Ambrx

Protein Medicinal Chemistry with an Expanded Genetic Code

Oncology Product and Platform Partnering Opportunity

April 2017
Ambrx has Made Advances in Proprietary Platform and Titer while Achieving Clinical Validation

- Private company based in La Jolla, California
- Focused development of bio-conjugates utilizing propriety site-specific non-natural amino acid
- Diverse portfolio of novel wholly owned product candidates including Antibody-Drug Conjugates (ADC) and Bi-Specifics
  - ADC: ARX-788 (Phase I) clinical validation of platform technology and cost effective titer yields have been achieved
  - Bi-Specific: Anti-CD3 Folate (Pre-Clinical) incorporates platform technology allowing for differentiating optimal balance of efficacy / toxicity
- Major product and platform partnerships with Astellas / Agensys, BMS and Eli Lilly and Company
- Significant improvements in mammalian expression platform with titer up to 1.5 - 2.0 g/L
Ambrx Portfolio Includes an Array of Wholly Owned and Partnered Based on Technology Platform

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<th>Ambrx Programs</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
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<td>ARX-788 Anti-HER2 ADC - Oncology&lt;sup&gt;1&lt;/sup&gt;</td>
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<td>Anti-PSMA ADC - Oncology</td>
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<td>Anti-CD70 ADC - Oncology</td>
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<td>ARX-618 FGF21 - NASH</td>
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<td>Relaxin (Next Generation) - Heart Failure</td>
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<td>Bio-Conjugates for Animal Health (multiple)</td>
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<sup>1</sup> Partnered in China with Zhejiang Medicine. Ambrx retains rest-of-world rights for ARX788 development and commercialization.
Ambrx Platform Technology Remains Differentiated and Best-in-Class within ADC Field

**Proprietary Site-Specific Non-Native Amino Acid Incorporation Technology is Least Limiting Conjugation Tool**

- Most elegant way to build a site-specific ADC through direct conjugation
- No complex work-arounds necessary (e.g. de-capping, re-oxidizing and ring opening for engineered cysteine, etc.)
- No ligation enzyme and its corresponding recognition sequence on antibody necessary
- Highly stable linker enables wild-type antibody-like *in vivo* PK
- Interchangeable platform that allows for incorporation of other innovator technologies (e.g. warhead, linker, etc.)
- Sole technology with complete and all encompassing IP protection
- Robust manufacturability with titer up to 1.5 - 2.0 g/L
Site-Specific Incorporation of Ambrx Amino Acid Leads to Robust Manufacturability Using Traditional Facility

- E. coli strains and stable CHO cell lines with build-in Ambrx technology
- Multiple Ambrx amino acid amenable for wide selection of orthogonal conjugation chemistries
- Highly compatible with current manufacturing facility and process
- Robust scalability: E. coli-50,000 L; CHO-2,000 L

The unique codon ④ is placed at a precise position in the DNA sequence and this is transcribed to a unique codon in the mRNA. The Ambrx synthetase ② and Ambrx tRNA ③ translate and transcribe the DNA sequence and incorporate the Ambrx amino acid ① into the specified site of the protein product ⑤.
ARX-788 is an anti-HER2 ADC that incorporates non-natural amino acid

ARX-788 is currently in a Phase 1 trial to define the recommended dose for Phase 2

Payload is Amberstatin (AS269), a proprietary Ambrx microtubule inhibitor

Conjugation of Amberstatin to anti-Her2 antibody is site-specific and quantitative (DAR = 1.9)
Potential best and first-in-class ADC therapeutic

- Pre-clinical models suggest anti-PSMA ADC is more efficacious and stable compared to competition
- Ambrx site-specific conjugation technology embedded within anti-PSMA ADC has been clinically validated in ARX-788

Target market is relapse / refractory prostate cancer
Ambrx Has Built a Robust Bi-Specific Product and Platform Based on Proprietary Technology

**Product**
- Only anti-CD3 Folate bi-specific that is conjugated to a small molecule (folate) for tumor targeting. Asset is 18 months from IND.
- Potential indications in ovarian, NSCLC and triple negative breast cancer
- Humanized and cyno cross-reactive anti-CD3 antibody
- Full set of variants with different anti-CD3 affinity to optimize efficacy while reducing the potential for cytokine-release storm / toxicity
- Half-life extender allows for improved PK

**Platform**
- Next generation anti-CD3 bi-specific based platform with potential applications in multiple oncology targets
- Ambrx technology allows for direct conjugation between anti-CD3 antibody and anti-tumor ligand (e.g. whole antibody, fab or folate) which facilitates improvements in half-life and manufacturability over competition
Ambrx is Seeking Global Product and Platform Partnerships for ADC and Bi-Specific Fields

• **Product Collaboration**
  – Includes ARX-788 (Phase I), anti-PSMA and anti-CD3 Folate (both 18 months to IND)
  – Flexible in deal structure (exclusive to geographical regions, joint development and/or option of joint-development, etc.)

• **Platform Collaboration**
  – Utilize partner target and/or warhead, antibody, etc. for ADC
  – Ambrx would re-engineer antibody to enable un-natural amino acid conjugation
  – Flexible in deal structure

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