Solving Unmet Patient Needs with Strong Scientific Foundations

IDERA PHARMACEUTICALS
Jefferies 2015 Global Healthcare Conference
Forward-Looking Statements and Other Important Cautions

This presentation contains forward-looking statements that involve substantial risks and uncertainties. Any statements in 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 annual report on Form 10-Q that we filed with the U.S. Securities and Exchange Commission for the period ended March 31, 2015. 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.
Our goal is to translate scientific breakthroughs into important medicines for patients

Committed to advancing patient care

Focused on serious unmet needs in oncology & rare diseases

Leading scientific discovery in immunotherapy & gene silencing
Scientific platforms support broad pipeline opportunities

SERIOUS UNMET PATIENT NEEDS

- Genetically defined forms of B-cell lymphoma
  - Immuno-oncology
  - Rare diseases

- Multiple targets in cancer and rare diseases

TOLL-LIKE RECEPTOR IMMUNE MODULATION

GENE SILENCING OLIGONUCLEOTIDES
Idera is a pioneer of immunotherapy and gene silencing technologies

**THIRD GENERATION CHEMISTRY**
Gene silencing oligonucleotides

**IMMUNE BLOCKADE**
Toll-like receptor antagonism

**SECOND GENERATION CHEMISTRY**
Modified RNA-DNA hybrid structure;
Most successful to date, but limitations persist

**ANTISENSE CONCEPT**
Idera scientists were early pioneers

**FIRST GENERATION CHEMISTRY**

**IMMUNE ACTIVATION**
Toll-like receptor agonism
# Idera’s growing pipeline

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B-cell lymphoma programs

Committed to advancing patient care

FOCUSED ON SERIOUS UNMET NEEDS IN ONCOLOGY & RARE DISEASES

Leading scientific discovery in immunotherapy & gene silencing
B-cell lymphomas characterized by the MYD88 L265P mutation are rare and have limited treatment options

**Waldenström’s Macroglobulinemia (WM)**
- Rare and slow-growing form B-cell lymphoma\(^1\)
- ~1,000-1,500 new cases diagnosed annually in US\(^1\)
- Currently incurable\(^1\)
- 90% carry MYD88 L265P mutation\(^2\)
- Serious complications include anemia, retinopathy and peripheral neuropathy\(^1\)

**Diffuse Large B-Cell Lymphoma (DLBCL)**
- Fast growing and potentially lethal form of B-cell lymphoma\(^1\)
- ~20,000 new cases diagnosed annually in US\(^3\)
- ~10% carry MYD88 L265P mutation\(^4,5\)
- Data show poor prognosis in MYD88 L265P+ population\(^6\)

MYD88 L265P mutation also present in chronic lymphocytic lymphoma (5-10%)\(^7\), splenic marginal zone lymphoma (13%)\(^8\), primary CNS lymphoma (36%)\(^9\), and other cancers

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Targeted therapy for B-cell lymphoma patients carrying oncogenic mutation in TLR signaling pathway

IMO-8400 inhibits tumor cell viability

IMO-8400 suppresses tumor-associated cytokines

Graphic adapted from Cancer Res. 2013, 73 Suppl. 1.2332. IMO-8400 data presented at AACR 2014.
IMO-8400 has demonstrated tolerability and evidence of clinical activity

IMO-8400 blocks TLR signaling and immune system activation

- IMO-8400 is a synthetic oligonucleotide-based antagonist of TLRs 7, 8 and 9
- Activity observed in preclinical models of autoimmune diseases and lymphoma
- Evidence of TLR antagonism observed in human clinical trials in psoriasis
- IMO-8400 generally well tolerated in ~85 patients and healthy subjects with >550 doses administered to date
Waldenström’s clinical trial data available in Q4 2015

- Received FDA orphan drug designation for IMO-8400 in Waldenström’s in December 2014
- Completed enrollment; data available in 4Q 2015

Study objectives: demonstrate safety, clinical activity and optimized dosing regimen; Target enrollment: up to ~30 patients

*DRC recommendations on dose escalation based on 4-week safety data from cohorts 1 and 2, respectively
DLBCL program updates

- Completed initial development of prototype CDx under collaboration with Abbott Molecular
- Activated multiple clinical sites and enrollment commenced in DLBCL clinical trial
- Received FDA orphan drug designation for IMO-8400 in DLBCL in April 2015

Study objectives: demonstrate safety, clinical activity and optimized dosing regimen; Target enrollment: up to ~30 patients

*DRC recommendations on dose escalation will be based on 4-week safety data from cohorts 1 and 2, respectively*
Immuno-oncology program

Committed to advancing patient care

FOCUSED ON SERIOUS UNMET NEEDS IN ONCOLOGY & RARE DISEASES

Leading scientific discovery in immunotherapy & gene silencing
Cancer immunotherapy with intratumoral TLR9 agonist and checkpoint inhibitors

