



Genzyme Supply Update

August 17, 2009

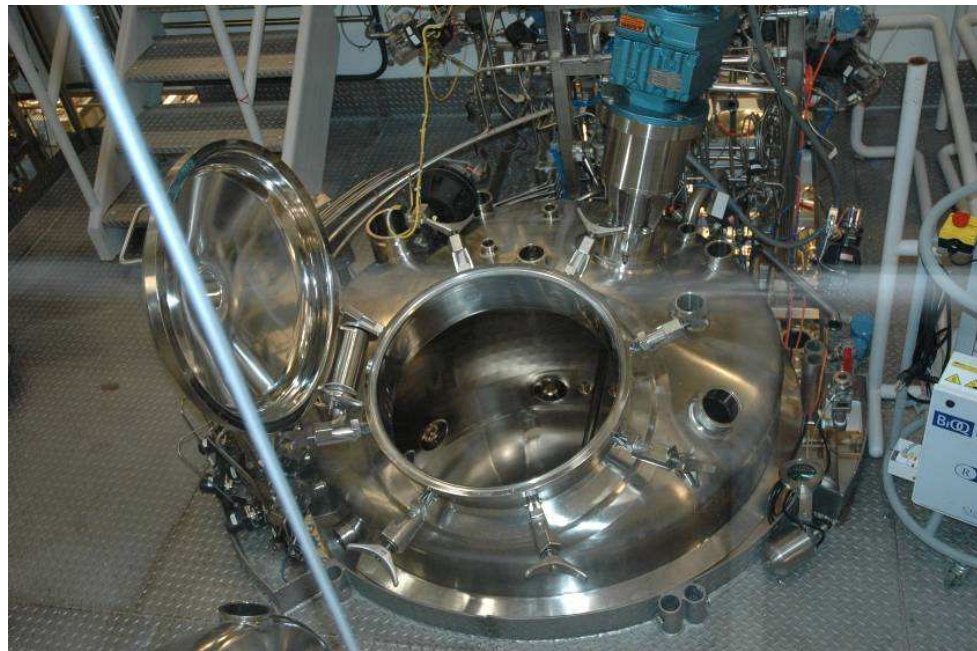
Agenda

- **Biologics Manufacturing at Allston Landing**
- How We Got Here
- Where We Were
- Where We Are
- Where We Are Going

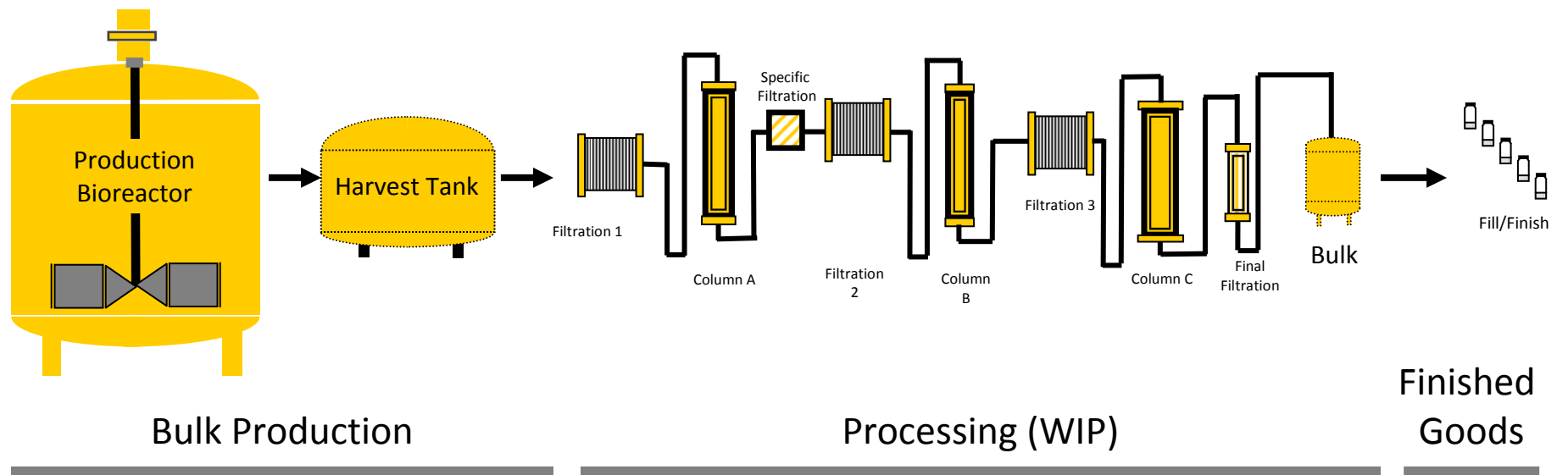
Allston Landing - Boston, Massachusetts, USA



