Forward Looking Statements

- This presentation contains forward-looking statements that involve substantial risks and uncertainties. Any statements in or made orally during this presentation about future expectations, plans and prospects for the company, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. Important factors that may cause or contribute to such differences include the factors set forth under the captions “Risk Factors” in our most recent annual report on Form 10-K and quarterly report that we filed with the U.S. Securities and Exchange Commission for the periods ended December 31, 2015 and March 31, 2016, respectively. The forward-looking statements contained in this presentation reflect our current views with respect to future events, and we assume no obligation to update any forward-looking statements except as required by applicable law.
Two unique scientific platforms serve as engines for continuous growth

SERIOUS UNMET PATIENT NEEDS

Genetically defined forms of B-cell lymphoma
Dermatomyositis
Immuo-Oncology

Multiple targets in cancer and rare diseases

TOLL-LIKE RECEPTOR IMMUNE MODULATION
THIRD GENERATION ANTISENSE (3GA)

© 2016 Idera Pharmaceuticals
# Growing Development Pipeline Advancing

## Rare Diseases – IMO-8400

<table>
<thead>
<tr>
<th>DEVELOPMENT PROGRAM</th>
<th>PRECLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PIVOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waldenström’s macroglobulinemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse large B-cell lymphoma (MYD88 L265P+)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Immuno-Oncology – IMO-2125

<table>
<thead>
<tr>
<th>DEVELOPMENT PROGRAM</th>
<th>PRECLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PIVOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractory/Relapsed Melanoma w/ CTLA4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional Tumor Types / CPI Combos</td>
<td></td>
<td></td>
<td>Planning underway</td>
<td></td>
</tr>
</tbody>
</table>

## RESEARCH PROGRAM

<table>
<thead>
<tr>
<th>RESEARCH PROGRAM</th>
<th>PRECLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PIVOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>THIRD GENERATION ANTISENSE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NLRP3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DUX4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undisclosed Targets</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Immuno-Oncology Clinical Development Program

Intratumoral Therapy with IMO-2125, A TLR9 Agonist
Tumor microenvironment is key to clinical outcome in cancer immunotherapy

Figure from: Pardoll, D, *The blockade of immune checkpoints in cancer immunotherapy;* Nat Rev Cancer. 2012; 252-64
Toll-like receptor 9 is a rationale target for induction of anti-tumor immunity

Toll-like receptor (TLR) 9
- Activator of innate immunity
- Preferentially expressed on plasmacytoid dendritic cells and B-cells
- Natural ligand is CpG DNA
- Targetable with nucleic acid therapeutics

IMO-2125
- Synthetic oligonucleotide agonist of TLR9
- Novel structure based on proprietary Idera drug discovery technology
- Safety and tolerability of subcutaneous administration demonstrated in 80+ subjects
- Triggers maturation of dendritic cells

Systemic IMO-2125 induced IFN-α in phase I trial

In a Phase 1 trial, IMO-2125 was administered at doses 0.04, 0.08, 0.16, 0.32, and 0.48 mg/kg/week subcutaneously in null responder HCV patients. Data presented at AASLD 2010. *p=0.005, **p<0.0001. IFN-α shown at day 23
Intratumoral IMO-2125 Mechanism of Action

Simplified Graphical Representation

- Intratumoral Delivery of IMO-2125
- Draining Lymph node
- Primed T-cells invade treated as well as distant tumor sites
- DC maturation
- Antigen presentation to T-cells
- T-cell activation/expansion
- T-cell migration
- Tumor cell-killing
- Increased TIL Infiltration
- IFN-α & Th1 type cytokines
- Metastases are targeted by primed anti-tumor T-cells
- Tumor specific antigens
- Dendritic Cells
- NK cells
- CD8+ T-cells

© 2016 Idera Pharmaceuticals
Pre-clinical i/t 2125/Check Point Inhibitor combination studies demonstrated tumor regression and systemic effects

BALB/c mice (n=8 per group) were implanted s.c. with 2 x 10^7 murine colon carcinoma CT26 cells in right flank (Tumor 1) and 3 x 10^6 murine colon carcinoma CT26 cells in lungs (Tumor 2). Treatment was initiated on Day 5. On Days 5, 6, 8 and 9, treatment with IMO-2125 a dose of 2.5 mg/kg (50 μg in 100 μl PBS) was administered intratumorally in right tumor nodules and treatment with anti-mouse CTLA4 mAb (10 mg/kg, 200 μg/mouse) was administered by i.p. injection.
IMO-2125 + anti-CTLA4 has abscopal effect

Antitumor activities of IMO-2125 on systemic lung metastasis

* Picture was taken on Day 13 after tumor implantation.