**Therapeutic Rationale**

- Emerging class of checkpoint inhibitors (CPIs) represents a significant advance in cancer immunotherapy
  - Designed to block pathways that inhibit anti-tumor immune responses
  - PD-1 and CTLA-4 inhibitors are FDA approved for the treatment of melanoma; clinical development in additional cancer types is ongoing
- Intratumoral administration of TLR9 agonists have demonstrated immunostimulatory activity in preclinical models of cancer

**Opportunity**

- Combination of complementary cancer immunotherapy agents may increase the duration and durability of clinical responses
Systemic Treatment vs Intratumoral Administration of TLR9 Agonist

**Systemic Treatment**

- Tumor Antigens
  - Recognition by the immune system heightened by TLR9 agonist
  - Activation of B-cells and pDCs

**Intratumoral Administration**

- Intratumoral injection
  - Cytotoxic T Cells
  - Tumor infiltrating lymphocytes (TILs)

**Systemic Responses**
Intratumoral TLR9 agonist stimulates immune response while CPI inhibits tumor defense against immune attack

Modulation of the Tumor Microenvironment

- Intratumoral TLR9 agonist stimulates dendritic cell maturation and T-cell activation; induces interferon-α
- CPIs block inhibitory pathways enabling activation of CD4+ and CD8+ T-cell responses
- Dying tumor cells release antigens enabling T-cell memory, systemic anti-tumor immune responses
Intratumoral TLR9 Agonist and anti-CTLA-4 mAb inhibited the growth of treated tumors in preclinical models

Data from CT26 colon carcinoma model. Presented at AACR Tumor Immunology 2014.
Intratumoral TLR9 Agonist and anti-CTLA-4 mAb induced a systemic anti-tumor response in preclinical models

AH1 antigen presented in locally treated tumors

β-gal antigen presented in disseminated lung metastases

*Data from CT26 colon carcinoma model. Presented at AACR Tumor Immunology 2014.*

*Fisher's exact test and two-tailed Mann-Whitney U Test: *p*<0.05; **p*<0.01 (compared with IMO-2055 or anti-CTLA-4 mAb treatment alone)*
IMO-2125 & IMO-2055 are clinical-stage TLR9 agonists

IMO-2125 and IMO-2055 stimulate TLR signaling to induce an immune response

- IMO-2125 and IMO-2055 are synthetic oligonucleotide-based agonists of TLR9

- Idera’s TLR9 agonists have demonstrated evidence of anti-tumor activity in multiple settings
  - Clinical trial in non-small cell lung cancer
  - Preclinical models
IMO-2125 showed preliminary indication of safety and tolerability in clinical study with systemic administration

- Completed trials involving systemic administration of IMO-2125
  - 2 Hepatitis C Clinical Studies
- Well tolerated by HCV patients (N=48 null responders; N=48 treatment naïve, with ribavirin),
  - 4 weeks of dosing; once or twice/week
- No treatment-related discontinuations or serious adverse effects
- No safety lab changes attributed to IMO-2125
- Adverse events in >10% of patients limited to
  - Mild to moderate injection site reactions
  - Flu-like symptoms of typically short (<24 h) duration
- No development of tolerance to induction of serum IFN-\(\alpha\)
Priorities for immuno-oncology program

- Rapidly advance a combination regimen with an intratumoral TLR9 agonist and a CPI into clinical development
- Complete ongoing preclinical studies to characterize potential combination regimens with various CPIs

_Intratumoral TLR9 agonism has the potential to enhance cancer immunotherapy regimens with CPIs_
Rare disease programs - IMO-8400

Committed to advancing patient care

FOCUSED ON SERIOUS UNMET NEEDS IN ONCOLOGY & RARE DISEASES

Leading scientific discovery in immunotherapy & gene silencing
Scientific rationale for TLR antagonism in autoimmune diseases

Damaged cells release self DNA, self RNA and other molecules to form Damage Associated Molecular Patterns (DAMPs).

DAMPs stimulate TLR signaling to promote inflammation.

Inflammation causes additional cellular damage, thereby propagating the diseases process.

Adapted from Rayavarapu, et al. Skeletal Muscle 2013.
Clinical proof-of-concept established for TLR antagonism in an autoimmune disease

Safety
- Treatment well tolerated for up to 12 weeks*
- No treatment-related discontinuations, serious adverse events or dose reductions*
- Dosages up to 0.6 mg/kg per week*

Clinical Activity
- PASI score improvement observed*
- Full data from the Phase 2 trial of IMO-8400 in psoriasis was presented in March at the Annual Meeting of the American Academy of Dermatology

*Top-line data from Phase 2 Trial of IMO-8400 Press Release (March 28, 2014)
Dermatomyositis is a rare and disabling inflammatory muscle disease with skin involvement

**Therapeutic Rationale**

- Cell damage may be caused by stress, injury or infection
- TLR 9 and mRNA for MYD88 significantly over-expressed
- 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

Duchenne muscular dystrophy is a rare and universally fatal neuromuscular disorder

**Therapeutic Rationale**
- Muscle cell damage caused by lack of functional dystrophin protein
- TLR 7 significantly over-expressed, even in pre-symptomatic infants
- Corticosteroids are standard of care, but have limited efficacy and serious side effects
- ~15-20k patients in U.S.