**Inside a 2000 L
Bioreactor**



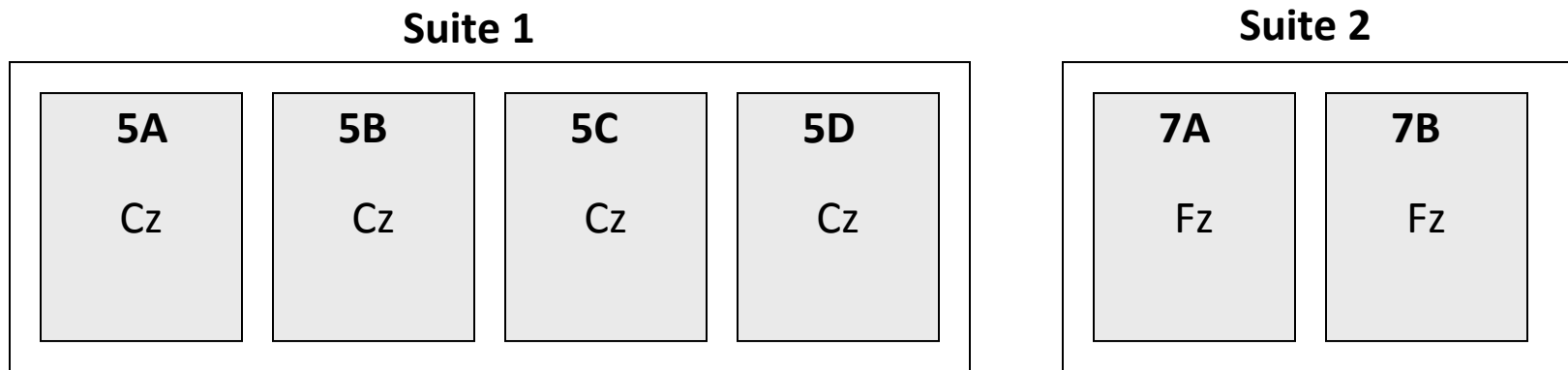
Biologics Manufacturing Process*



* Graphic depicts the manufacturing process generally and is not specific to any particular Genzyme product. Earlier stages of the production process are not shown in this graphic.

Current Allston Bulk Product Allocation

- Allston Landing is a multi-use facility primarily dedicated to Cerezyme[®] (imiglucerase for injection) (CZ) and Fabrazyme[®] (agalsidase beta) (FZ)
- It contains 6 2000 L bioreactors in 2 suites



