Commercial Production and Distribution of Astatine-211 for Targeted Alpha Therapy

Astatine-211 User Group Meeting
September 6, 2022

David M. Eve
VP, Medical Affairs
Ionetix Corporation was founded in 2010 with a revolutionary concept to create a new paradigm for isotope access centered on proven superconducting cyclotron technology developed at the MIT Plasma Fusion Laboratory.

**Lansing, Michigan** - Company HQ and home of the DoE’s Facility for Rare Isotope Production

**Production and Supply Platform**

**Cyclotron Technology**: In-house expertise to design, engineer, build, and service “next generation” cyclotrons.

**Isotope & Radiopharmaceutical Manufacturing**: Vertical integration - cyclotron deployment, isotope production, drug manufacturing and “white glove” distribution.

**Quality & Regulatory**: Highly experienced regulatory affairs team with a proven track record with the FDA and NRC agencies.

**Achievements and Milestones**

**Cyclotron Technology**: Two cyclotrons, one for short-lived positron-emitting and now one for therapeutic alpha-emitting radioisotopes.
- 12 MeV Cyclotron – 2013
- 30 MeV Cyclotron – 2021

**Isotope &Radiopharmaceutical Manufacturing**: 9 locations, including new alpha isotope facility.
- ANDA for N-13 Ammonia (210524) – approved 2018
- NDC: 71162-0001-10 & 71162-0001-05

**Quality & Regulatory**: 8 Successful FDA inspections to date across all manufacturing sites.
Targeted Alpha Therapy Radionuclide Supply: Astatine-211

Growing demand in TAT raises need for supply

1. New facility in **Lansing, Michigan** dedicated to high-yield alpha isotope production and distribution
2. Optimization of **existing cyclotron** technology for improved At-211 production
3. Planned growth for **Regional Production Facilities** for expanded access & availability
4. Development of **new cyclotron** system to support regional growth

Astatine-211 production in the U.S.

- University of Washington
- University of Pennsylvania
- University of California, Davis
- Texas A&M University
- Duke University

Ionetix commercial Astatine-211 supply

- **New facility in Lansing, Michigan** dedicated to high-yield alpha isotope production and distribution
- Optimization of **existing cyclotron** technology for improved At-211 production
- Planned growth for **Regional Production Facilities** for expanded access & availability
- Development of **new cyclotron** system to support regional growth

---


Targeted Alpha Therapy Manufacturing Services and Solutions – Cyclotron and Vault

Lansing, Michigan

Cyclotron Assembly and Installation

Magnet Installation and Magnetic Field Mapping Completed in May 2022

Cyclotron Vault

Vault Completed in August 2022
## Alpha Facility Timeline and Astatine-211 Drug Development Collaboration

### Lansing, Michigan

#### Facility Project Timeline

<table>
<thead>
<tr>
<th>Program</th>
<th>Completion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclotron</td>
<td>December 2022</td>
</tr>
<tr>
<td>Radiochemistry Lab</td>
<td>March 2023</td>
</tr>
<tr>
<td><strong>Astatine-211 Production – Distribution Ready</strong></td>
<td><strong>April 2023</strong></td>
</tr>
<tr>
<td>Astatine-211 Drug Master File (DMF)</td>
<td>July 2023</td>
</tr>
</tbody>
</table>

#### Customer At-211 Pipeline

<table>
<thead>
<tr>
<th>Program</th>
<th>Lead Compound</th>
<th>Indication</th>
<th>Discovery</th>
<th>Preclinical</th>
<th>IND-Enabling</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMI21</td>
<td>PSMA</td>
<td>Prostate Cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATO-101</td>
<td>Girentuximab</td>
<td>Bladder Cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Ionetix 30 MeV Cyclotron Development Roadmap – Astatine-211 Production Cyclotron

#### 30 MeV, Alpha Particle Cyclotron

<table>
<thead>
<tr>
<th>Year</th>
<th>Model</th>
<th>Details</th>
</tr>
</thead>
</table>
| 2019 | CS-30 Cyclotron | Duke University  
       Contracted to support cyclotron upgrades |
| 2021 | CS-30 “Upgraded” Cyclotron | Ionetix Alpha Facility, Lansing  
       Modified CS-30 – **Optimized for Alpha Particles**. (University of Michigan 1982)  
       Internal Target  
       New main coils, trim coils, central region, magnet sectors, power supply, operating system, target |
| 2024 | R&D ION-30 Cyclotron | Ionetix Manufactured Cyclotron  
       4-sector magnet  
       Internal Target |
| >2024 | R&D ION-30X Cyclotron | Ionetix Manufactured Cyclotron  
       High Intensity  
       4-sector magnet with central hole of 30 mm in radius  
       External ion source: Injection line/Spiral inflector |
## Ionetix 30 MeV Cyclotron Development Roadmap: Technical Specifications