PBS group: a few T cells are present in the tumor tissues bordering normal tissue.
IMO-2125 group: increased T cells are infiltrating into tumor tissues.
Anti-CTLA-4 mAb group: increased T cells are infiltrating into tumor tissues.
Combination group: massive T cell infiltrate into tumor tissue.
Ongoing Phase 1/2 clinical trial of IMO-2125 in relapsed or refractory metastatic melanoma following anti-PD-1 therapy

**Cohort 1: Enrolling**

Phase 1 Dose Finding  
IMO-2125 (i.t.) + ipilimumab (i.v.)  
Phase 2 Expansion

**Cohort 2: Planned**

Phase 1 Dose Finding  
IMO-2125 (i.t.) + pembrolizumab (i.v.)  
Phase 2 Expansion

Trial supported through strategic alliance with MD Anderson Cancer Center

**Trial design**

- Open-label 3x3 design with Bayesian component
- IMO-2125 administered by intratumoral injection at weeks 1, 2, 3, 5, 8, 11
- Ipilimumab and pembrolizumab administered by intravenous injection on approved dose schedules
- Enrolling patients with relapsed or refractory metastatic melanoma following anti-PD-1 therapy

**Objectives**

- Safety and tolerability
- Recommended Phase 2 dose
- Preliminary response rate (immune RECIST criteria)
- Exploratory markers of immune activation
Targeting immune stimulator and regulatory pathways may achieve optimal anti-tumor effects

• IMO-2125 is a novel oligonucleotide-based TLR9 agonist
  – Potent inducer of interferon-alpha and other Th1 cytokines
  – Only TLR9 agonist with human clinical data experience to date from previous development in HCV
  – Compelling preclinical data in intratumoral models

• A Phase 1/2 clinical trial of IMO-2125 in combination with ipilimumab is enrolling patients with metastatic melanoma unresponsive to anti-PD-1 therapy

• Expanded clinical development program targeting additional tumor types and checkpoint combinations is being planned for initiation in 1st Half 2017

Initial Translational Data Planned for Presentation in Fall 2016
Toll Like Receptor (TLR) Antagonism Clinical Programs
Treating Mutation-driven B-cell Lymphomas

Waldenström’s Macroglobulinemia (WM)

- Rare and slow-growing form B-cell lymphoma
- ~1,000-1,500 new cases diagnosed annually in US
- 90% carry MYD88 L265P mutation
- Serious complications include anemia, retinopathy and peripheral neuropathy

Diffuse Large B-Cell Lymphoma (DLBCL)

- Fast growing and potentially lethal form of B-cell lymphoma
- ~20,000 new cases diagnosed annually in US
- ~30% in ABC-DLBCL carry MYD88 L265P mutation
- Data show poor prognosis in MYD88 L265P+ population

MYD88 L265P mutation also present in chronic lymphocytic lymphoma (5-10%), splenic marginal zone lymphoma (13%), primary CNS lymphoma (36%), and other cancers

Survival is impaired in MYD88 L265P+ DLBCL patients

MYD88 L265P is an important target in B-cell malignancy

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incidence of Disease&lt;sup&gt;a,b&lt;/sup&gt;</th>
<th>MYD88 L265P mutation % Patients</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC-DLBCL&lt;sup&gt;c&lt;/sup&gt;</td>
<td>4,868</td>
<td>29%</td>
<td>1,412</td>
</tr>
<tr>
<td>Waldenström’s Macroglobulinemia</td>
<td>876</td>
<td>91%</td>
<td>797</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia</td>
<td>14,586</td>
<td>5%</td>
<td>729</td>
</tr>
<tr>
<td>Primary CNS lymphoma</td>
<td>1,200</td>
<td>37%</td>
<td>444</td>
</tr>
<tr>
<td>Marginal Zone Lymphoma&lt;sup&gt;d&lt;/sup&gt;</td>
<td>4,868</td>
<td>6.5%</td>
<td>316</td>
</tr>
<tr>
<td>Sanctuary Site Lymphomas&lt;sup&gt;e&lt;/sup&gt;</td>
<td>?</td>
<td>&gt;70%</td>
<td></td>
</tr>
</tbody>
</table>