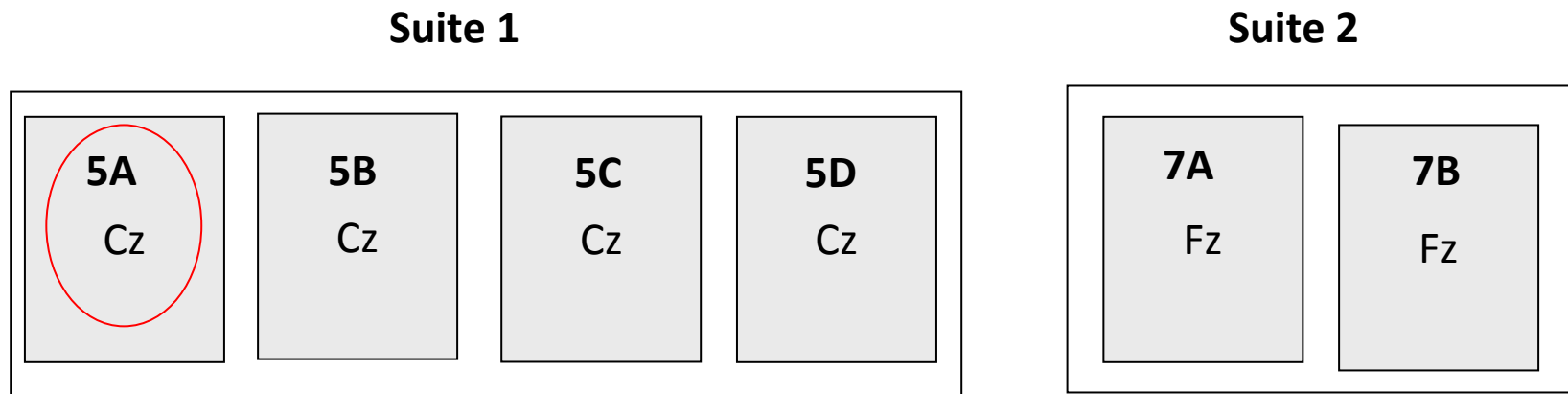
- For the past 3 years, Allston Landing was also producing Myozyme[®] (alglucosidase alfa)/Lumizyme[™] (alglucosidase alfa) at the 2000 L scale

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How We Got Here: Identification of a Virus

- Inventories of Cerezyme were relatively low and were being replenished at Allston
- The Vesivirus was identified in Bioreactor 5A over the weekend of June 13-14



