Resusix™ – Spray Dried Solvent Detergent Treated

Remote Damage Control Resuscitation Symposium
Norway, June 2012

Mike Galiger
Vice President Product Development,
• Our Mission for blood component therapy
  – Safety
  – Availability
  – Potency
  – Characterization
Resusix™: a biopharmaceutical plasma-based therapeutic

- Released to set criteria based on EU pharmacopeia
- Pathogen reduced
- Standardized
- Provides benefits equivalent to FFP without:
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  - TRALI
  - Viral transmission
  - Cell Fragments
  - Variability
Resusix™: a biopharmaceutical plasma-based therapeutic

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- Pathogen reduced
- Standardized
- Provides benefits equivalent to FFP without:

  ✓ TRALI
  ✓ Viral transmission
  ✓ Cell Fragments
  ✓ Variability
  ✓ Allergic reactions
  ✓ Lipids
  ✓ Other Micro particles
  ✓ TRIM
Resusix™ – Product Description

• USFDA Licensed source Plasma, Pooled (> 90 liters)
  – Standardized concentration of Proteins
  – Dilutes specific antibodies, allergens, and active substances such as histamines
  – Full testing for standard pathogens
  – Can neutralize antibodies if respective antigens are present
Clinical advantages of Pooling Plasma (Solheim):

- Standardized content provides a more predictable effect
- “Eliminates” TRALI – the leading cause of transfusion related death
- Explained by dilution and neutralization of leukocyte antibodies and elimination of activated lipids (in SD processing)
- Pooling reduces the rate of allergic/immunologic adverse events by 60–80%
Resusix™ – Product Description

• Solvent Detergent Treated
  – Reduced risk of Transfusion Transmitted Infection (TTI)
  – Eliminates all enveloped viruses and bacteria
  – Excellent safety profile

  • In the almost 20 years of European experience with patients treated with S/D plasma (including therapy with over 10 million units of S/D plasma used in routine medical care), there have been no documented cases of TRALI or transmission of hepatitis B virus (HBV), hepatitis C virus (HCV), or human immunodeficiency virus (HIV) (Hellstern 2010).

  – Final filtration (.22μ) reduces lipids,
Resusix™ – Product Description

- **Spray Dried**
  - Spray drying – Liquid solvent is forced through heated gas resulting in rapid dehydration on a sub-second timescale
  - Resulting powder has approximately 2.5% moisture content (long term storage)
  - Rehydration fluid is a Citrate/Phosphate Buffer, pH adjusted

Spray Dried Plasma – SEM
**Resusix™ – Concentration**

- Final presentation is flexible
  - 3x – Reconstituted with 1/3 original plasma volume
    - 1x – 14g powder/200mL fluid or 28g/400mL
    - 3x – 14g powder/67mL fluid or 28g/133mL
  - Similar to PCC’s without the thrombotic complications
  - Reduces risk of volume overload
  - Hyperoncotic and hyperosmotic
### Resusix™ – IND Data

#### Release Criteria:

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*onsdag 5. september 2012*
Resusix™ - IND Data

EU PH 7.0
Resusix™ - IND Data

EU PH 7.0
Resusix™ - Preclinical

• Proteomics
  – 9000 unique proteins identified
  – 96% similarity between pre and post spray dried material

• In Vivo
  – Coumadin reversal in swine
    • INR to 1.5 in warfarin treated swine
  – Dose response in swine
    • ROTEM directed infusion
Resusix™ – Preclinical Testing

UNC Coumadin
Resusix™ – Preclinical Testing

UNC Swine dose response
Resusix™ Clinical Program

• U.S. IND 15091
  – Submitted to FDA 03 May 2012
  – FDA allowed IND to proceed to phase 1
    • No additional data required
    • Additional infusions requested for phase 1 study
• Phase 1 Safety Study
  – Single site, open-label, uncontrolled
  – Healthy, normal volunteers
  – Single dose, 4 cohorts
    • n=4: 100mL Resusix™
    • n=4: 200mL Resusix™
    • n=8: 500 mL Resusix™
    • n=8: 1,000 mL Resusix™
  – 1-week observation after 1st subject in each cohort
  – 12-week study duration following infusion
Resusix™ Clinical Program

- Phase 2a – acquired coagulopathy due to Liver disease
  - Multi-center, double-blind, randomized, controlled
    - 15 U.S. sites planned
    - 1:1 FFP:Resusix™
    - Dose: 2 to 4 units
Resusix™ Clinical Program

- **Phase 2b Study – Significant bleeding/Burns**
  - Multi-center, double-blind, randomized, controlled
    - 15 U.S. sites planned
    - 1:1 FFP:Resusix™
    - Dose: ≥4 units
  - Patients with significant bleeding (requires ≥4 units)
    - n=up to 125 (for 100 evaluable patients)

- **Phase 3 Studies**
  - Multi-center, double-blind, randomized, controlled
    - Patients with acquired coagulopathy due to liver disease
    - Significant Bleeding/Burns
Resusix™ – Questions?

onsdag 5. september 2012