International Partnership Model: Celltrion in South Korea♪

August 29, 2013
Bangkok, Thailand

Seung-il Shin, Ph.D.
Former Senior Advisor for International Development, VaxGen
Former Chair, Scientific Advisory Board, Celltrion
External Board Member, GSID

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Celltrion, Inc. - Overview

- Established in 2002 in South Korea to produce AIDSVAX® for the global market
- A US-Korea joint venture between VaxGen/GSID (South San Francisco, CA, USA) and three Korean partners
- Now is the global leader of biosimilars development and production, with a market capitalization of $6 billion

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Historical Setting, 1999♪

- VaxGen (GSID) expected to conclude the Phase III clinical trials of AIDSVAX by the end of 2003,
- But Genentech was not prepared to produce AIDSVAX for the global market.
- VaxGen (GSID) had to find a solution to supply the vaccine to the world,
  - At low cost
  - In large quantity
  - As soon as possible
  - At low capital cost

♪

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Potential Options for VaxGen

1. Partner with a major global vaccine company to share manufacturing and marketing rights to AIDSVAX
2. Partner with a vaccine producer in an emerging country, and focus on supplying AIDSVAX to low income countries
3. Pay costly reservation fees to reserve future manufacturing capacity with a CMO
4. Create VaxGen's own manufacturing capability

Search for Solutions, 1999-2000

- VaxGen(GSID) carries out a global search for potential manufacturing partners and CMOs
- A commissioned study in 2000 concludes that a new 50,000 L facility in CA will cost ~$160 million, take 36-48 months to build
- Three major Korean engineering companies report that the same plant could be built for ~$100-$120 million in 24 months, if built in Korea
- VaxGen concludes that the only feasible option, consistent with its desire to shorten the time to the market, is to create its own manufacturing facility at an ex-US site

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Proposed Solution, 2000

- VaxGen(GSID) moves to create a joint venture in an East Asian country by hedging the risk of an AIDSVAX failure by designing a facility that can produce either rgp120 or MAbs
- Basic requirements for the JV partner:
  - Existence of strong legal systems for IP and technology protection, biologics licensing regulations, and cGMP compliance practices
  - Adequate engineering, construction, industrial and technology-service infrastructure for biopharmaceuticals manufacturing
  - Strong local leadership and managerial expertise
  - Sufficient manpower pool already trained in bio-manufacturing
  - Available capital

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Search for Partners, 2000-2001

- Explorations for potential JV partners carried out in Japan, South Korea, Taiwan and Singapore
- A South Korean consortium (consisting of Nexol Corp., KT&G and J Stephen & Ventures) selected as JV partners
- The City of Incheon offers a package of incentives to locate the manufacturing facility in Songdo, in the Incheon Free-economic Zone
- Celltrion is formally launched in February 2002

Celltrion: US-Korea Joint Venture♪

- US Partner (VaxGen/GSID):
  - Proprietary product (AIDSVAX®)
  - Technology transfer, including large-scale manufacturing processes for complex recombinant proteins
  - On-site technical oversight and staffing of key experts
  - Marketing rights (ex-US) for AIDSVAX
- Korean Partners:
  - Capital and land for construction of a 50,000 L plant
  - Engineering oversight, management for facility construction and operational responsibility
  - On-going management and business development

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Celltrion:
Fast Planning and Implementation

- **February 2002:** Celltrion incorporated as a Korean company and acquires the land to build the facility
- **Summer 2002:** Competitive bids to select firms for conceptual design, detailed design and engineering, bioreactor fabrication, and primary construction contractor
- **March 2003:** Official groundbreaking at the Songdo site

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Celltrion Plant I: Conceptual Site View (2002)

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

2002: Songdo New City before…

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

…and after: Celltrion Plant I, Completed in 2005♪

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Bioreactor Hall, Plant I
(12,500 L X 4)

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Cell Harvest Suite

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Purification Suite

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Celltrion Plant II, Completed in 2010♪

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Bioreactor Hall, Plant II

(15,000 L X 6)♪

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Celltrion Facility: Summary

- Plant I: 50,000 L (4 X 12,500 L bioreactors)
- Construction period: 19 months to mechanical completion (March 2003 – October 2004)
- Validation and facility licensure: End of 2005
- Commercial launch of facility: Early 2006
- Plant I construction budget: $95 million
- Plant II: 90,000 L (6 X 15,000 L bioreactors) and finish/fill facility completed in 2010; licensure expected in 2013

Celltrion's Strategy for Success

1. Celltrion, after "AIDSVAX failure", retooled and won the largest CMO contracts ever awarded in Asia in 2005
2. Celltrion leveraged its contract manufacturing business to fund expansion of its infrastructure and development of its own biopharmaceutical products
3. Celltrion received marketing approval in 2012 from the KFDA for Remsima™, the world's first antibody biosimilar, and in 2013 from the EMA
4. Celltrion established strategic alliances and partnerships to fuel a pipeline of biosimilar drug candidates
5. Celltrion now the global leader in biosimilar programs

In hindsight: Keys to a Successful International Partnership♪

1. Excellent starting base: adequate lead funding and good local infrastructure
2. Efficient management structure: A strong and effective leadership able respond quickly, proactively and decisively
3. Local availability of experienced and dedicated technical and managerial staff
4. Proven manufacturing technology (Genentech) and on-site technical support in critical early years (VaxGen/GSID)
5. Viable alternate business strategies (multiple “Plan B’s”)
6. Good timing, plus a measure of GOOD LUCK

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Next Steps: Efficacy Testing♪

Assume a 3 arm trial:

- ALVAC
  AIDSVAX (with booster doses)
- ALVAC
  AIDSVAX (new antigens)
- Placebo

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Next Steps: Manufacturing♪

- Short-term:

  Produce vaccine for Phase III Trial by contract manufacture

  - Identify organization
  - Transfer technology
  - Manufacture and deliver

- Long-term:

  Identify/create a Thai company

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Long-term: Thai Manufacture♪

- Agreements/Licensure
  - Sanofi
  - GSID
  - ?Other
- Manufacturing Plan
  - Facility
  - Staffing
  - Funding

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Long-term: Actions to follow ♪

- Conduct Phase III trial
- Construct Thai manufacturing facility
- Make back-up plan (alternate product)
- Transfer technology to Thailand
- Train staff
- Make pilot lots
- Obtain facility licensure

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Looking forward: Manufacturing capability for a future HIV vaccine♪

1. Establish a lead group to manage the task now
2. Negotiate IP licensure, technology transfer, etc.
3. Provide sufficient funding, and give full independence to the project manager ("do not manage by committees")
4. Obtain experienced outside help (for site plan, engineering, construction management, manufacturing and regulatory issues)
5. Engage a good biotech partner for staff training and technology transfer on-site
6. Have a "Plan B" in case the vaccine project does not work
7. Start as soon as possible.

♪

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES

Thank you!♪

GS ID GLOBAL SOLUTIONS FOR INFECTIOUS DISEASES