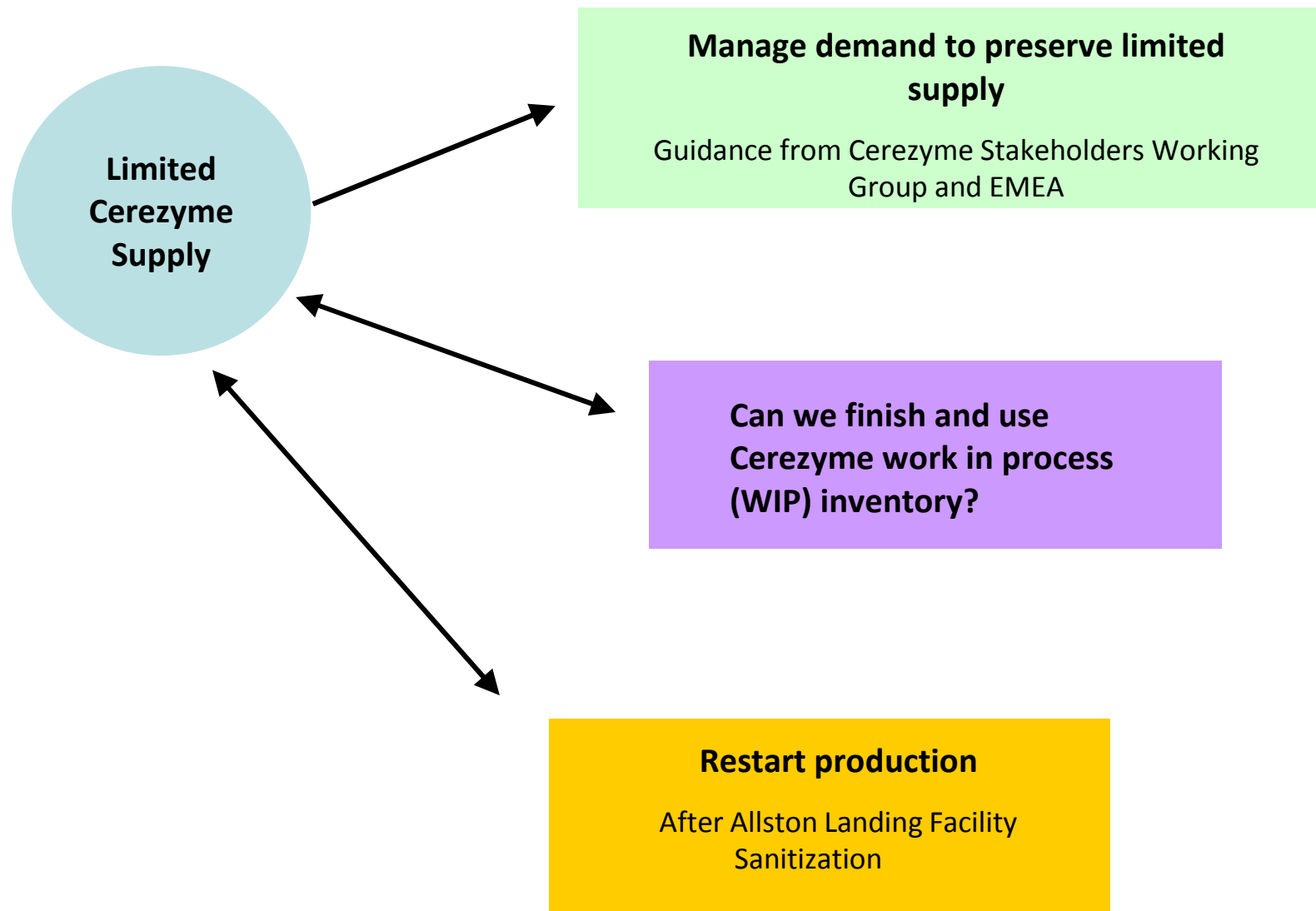
How We Got Here: Impact of Vesivirus

- Evidence suggests that the Vesivirus can only grow in CHO cells, which are the cells Genzyme uses in manufacturing. Furthermore, this particular strain, Vesivirus 2117, is not known to infect humans
- Vesivirus was not detected in the finished vials of Cerezyme that we tested
- Furthermore, the purification process in place would likely remove any virus in the product
- Because the virus impairs cell growth during production, we temporarily suspended bulk production of Cerezyme and Fabrazyme and sanitized the Allston Landing facility
 - This temporary shut down contributed to the lack of available product in the second half of this year
- Our first priority today and everyday is patient safety

How We Got Here: Guiding Principles

- From the outset, as we've worked to understand this situation, we've been focused on the impact to patients, families, and healthcare providers with three basic principles:
 - First, try to ensure therapy for the most vulnerable patients;
 - Second, try to ensure equity on a global basis so that no one country is contributing disproportionately compared to others; and
 - Third, that we would not discriminate between charitable and commercial patients in managing the allocation of what Cerezyme is available.
- In consultation with key stakeholders, we worked to develop Cerezyme and Fabrazyme dose conservation guidelines.

