ATNM-US Department of Energy

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Actinium is on the cusp of clinical successes that can realize our vision for a fully integrated specialty oncology company built on our innovative R&D capabilities

Leading radiotherapy company with a late-stage pipeline focused on conditioning for bone marrow transplant (BMT)

Iomab-B, a Ph III-complete, paradigm shifting induction and conditioning agent, for R/R AML; topline data expected in Q3:2022. Immedica AB secured as EU commercial partner

Actimab-A investigated in R/R AML trials including in combination with Bcl-2 targeted venetoclax and the salvage chemotherapy CLAG-M, the latter demonstrating 80% ORR

Next-generation clinical-stage targeted conditioning pipeline for the large and rapidly growing Cell and Gene Therapy markets advancing

Leading edge innovation in radiopharma R&D drives partnerships including Astellas in solid tumor theranostics, AVEO with first in class HER3-targeted radiotherapy, EpicentRx with CD47 immunotherapy and proprietary radiotherapy combinations in solid tumors

r/r AML – Relapsed/Refractory Acute Myeloid Leukemia
* Unaudited proforma cash figure based on cash on hand and $35 million upfront payment from Immedica
AWE Platform Powers Our Pipeline of ARCs

Deep pipeline of potent Antibody Radiation-Conjugates with significant therapeutic and combination potential in hematology and oncology

<table>
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<th>Targeted Conditioning &amp; CD33 Therapeutic Pipeline</th>
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<td>r/r AML 55+</td>
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<td>EU/MENA Commercial Partner</td>
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<td>Iomab-ACT CAR-T – CD45</td>
<td>CD19 r/r B-ALL, DLBCL</td>
<td>Phase 1/2</td>
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<td>Data update at TCT</td>
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<tr>
<td>Iomab-ACT GeneTx – CD45</td>
<td>Anti-HIV</td>
<td>Phase 1/2</td>
<td></td>
<td>Top line data Q3 2022</td>
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<td>R/R AML</td>
<td>Phase 1 – Complete</td>
<td>Developing registration-enabling regulatory strategy</td>
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<tr>
<td>Actimab-A + venetoclax</td>
<td>R/R AML</td>
<td>Phase 1/2</td>
<td>Determine Phase 2 dose</td>
<td></td>
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</table>

**AWE Platform Collaborations**

- Ac-225 + undisclosed Astellas targeting agents for solid tumor theranostics
- Ac-225 HER3 ARC for solid tumor indications
- Ac-225 + RRx-001 (small molecule CD47-SIRPα inhibitor) in AML

**AWE Preclinical Programs**

- HER2 ARC + Magrolimab (CD47) in solid tumors
- Actimab-A + Magrolimab (CD47) in AML
- Ac-225- Daratumumab (CD38)
- ARCs + undisclosed targets

AML – Acute Myeloid Leukemia, MM – Multiple Myeloma, ALL – Acute Lymphoblastic Leukemia, DLBCL – Diffuse Large B-Cell Lymphoma, HIV = Human Immunodeficiency Virus r/r= relapsed/refractory
AWE Platform Drives Pipeline, Enables Future Opportunities

*Our AWE technology platform allows us to create ARCs for multiple areas of clinical development*

### AWE Technology Platform

**Scientific Founders**

- Memorial Sloan Kettering Cancer Center
- Organon

**Collaborators**

- astellas
- EpicentRx

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**Strong, Growing IP Portfolio of 170+ Patents**

### Multiple Validated Targets

- **CD45**
  - Leukemia, Lymphoma and immune cells

- **CD33**
  - AML, MDS and MM

- **Undisclosed**
  - Solid tumor theranostics

- **CD38**
  - MM and leukemia cells

- **HER2 & HER3**
  - Solid tumors

- **CD47**
  - Solid tumors and blood cancers

### Multiple Therapeutic Isotopes

- **Iodine-131**
  - Range: 2.3 mm
  - Energy: 0.6 MeV

- **Actinium-225**
  - Range: 0.048 mm
  - Energy: 5.8 MeV

- **Lutetium-177**
  - Range: 1.8 mm
  - Energy: 0.50 MeV

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**Areas of Focus**

**Targeted Conditioning**

- CD45
- CD33

**Solid Tumor Therapeutic Combinations**

- astellas
- CD47
- HER2/3

**Next-Generation ARCs**

- CD33
- CD47
- CD38
- Undisclosed

**Enhanced R&D Infrastructure & Capabilities**

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Highly Differentiated CD33 Program

Focused on establishing Actimab-A as a backbone therapy for r/r AML

- Actimab-A targets highly validated CD33 with potent Ac-225 alpha emitter
- Clinical experience in ~150 patients in 6 clinical trials driving combination “backbone” strategy with high response rates
- Minimal non-hematologic toxicities > grade 3 outside of myelosuppression in Phase 1/2 trial
- Multiple opportunities to use Actimab-A in combination with chemotherapy, targeted agents and immunotherapy

### Actimab-A Phase 1/2 Results

<table>
<thead>
<tr>
<th>Dose Level (µCi/kg/fraction)</th>
<th>Response Rate (%) (CR, CRp &amp; Cri)</th>
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<tbody>
<tr>
<td>0.5 µCi/kg</td>
<td>0%</td>
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<tr>
<td>1.0 µCi/kg</td>
<td>17% (1 CR)</td>
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<tr>
<td>1.5 µCi/kg²</td>
<td>22% (3 CRp, 3 CRi)</td>
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<tr>
<td>2.0 µCi/kg³</td>
<td>69% (1 CR, 2 CRp, 6 CRi)</td>
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### Broad Applicability
- CD33 is expressed in virtually all patients with AML
- CD33 is expressed regardless of cytogenetics or mutations