DLBCL, Diffuse Large B-cell Lymphoma; ABC, Activated B-cell (type)

<sup>a</sup> Diagnosis-specific incidence in US based on 2011 SEER dataset estimate of 70,800 NHL cases per year and the relative counts of specific diagnoses.

<sup>b</sup> Estimated incidence of L265P mutation is based on disease incidence and the reported frequency of the mutation in the disease.

<sup>c</sup> ABC-type represents 28% of all DLBCL. Among patients with DLBCL, almost all instances of L265P mutations have been in those with ABC-subtype.

<sup>d</sup> Also known as Mucosa-Associated Lymphoid Tissue Lymphoma (MALT).

<sup>e</sup> Kraan Blood Cancer J, 2013.
Recent Update on Clinical Activity with 8400 in WM

- In the highest dose cohort studied to date (1.2 mg/kg twice a week):
  - 9 of 10 patients demonstrated reductions in IgM or M-Protein levels from baseline
Safety Profile of IMO-8400 Continues to Impress

- IMO-8400 was generally well tolerated at all dose levels tested
- Most reported adverse events (AEs) were mild or moderate (grade 1 or 2)
- The most common AEs observed were fatigue, injection site erythema, headache, injection site pain, nausea and pain in extremity
- Grade 3 AEs reported as possibly or probably related to study drug included neutropenia, anemia and arthritis
  - 1 of 8 patients treated with 2.4 mg/kg in the safety population had a dose-limiting toxicity (DLT) deemed possibly related to study drug. This patient experienced a grade 3 probable flare of pre-existing arthritis

Dose Escalation Continues to Progress
Targeting Recommended Phase 2 Dose by Year End 2016

- Both DLBCL and WM study protocols evaluating higher and more convenient dosing (2.4 mg/kg once weekly and 3.6 mg/kg once weekly)
- Development strategy centered on demonstrating efficacy in largest unmet need – DLBCL
- Prioritizing recruitment of ibrutinib-refractory subjects in WM

Trial Data for WM and DLBCL expected in 1st Half of 2017
Applying TLR Platform to Rare Disease

Dermatomyositis

Therapeutic Rationale

• Cell damage may be caused by stress, injury or infection
• Onset typically occurs between ages 40-60 years
• Symptoms can be severely disabling, and include:
  – Muscle weakness, skin rash and/or calcinosis, joint pain, and difficulty swallowing
• Corticosteroids and immunosuppressive drugs have limited efficacy and serious side effects
• ~25k patients in U.S.

Opportunity

• TLR antagonism may disrupt the autoimmune cycle of tissue damage to improve disease symptoms
TLRs Play Role in Pathogenesis of DM

- Damaged skeletal muscle and skin tissue release Damage Associated Molecular Patterns (DAMPs)
- DAMPs bind to and initiate immune signaling through TLRs 7, 8 and 9 in skeletal muscle fibers and immune cells
- TLR signaling induces pro-inflammatory cytokines, driving downstream effects including damage to capillaries and hypoxia in affected tissue, inhibition of new muscle fiber formation, and cell death
DM Phase 2 Study Underway

Study 211: Double-Blind, Placebo-Controlled Phase 2 Trial

Randomization

N = 12
0.60 mg/kg weekly

N = 12
1.8 mg/kg weekly

N = 12
Placebo

Screening: ≤ 28 days 24 weeks

Study Design

- 24-week randomized, double-blinded placebo-controlled assessment

Major Eligibility Criteria

- DM diagnosis, aged 18-75 years, active skin and muscle disease, stable regimen of con-meds

Primary endpoint

- CDASI activity score

Exploratory endpoints

- MMT-8, 10-meter run walk, Timed Up and Go test, Four Stair Climb, 5D itch scale, SF-36 health survey
Third Generation Antisense (3GA) Platform
Applied learnings to create third generation antisense

Development of a thorough understanding of interaction of nucleic acids and innate immune receptors
Why is third generation antisense (3GA) needed?