How We Got Here: Cerezyme - Where We Were in June/July



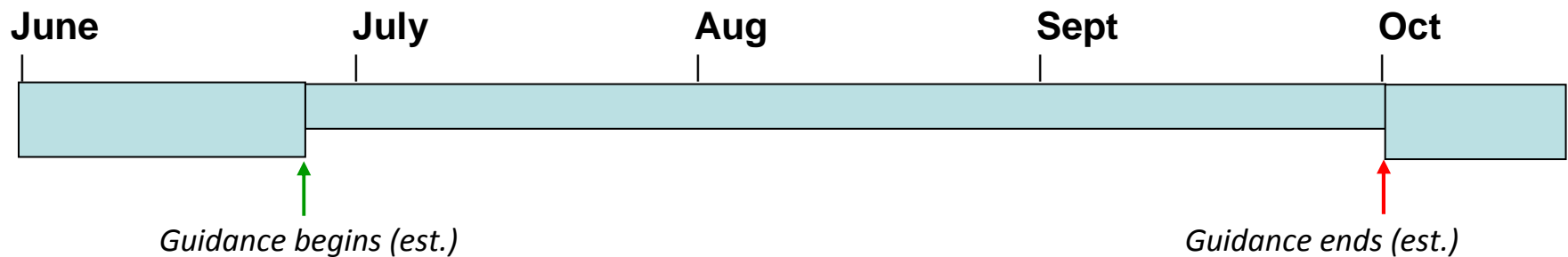
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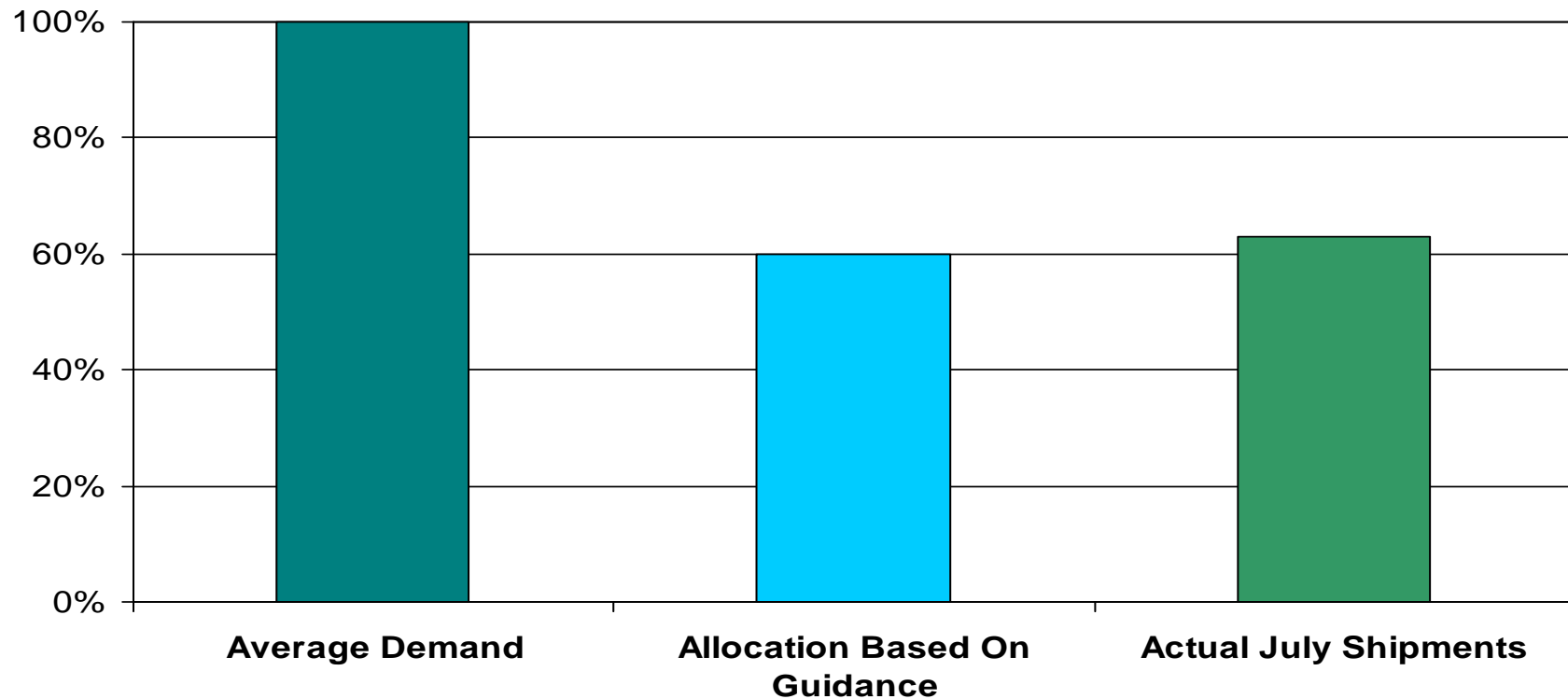
Where We Were: June/July