### Differentiated MoA
- Potent radiation via Ac-225 directed at radiosensitive AML cells
- ARCs are agnostic to cytogenetics or mutations

### Targeted Precision
- Short path length of Ac-225 limits bystander effect
- Well-tolerated
- Minimal extramedullary toxicity
Promising Phase 1 Results: Actimab-A + CLAG-M Combo

High remission and MRD- rates vs approved agents from Actimab-A + CLAG-M combo in R/R AML

- 100% remission rate (1 CR, 2 CRp) in cohort 3, which has been determined Phase 2 dose
- CR/CRp in all dose cohorts, including subtherapeutic doses
- 80% ORR in patients receiving less than 4 prior therapies
- 60% ORR in patients with prior venetoclax treatment

- MRD negativity in 72% of all patients with remissions (9/12)
- CR/CRi and MRD- observed in all dose cohorts
- No 30-day mortality reported in any cohort

High MRD negativity rates and ORR in patients with prior venetoclax therapy support continued development

Actimab-A + Venetoclax Combination Trial

Venetoclax is used widely across AML segments, however, most patients ultimately relapse - preclinical and clinical data support mechanistic synergy of Actimab-A with Venetoclax

- Venetoclax is a Bcl-2 inhibitor approved in 3 hematologic indications and is recommended for fit and unfit patients with AML with HMA or LDAC per NCCN guidelines. Venetoclax showed a 19% ORR in R/R AML as single agent

Actimab-A + Venetoclax Phase 1 Results

- 67% ORR in Patients with TP53 mutation, including one patient in follow-up 200+ days
- Trial to advanced to dose cohort 3 of 1.5 μCi/kg of Actimab-A
- No early deaths reported
- Additional Phase 1 data from continued dose escalation expected in 2022

Actimab-A restores sensitivity to venetoclax and has single agent anti-leukemic activity supporting the rationale for ongoing Phase 1/2 combination trial

Rationale: Actimab-A depletes Mcl-1, a mediator of venetoclax resistance

Demonstrable Mechanistic Synergy

Actimab-A Combinations Showing Impressive Results in R/R AML

Potential best in class profiles for both fit and unfit patients with R/R AML

- Actimab-A + CLAG-M (16)
- CLAG-M (1)
- FLAG-Ida (2)
- MEC (3)
- Gilteritinib (FLT3) (4)
- Uproleselan (E-selectin) + MEC (5)
- Alvocidib (CDK9) + Cytarabine + MEC (6)
- Magrolimab (CD47) + Aza (7)
- Alvocidib (CDK9) + Cytarabine + MEC (6)
- Uproleselan (E-selectin) + MEC (5)
- Gilteritinib (FLT3) (4)
- MEC (3)
- FLAG-Ida (2)
- CLAG-M (1)
- Actimab-A + CLAG-M (16)

Fit R/R AML ~50%¹⁷
Unfit R/R AML ~40%¹⁷
Supportive Care ~10%¹⁷

~10,000+ R/R/ AML Patients

Actinium has data demonstrating the potentiating and synergistic effect of targeted radiotherapy.
# Actimab-A Clinical Development Timelines

<table>
<thead>
<tr>
<th>Year</th>
<th>2022</th>
<th>2023</th>
<th>2024</th>
<th>2025</th>
<th>2026</th>
<th>2027</th>
<th>2028</th>
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<tbody>
<tr>
<td><strong>Pivotal Trial:</strong> Actimab-A + CLAG-M</td>
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<tr>
<td><strong>Ph 1b/2 Trial:</strong> Actimab-A + Venetoclax + Azacitidine</td>
<td>Ph 1 Data: Actimba-A + Venetoclax</td>
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<tr>
<td><strong>Ph 1b/2 Trial:</strong> Actimab-A + Azacitidine</td>
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<tr>
<td><strong>Dose Selection/POC Trials:</strong> Actimab-A + CD47</td>
<td>IND-enabling Data</td>
<td>IND Filing</td>
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Single-dose potency of Actimab-B ($^{225}$Ac-BC8) activity in Multiple Myeloma

- Single dose treatment of subcutaneous xenografts of MM tumors with Actimab-B effected complete tumor growth control for the duration of study.
- Neither cold BC8 or nonspecific control $^{225}$Ac-18B7 had any anti-tumor effect demonstrating the selective tumor killing of Actimab-B.

**U266 Tumor xenograft**

**H929 Tumor xenograft**
Radio-Conjugation with $^{225}\text{Ac}$ Empowers Daratumumab (Anti-CD38 mAb)

Xenograft Model of Multiple Myeloma

Dawicki et al. OncoImmunology (2019)
ATNM is committed to Ac-225 Solid Tumor Programs

HER3 Is Widely Expressed Across Solid Tumors

First-in-Class $^{225}$Ac-HER3 ARC Leads to Dramatic Tumor Regression

$^{225}$Ac-HER3 ARC Potentiates CD47 Immunotherapy


Our $^{225}$Ac ARCs have the potential to treat numerous patients with limited options:

+ Monotherapy
+ Combination with immunotherapy

Actinium Pharmaceuticals is also generating $^{225}$Ac conjugates against multiple undisclosed tumor targets including ongoing collaboration with Astellas.
ATNM proudly holds the leadership position in the development of Ac-225 radiotherapies and has the most clinical experience with over 100 patients dosed with Actimab-A, our clinical stage Ac-225 ARC.

Actimab-A is poised to move into phase 3 as a ‘backbone” therapy for treatment of patients with AML, an area of high unmet need and low survival outcomes.

Reliable and high-quality supply of Ac-225 is critical to bringing patients this potentially transformative option.

ATNM sincerely appreciates the ongoing support from DOE and is eager to expand and further develop its partnership with DOE and enabling our commitment to bring better options to cancer patients.