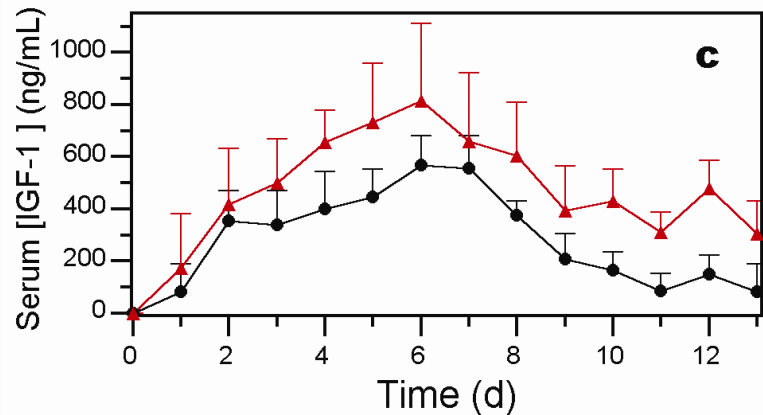
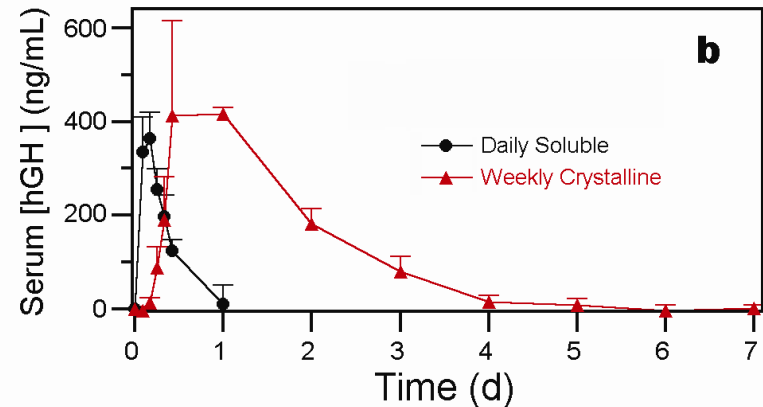
**Administration of proteins at higher concentrations (e.g. antibodies) requires IV delivery due to increased volume needed to lower viscosity, crystallization overcomes this problem**

# Long Acting Protein Formulations

- Crystallization can overcome many formulation challenges such as,
  - Modifications to the protein, polymer encapsulation, and/or non-aqueous vehicles for extended-release formulations
  - Complicated manufacturing processes
  - Poor stability profile
  - Inability to concentrate
  - High viscosity/poor syringeability
  - Initial burst
  - Inadequate or exaggerated PD response

# Proven Formulation Benefits: *Extended Release Profile via Crystallization*

- Time actions profile of soluble and crystalline rhGH formulations in female cynomolgus monkey model. Insulin-like growth factor-1 (IGF-1) is a diagnostic for growth hormone deficiency
- Crystalline hGH formulation serum hGH levels provided a significantly prolonged PK profile compared to daily soluble rhGH serum levels
- The IGF-1 serum level from one weekly crystalline hGh dose is similar to seven daily soluble injections



**Crystalline proteins can convey extended release without modifying the protein**

# Why ProCrysta Technology?

- The protein molecules are not chemically modified, conjugated or encapsulated with polymers
- Formulates drugs in an aqueous suspension with lower viscosity, allowing administration with 29-31G needle
- Possible to change route of administration from intravenous to subcutaneous
- Delivers drugs at higher concentrations
- Various drug delivery options
- Imparts stability to formulations
- Extends Patent life



# Executive Summary

**Accelerate your drug development program by collaboration with our dedicated and experienced team**

- State of the art Technology
- Expertise in protein crystallization, purification and formulation
- Dedicated team delivering quality work
- Outstanding problem solving skills
- Result driven approach
- Demonstrated technology