Cerezyme Stakeholder Working Group (CSWG) and EMEA Guidance was developed and disseminated

- *If*
 - All finished and most work-in-process Cerezyme can be used
 - Allston facility is sanitized and restarted in second half of July
 - Most vulnerable patients continue using Cerezyme without interruption
 - All other patients reduce Cerezyme use by 50% immediately
- *Then*
 - Cerezyme should **not** completely stock-out



Where We Were: End of July Cerezyme Supply (Global)



- Changed shipping and demand management practices in the U.S.
- Global results were within our allocation guidance

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Where We Are: Fabrazyme Supply Update

- Initial adoption of the FSWG guidelines appears to be strong
- Genzyme does not need to change the original guidance on the period of supply constraint or on the period of dose conservation at this time
- Those in the Fabry community that have adopted the FSWG guidelines should be encouraged to continue to do so
- Those in the community that have not yet adopted the FSWG guidelines are encouraged to consider doing so
- A continuing high level of participation is needed to manage through the period of temporary supply constraint through the November-December timeframe

Where We Are Now: Cerezyme Work In Process (WIP)

- Original guidance assumed most WIP could be used
- There was around 2.5 months of WIP inventory at risk
- A key determinant is whether any WIP material presents a potential risk of re-contaminating the Allston Landing facility
- On August 10th, we announced that we decided not to further process **~80% of current Cerezyme WIP** (retaining the remaining ~20% for further testing)
- Not having this material available for use has significantly changed the Cerezyme supply situation
- Therefore, our current projected levels of inventory of Cerezyme are at a point where we will stock out of Cerezyme **globally** if we continued to ship at current levels

Where We Are: Cerezyme Allocation

- We have reduced the amount of Cerezyme we are shipping to every country that uses Cerezyme commercially or in charitable programs
- Country shipments are being reduced such that no one country feels a greater impact than another
- Country inventories will be managed in a manner intended to best meet the needs of the patients who use Cerezyme in that country in conjunction with regulatory authorities, physicians, and patient organizations
- *By reducing shipments globally to ~20% of normal consumption, we hope to conserve supply for the most vulnerable patients until new supply of Cerezyme becomes available in the November-December timeframe*
- Even with this plan, we cannot guarantee supply of Cerezyme

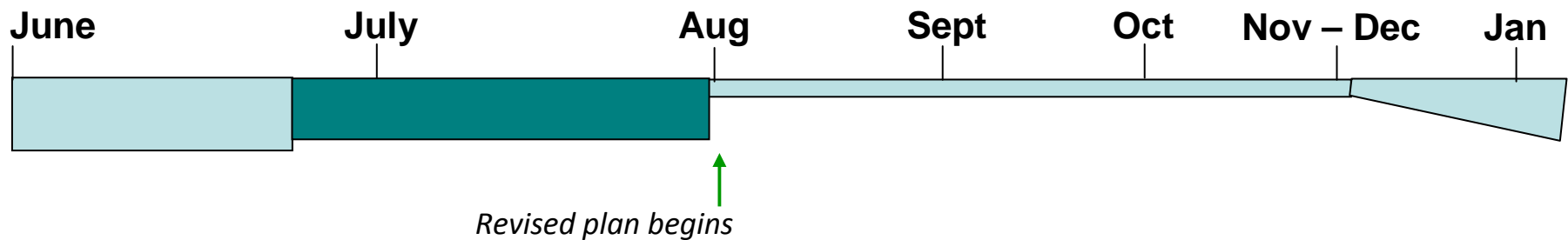
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Where We Are Going

Active supply management

- *Actions*
 - Revised local supply management
- *Result*
 - Cerezyme supply will be reserved for most vulnerable patients as defined by country
 - Most patients will need to temporarily interrupt Cerezyme infusions
 - Some patients may switch to investigational therapies through treatment-IND protocols or clinical trials during this period