### 30 MeV, Alpha Particle Cyclotron

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Cyclotron</th>
<th>Ion Source</th>
<th>Central Region</th>
<th>Magnet</th>
<th>Target</th>
<th>Current (alphas)</th>
<th>Energy (alphas)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Cyclotron Corporation (TCC)</td>
<td>CS-30</td>
<td>Internal</td>
<td>Factory Original</td>
<td>Factory Original 3-sectors</td>
<td>Internal</td>
<td>90 µA</td>
<td>~28.7 MeV</td>
</tr>
<tr>
<td>The Cyclotron Corporation (TCC) – Ionetix Upgrade</td>
<td>CS-30 “Upgraded”</td>
<td>Internal</td>
<td>New</td>
<td>New 3-sectors</td>
<td>Internal</td>
<td>90 µA</td>
<td>~28.7 MeV</td>
</tr>
<tr>
<td>Ionetix – R&amp;D</td>
<td>ION-30</td>
<td>Internal</td>
<td>New</td>
<td>4-sectors</td>
<td>Internal</td>
<td>~150 µA</td>
<td>30 MeV</td>
</tr>
<tr>
<td>Ionetix – R&amp;D</td>
<td>ION-30X</td>
<td>External Injection Line Spiral Inflector</td>
<td>New</td>
<td>4-sectors, Central hole Radius 30mm</td>
<td>Internal/External</td>
<td>~400 µA</td>
<td>30 MeV</td>
</tr>
</tbody>
</table>

---

*Note: Values are approximate and subject to change.*
Ionetix Upgraded CS30 for Astatine-211 Production: New Central Region

30 MeV, Alpha Particle Cyclotron

Complete electrical and magnetic field analysis of the CS-30.

- **Objective:** Precisely calculate beam transmission and delivery on target.
- **Result:** Redesign of the central region and sectors.
- **Impact:** Improved beam capture efficiency to accelerate more particles to the target while maintaining consistency of beam spot and spread on target.

**TCC CS-30**
Factory Central Region

**Ionetix Upgraded CS-30**
New Central Region

**Internal Target Beam Spot on Target**
Ionetix Upgraded CS30 for Astatine-211 Production: New Sectors

30 MeV, Alpha Particle Cyclotron

- TCC CS-30 Magnet Sectors and Field MAP
- Ionetix Upgraded CS-30 Magnet Sector Shims

- 1st harmonics magnetic field amplitude limited to ~20 gauss in the acceleration region
- Isochronous magnetic field errors reduced significantly for both proton and alpha particles
- Impact: Improved beam transmissions efficiencies from the ion source to the target and better beam spot distributions on the target for At-211 production

Ionetix Upgraded CS-30 Factory Sectors

- TCC CS-30 Factory Sectors
- Isochronous Field for Alpha particles
- Isochronous Field for Proton particles

Impact:
- Improved beam transmissions efficiencies from the ion source to the target and better beam spot distributions on the target for At-211 production
Ionetix Upgraded CS30 for Astatine-211 Production: Astatine-211 Targetry

30 MeV, Alpha Particle Cyclotron

- **Internal Target**
- **New Upgraded Target Control Arm**
  - Added additional controls
  - The target angle can be changed or rotated for improved beam alignment
- **Bismuth-209 Target**
Ionetix Alpha Isotope Supply Chain Solution - Summary

Lansing, Michigan

At-211 Production beginning in 2023
- Upgraded CS-30 Cyclotron for near term At-211 Production

Alpha Radionuclide API Supply
- Commercial Processing and Purification Solutions
- DMF for At-211
- Batch Quality Control / Certificate of Analysis release

Full cGMP Facility for Radiolabeling
- Contract Manufacturing
- Manual and Automated Commercial Synthesis Solutions
- Independent Clean Room available for Research Work

Regional Production and Distribution Model
- Ship target, processed At-211 or final drug product
Ionetix Alpha-Emitting Radionuclide Production Team

Acknowledgements:

**Cyclotron Team**
- John Vincent, Ph.D., VP of R&D, Project Leader
- Xiaoyu Wu, Ph.D., Senior Physicist
- Mark Leuschner, Ph.D., VP of Special Projects and Strategy
- Gary Horner, Accelerator Engineer
- Gabe Blosser, Mechanical Engineer
- Zachary Neville, Mechanical Engineer
- S. Vorozhtsov, Ph.D., Consultant Scientist
- V. Smirnov, Ph.D., Consultant Scientist

**Operations Team**
- Anthony Stagnolia, COO
- Alex Yordanov, Ph.D, Director of CMC, Product Development
- Jill Wilson, Senior Director, Regulatory Affairs & QA
- Michael Levy, Director, Radiation Compliance, RSO
- Rick Hart, Cyclotron Operator and QC Production Technician
For more information, please contact:

David Eve
deve@ionetix.com

Alex Yordanov
ayordanov@ionetix.com

Alpha Isotope Facility
6424 Westland Way
Lansing, MI 48917

Corporate Office
3130 Sovereign Drive, Suite 5D
Lansing, MI 48911

Executive Offices
101 The Embarcadero, Suite 210
San Francisco, CA 94105

www.ionetix.com