3GA Platform Built upon the lessons learned from Idera’s Pioneering work with 1st and 2nd Generations of Antisense

• To realize the full potential of antisense technology for the treatment of diverse diseases
• To overcome the limitations of the first and second generation antisense technology:
  – Immunotoxicities (i.e. thrombocytopenia)
  – Therapeutic Index

Assays were conducted with antisense constructs in Hepa 1-6 cells; RNA levels were quantified by qPCR
Our 3GA disease prioritization process

Key Considerations

• Gene target associated with the disease
• Over expression of the gene correlates with disease
• Gene target/pathway proof-of-concept established
• Gene target/pathway not “druggable” with small molecules or antibodies
• Rare disease and oncology indications with commercial viability
• Possibility of local delivery to the site of gene expression
  – Bladder, Ocular, Intratumoral, Lungs, GI/Colon
3GA Platform Path to Validation

Progressing Towards Human Proof of Concept

✓ Gene Target Selection
✓ Target Disease Development and Commercial Pathway Analysis
✓ Pre-clinical Animal Model Studies
✓ 3GA Clinical Candidate Selection
  Toxicology - Underway
  IND Submission – Planned for 2017
  Clinical Trial Initiation – Planned for 2017
3GA platform is ready to realize the full potential of antisense technology

- 3GA is designed to address the shortcomings/limitations of 1st and 2nd generation ASO
- Distinct mechanism with potent gene knockdown
- Rapid process from target selection to potential drug candidate
- We expect 1 to 2 targets per year to push into IND enabling studies for certain cancers and rare diseases
- Will announce 1st indication for clinical development 2nd half of 2016
- Plan to initiate first human clinical study in 2017 to establish proof of concept
- We believe we can further exploit the 3GA technology through partnerships with companies whose interests lie outside of oncology and rare diseases
- First license agreement entered into in 2015 with GSK for renal targets
Experienced Leadership

SUDHIR AGRAWAL, D.Phil. ~ President, Research

LOUIS ARCUDI ~ Chief Financial Officer

MARK CASEY ~ General Counsel

JILL CONWELL ~ Human Resources

ROBERT DOODY ~ IR & Comms

CLAYTON FLETCHER ~ Strategy & BD

JOANNA HOROBIN, MB, ChB ~ Chief Medical Officer

VIN MILANO ~ Chief Executive Officer
## Growing Development Pipeline Advancing

### DEVELOPMENT PROGRAM

<table>
<thead>
<tr>
<th>Rare Diseases – IMO-8400</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waldenström’s macroglobulinemia</td>
</tr>
<tr>
<td>Diffuse large B-cell lymphoma (MYD88 L265P+)</td>
</tr>
<tr>
<td>Dermatomyositis</td>
</tr>
</tbody>
</table>

### Immuno-Oncology – IMO-2125

| Refractory/Relapsed Melanoma w/ CTLA4 |
| Additional Tumor Types / CPI Combos |

### RESEARCH PROGRAM

<table>
<thead>
<tr>
<th>THIRD GENERATION ANTISENSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>NLRP3</td>
</tr>
<tr>
<td>DUX4</td>
</tr>
<tr>
<td>Undisclosed Targets</td>
</tr>
</tbody>
</table>

---

**Cash through Q3 2017**

© 2016 Idera Pharmaceuticals
Near Term Milestones

- Fall 2016 – Translational Data from IMO-2125 Melanoma Trial
- 1st Half 2017 – IMO-8400 WM and DLBCL Dose Escalation Data
- 1st Half 2017 – Initiate Second IMO-2125 Clinical Trial
- 1st Half 2017 – IMO-2125 Melanoma Study Phase 1 Clinical Data
- 2017 – Initiate First Human Proof of Concept Studies for 3GA
- 2017 – Complete Enrollment of IMO-8400 Dermatomyositis Trial
Thank You