Time periods are estimates

Where We Are Going – Remaining Variables

- FDA agreed with Genzyme's decision to release final two lots of finished Cerezyme
- Evaluation of these lots is in process at EMEA
- No further regulatory decisions remain regarding finished goods or work-in-process inventory
- Therefore, the main issue remaining is successful production in Allston facility

Where We Are Going: Allston Landing Update

- Process of sanitizing the Allston Landing facility is complete
- Production of new Cerezyme and Fabrazyme have begun
 - By end of August, all 6 bioreactors (2 FZ and 4 CZ) are expected to be running
- New inventories available in the November/December timeframe



Where We Are Going: Alternatives During This Time

1. Phase 3 trials for Type I Gaucher patients
 - a. GENZ-116238 small molecule
 - a. ENGAGE – Naïve patients
 - b. ENCORE – Switch patients
 - a. Possibly Increase the number of participants and sites
 - b. Amend criteria to accommodate patients that missed infusions
2. Special Access Protocols
 1. In the U.S., there is a possibility of a Treatment IND (T-IND) for GENZ-116238 (filed in July; awaiting FDA decision)
 2. Compassionate use access options for Europe under development
 3. In the U.S., Shire's and Protalix's T-INDs have been approved

Contact Shire, Protalix, or Genzyme directly for information about access to investigational products

Staying Informed: Supply Update Website

Genzyme supply update
Information related to the production and availability of Cerezyme® and Fabrazyme®

[Home](#) | [Latest News](#) | [Archives](#) | [Contact](#) | [FAQs](#) | [Glossary](#)

Keeping you informed

On June 16th, Genzyme communicated that we temporarily suspended manufacturing of Cerezyme® (Imiglucerase for injection) and Fabrazyme® (agalsidase beta) at our Allston facility in Massachusetts after identifying a viral contamination in a bioreactor used for Cerezyme production. We are currently sanitizing this facility and plan to resume full production by the end of July.

While production at our other manufacturing sites is not affected, the temporary suspension of production at the Allston facility will constrain supply for Cerezyme and Fabrazyme. We know the critical importance of these therapies to patients around the world, and our number one priority is to rapidly resume full production and minimize therapy disruption.

We want to assure you that the virus was not detected in any released lots of Cerezyme, the virus (Vesivirus 2117) has not been detected in the bioreactors specifically used in the production of Fabrazyme at the Allston facility, and the virus has never been shown to cause health problems in humans. The main consequence of the virus is to reduce the amount of enzyme produced by the CHO cells used in our manufacturing processes.

We are working closely with treating physicians, other health care providers, patient communities and regulatory officials worldwide to support patients with Gaucher and Fabry disease during this period of constrained supply.

We are committed to keeping you aware of our progress in overcoming the current supply situation, and encourage you to check back frequently for the latest information. We know that you would like to understand what to expect not just in the near term but also in the long term for your treatment and care. If you would like regular updates sent to your email, please submit your contact information via the "Stay Informed" section on this website. We also want to hear from you. If you have questions or feedback of any kind, [please contact us](#).

Allston Cleanup Checklist

- production stopped
- sanitization started
- sanitization completed
- facility reassembled
- production started

Recent Posts

- [Information about Today's Press Release \(07/22/09\)](#)
- [An Update on the Allston Facility Sanitization Process \(7/14/09\)](#)
- [Information about the Fabrazyme \(agalsidase beta\) Treatment Guidelines \(7/7/09\)](#)
- [Information about the Cerezyme \(Imiglucerase for injection\) Treatment Guidelines \(7/7/09\)](#)
- [Information about Genzyme's long term manufacturing capacity \(7/1/09\)](#)
- [Information About Supply Allocation Recommendations \(6/25/09\)](#)
- [Follow-up on June 25, 2009 press release \(6/25/09\)](#)
- [Is it safe for me to use the vials I currently have of Cerezyme \(Imiglucerase for injection\) and/or Fabrazyme \(agalsidase beta\)? \(6/25/09\)](#)
- [How is the supply situation managed? \(6/23/09\)](#)
- [Information about FDA approval of some inventory of Cerezyme \(Imiglucerase for injection\) on Wednesday, June 17, 2009 \(6/19/09\)](#)

