Update on LEU TechneLite® Generators

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Mo-99 Topical Meeting
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## Lantheus Medical Imaging (LMI)

| **Company Overview** | • A global leader in innovative diagnostic medical imaging agents  
| | • Pharmaceutical imaging agents used to diagnose coronary artery disease, congestive heart failure, stroke, peripheral vascular disease and other diseases |
| **Headquarters** | • N. Billerica, Massachusetts |
| **Offices** | • Canada, Puerto Rico, Australia |
| **Commercial Products** | • 10 |
| **Development Pipeline** | • Three next-generation product candidates that use Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI) |
TechneLite® Generator - History

- $^{99m}\text{Tc}$- generator developed in Brookhaven National Labs in 1958 and commercialized in the mid 1960s
- $^{99m}\text{Tc}$ generator manufactured by LMI and predecessors since 1967
  - New England Nuclear (NEN) introduced Tc-99m Generator based on Mo-99 produced by neutron capture ($^{98}\text{Mo (n,γ)}^{99}\text{Mo}$)
  - NDA for generator based on Mo-99 from fission of U-235 ($^{235}\text{U (n,f)}^{99}\text{Mo}$) approved in 1975
- TechneLite®, terminally sterilized generator introduced in 1993
- TechneLite®, CMS compliant LEU sourced Mo-99 introduced in 2013
Lantheus Medical Imaging
LEU Leadership

• **FIRST** – to receive FDA approval for LEU Mo-99 in North America:
  – ANSTO: May 2011
  – NTP: September 2010

• **FIRST** – to commercially sell a generator made with only LEU Mo-99 (December 2010)

• **FIRST** – to have LEU Mo-99 as a routine part of blended Tc-99m production (May 2011)

• **FIRST** – to commercially manufacture and regularly distribute CMS non-HEU incremental add-on HOPPS payment compliant generators (beginning Jan. 7, 2013)
Lantheus Medical Imaging adds the innovative LEU Technelite® (Technetium Tc 99m Generator) to our Nuclear Medicine Portfolio

Available NOW!

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LEU TechneLite® Manufacture

- Dedicated, weekly LEU TechneLite® generator runs 2013-15 (87.3%)
  - 2013 – 46 weeks
  - 2014 – 42 weeks
  - 2015 – (34 out of 35) (thru August 31) - 97%*

- Validated cleaning process after each run ensures manufacturing line is clean and meets the CMS >95% LEU content criteria

- TechneLite® LEU generators marked as eligible for CMS add-on HOPPS payment by circular green sticker affixed to top of generator can and unique item number

- LEU TechneLite® generator segregation and identification
  - manufacturing batch records - different code for LEU Mo-99 than HEU Mo-99
  - specific catalog/item number in the Lantheus product catalog and systems (18000-ML versus 18000-M for HEU generator)
  - identifying item number is also on packing, shipping documents and invoice
  - lot number unique identifier – with an “A” incorporated (non-HEU generator - M123456A)

- Certification document provided by LMI to customers receiving an LEU TechneLite® generator

*HEU shipped in error instead of LEU
LEU Technetium® Features

• Quality and properties of LEU Technetium® generators are equivalent to HEU or blended LEU/HEU Mo-99 generators
  – Radiochemical purity is the same
  – Mo-99 breakthrough is the same
  – Elution efficiency (see chart)
• Tc-99m produced from > 95% LEU content Technetium® generators meets the USP specification
• All aspects of LEU Technetium® generators including product insert and labeling are identical to blended or HEU generator
• Only difference is the “green dot”
Substantial misperceptions and misunderstandings continue to persist in the market about LEU availability and reliability, CMS add-on payment, etc.

Lantheus interacting with customers to promote uptake of LEU generators
   – Adoption is increasing at Rx level
     • new LEU dose business mostly from VA Hospitals (leveled off)
   – CMS data demonstrates steadily rising claims, though still small

Lantheus continues to provide information to increase LEU knowledge at hospitals (i.e. August 2014 webinar and planned 2015 webinar)

Continue to assess LEU supply chain ability to service additional or different days of LEU TechneLite® manufacture

Production volume increases and day of manufacture changes dependent upon demand and customer committed orders
LEU TechneLite® generators shipped activity

LMI Curies per Week
Full Transition to LEU

• LEU Mo-99 as proportion of total LMI purchased Mo-99:
  
  2013: 20%
  2014: 25%
  2015 ~35%

• LEU supply chain issues experienced in first half of 2014 were effectively addressed and remedied

• ANSTO plans capacity increase in existing plant starting June 2016 to 2250 Ci/week

• ANSTO ANM project (3500 Ci/week) commissioning 2H2016.

• IRE LEU conversion expected mid-year 2016 (hot runs in fall 2015; validation and qualification first half 2016)

• Lantheus currently anticipates a full transition to LEU by end of November 2016 (assuming IRE LEU conversion is on schedule)
Full Transition to LEU - Barriers

- Technical: none
- Market: already described in commercial status slide
- Logistical:
  - commercial cargo transport from Australia, Belgium, and South Africa poses challenges; occasional delays due to unexpected administrative issues
- Regulatory:
  - ANSTO and NTP LEU sources already FDA approved
  - IRE LEU conversion will require submission of Prior Approval Supplement (PAS) to Lantheus Technelite NDA:
    - 3 separate qualification batches, non-commercial (range of generator sizes produced) with kit testing (anionic, ionic, and neutral)
    - data package submission
    - 4 month statutory review period
    - each additional reactor (irradiation source) will require further FDA filing (TBD)
  - ANSTO ANM will likely also require PAS due to new target, process (same as NTP target and process)
  - FDA has worked diligently in the past to expedite reviews and approvals
LEU TechneLite® and Nuclear Pharmacies

• Lantheus LEU Webinar has been filmed for September roll out:
  – Provides a Nuclear Pharmacy’s 2-year experience
    • Implementation into pharmacy operation
      – Operation changes
      – System changes
    • Education of End Users in market
    • Delivery of LEU doses to End Users
  – Provides an End Users’ experience
    • Implementation into operation
      – Operation changes
      – System changes
    • Reimbursement process

  - NOT AS DIFFICULT AS OFTEN PORTRAYED

• UPPI “LEU Walk,” implementing in 30+ pharmacies
Xe-133

• Xe-133 used in U.S. for pulmonary imaging

• NRU is currently the only source of bulk Xe-133 gas; Lantheus only Xe-133 pharmaceutical product supplier in U.S.

• Lantheus announced new strategic agreement on January 21, 2015 with IRE for future supply of Xe-133 gas

• IRE will provide unprocessed radiochemical Xe-133 to Lantheus for processing and finishing

• Development and commercialization work in process, good progress to date
  – Type A transport container designed and fleet being fabricated
  – Argonne National Lab provided analytical assistance

• Regulatory review and approval will be required

• Lantheus estimates commercial production will occur in 2016

• Investigating additional diversification options and LEU-based Xe-133
Conclusions

- Lantheus has taken a leadership role in use of LEU Mo-99 in its TechneLite® generator supply chain
- Commercial adoption of LEU TechneLite® generators is steadily increasing
- LEU contributes to enhanced global nuclear security and creates foundation for more secure, reliable future supply of Mo-99
- Lantheus and IRE are working diligently to secure future Xe-133 supply
Thank you

Questions?