About This Site

We have temporarily suspended bulk production of Cerezyme® (Imiglucerase for injection) and Fabrazyme® (agalsidase beta) at our Allston Landing facility, and inventories are not sufficient to avoid shortages during this period of suspended

- Supplyupdate.genzyme.com
- Contains globally relevant information
- Frequent content changes including:
 - Supply management information
 - Information & links related to Treatment Guidelines
 - Updates on status of Allston clean up
 - Press releases
 - Frequently asked questions
 - Glossary of terms
 - Links to patient organizations
- Provides feedback mechanism for community to contact us directly



Frequently Asked Questions

“What steps are you taking to prevent this virus from coming back into the Allston Landing facility?”

- Integrate Vesivirus testing into our existing testing panel to make sure external raw materials are tested before use
- Enhance filtration to remove viruses

“How could the situation change so quickly? Just a few weeks ago, you said the problem would last through August?”

- From the point at which the bioreactor contamination was identified, this has been a dynamic situation. We have communicated with the community as readily, openly, and accurately as possible based on the information we have at each particular point in time. Genzyme communicated to physicians and patients throughout June regarding our projections of a supply shortage for Cerezyme beginning in August. The plan that was developed by the EMEA and CSWG in June was based on projections including the release of existing Cerezyme WIP inventory and an immediate high level of compliance with the dose reduction guidelines. The data we have developed on the WIP inventory has now defined our inventory position to be lower than we originally estimated when we first communicated in June. The change is based on subsequent data and analysis which suggests that although use of this material might pose no risk to patients, we could not exclude the possibility that processing the material might expose the plant to a risk of recontamination. Since the most important goal is to restore the plant to its original state capable of reliably producing Cerezyme, this was not an acceptable risk.

“What are you doing to increase supply levels for the future?”

- In 2008, we began construction of a new Framingham manufacturing facility to enable production of Cerezyme and Fabrazyme in an additional location to the Allston facility. The new bioreactors in Framingham will be 2000 liter capacity, the same size as our current Allston bioreactors. We are well underway with this expansion and currently anticipate receiving approval from regulators (e.g. the FDA in the United States and the EMEA in Europe) for the production of Fabrazyme in 2011 and for the production of Cerezyme in 2012.
- Moved all Myozyme production to Geel, Belgium to free up bioreactors in Allston. Myozyme made at the 4000 L scale was approved for use by the EMEA in February 2009.

“Why is your first communication about problems like this supply shortage via a press release and not directly to those who use your products?”

- As a U.S. publicly traded company, Genzyme is subject to certain rules and regulations regarding disclosures of material information (information that could be expected to affect a company’s stock price) to the public. Generally, this means that when the company publicly discloses this information, it must report it broadly, often via a press release, so that everyone learns the information at once. There are also laws and regulations that govern when, what and how we communicate information to patients, physicians and other audiences, which vary from country to country. We endeavor to provide updates to the Gaucher and Fabry communities as quickly as possible within these legal obligations. Communication with patients, physicians and other stakeholders remains a top priority. In countries where we are able to communicate directly to patients, we strive to communicate with you directly. In areas where direct communication with patients is not allowed, we plan to continue to work with patient organizations to provide updated information to the community. We have also developed the [supply update website](#) as a tool to help provide important information to the community. If you have ideas or suggestions on how we might improve this process, please feel free to submit them through the website or via your local patient association.

Who to Contact for Questions?

- Insert Appropriate Local Information Here
 - Patient Organization
 - Genzyme Office/Medical Information
 - Your physician