**Opportunity**
- TLR antagonism has the potential to reduce muscle inflammation and slow disease progression
- Immune modulation may potentiate dystrophin restoration therapies such as exon skipping by inducing immunologic tolerance to dystrophin

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**DELAYS IN DEVELOPMENT**
**PROBLEMS STANDING**
**PROBLEMS WALKING**
**FULL-TIME WHEELCHAIR USE**
**LIMITED USE OF ARMS**
**VENTILATION**
**DEATH**

Rare disease programs are advancing toward clinical development by year-end 2015/early 2016

**Duchenne Muscular Dystrophy**

- Collaborating with Parent Project Muscular Dystrophy
- Conducting additional preclinical studies in well-established *mdx* mouse model
- Evaluating potential clinical trial design options with disease experts, including population and endpoint selection

**Dermatomyositis**

- Collaborating with The Myositis Association
- Organized advisory board of expert clinicians to inform design of Phase 2 clinical trial
- Finalizing clinical trial plan with IMO-8400
Gene silencing oligonucleotide program

Committed to advancing patient care

Focused on serious unmet needs in oncology & rare diseases

LEADING SCIENTIFIC DISCOVERY IN IMMUNOTHERAPY & GENE SILENCING
Novel Gene Silencing Oligonucleotides (GSOs) overcome limitations of current antisense technologies

**FIRST GENERATION**

**Chemistry**
- Single-stranded structure with phosphorothioate backbone

**Clinical Activity**
- Severe off-target immune activation limited clinical utility

**SECOND GENERATION**

**Chemistry**
- Modified RNA-DNA hybrid structure pioneered by Idera
- Most successful antisense chemistry to date

**Clinical Activity**
- Immune activation, immunotoxicity, injection site reactions
- Hepatic toxicity with chronic dosing
- Limited therapeutic index

**THIRD GENERATION**

**Chemistry**
- Novel structure discovered by Idera
- 19- to 21-mer length is optimal for gene silencing
- No 5’-prime ends abrogates immune activation
- Accessible 3’-prime ends improves degradation and clearance
- Issued U.S. patent

**Activity in Preclinical Models**
- Reduced immunotoxicity
- Decreased hepatic toxicity
- Improved potency
- Increased therapeutic index

*In vivo proof-of-concept established against multiple gene targets*

PRIORITIZATION OF GSO TARGETS FOR CLINICAL DEVELOPMENT

- Evaluate targets based on scientific merit and technical feasibility
- Validate targets in preclinical models
- Assess clinical feasibility and commercial potential
- Initiate development plans based on strategic prioritization

Assessment of potential GSO targets in oncology and rare diseases is underway.
IMO-9200, an Antagonist of TLRs 7, 8 and 9

Phase 1 Healthy Subject Trial

- Placebo-controlled trial in 30 healthy subjects, subcutaneous administration, escalating single dose levels
- All dose levels were well-tolerated, with no serious adverse events related to IMO-9200 reported

Pre-clinical study of oral administration of IMO-9200 in Inflammatory Bowel Disease (IBD) Models

- Preclinical study conducted with orally delivered IMO-9200 in TNBS-induced Crohn’s disease and DSS-induced Ulcerative Colitis models
- Treatment with IMO-9200 showed improved pro-inflammatory cytokine gene expression and levels in colon and serum
- Improved body weight and survival with corresponding improvements in colon weight, length and histology
- Data demonstrate that TLRs are important therapeutic target in IBD
Enhanced executive management team has a track record of success across the industry

VIN MILANO  Chief Executive Officer
SUDHIR AGRAWAL, D.Phil.  President, Research
LOU ARCUDI  SVP, Chief Financial Officer
JILL CONWELL  VP, Human Resources
ROBERT DOODY  VP, Investor Relations and Corporate Communications
LIZ EBERHARDT  VP, Oncology Team
CLAYTON FLETCHER  SVP, Business Development and Strategic Planning
KATE HAVILAND  VP, Rare Diseases
Idera’s 2015/2016 Goals

- **Completion and results** from Waldenström’s clinical trial in 4Q 2015

- **Completion and results** of DLBCL clinical trial

- **Initiate two** clinical combination trials with IMO-2125/IMO-2055 with checkpoint inhibitor (CTLA4/PD1) and complete at least one

- **Initiate** Phase 2 clinical trial with IMO-8400 in patients with dermatomyositis and phase 1/2 trial in patients with Duchenne Muscular Dystrophy

- **Complete** disease model studies and begin IND-enabling development for two disease indications with GSO platform
Idera’s long-term value drivers

• **Immunotherapy and gene silencing platforms** are the foundation for our development efforts in cancer and rare diseases

• **Genetically defined B-cell lymphoma programs** are progressing in the clinic

• **New immuno-oncology program** offers opportunity to enhance emerging class of checkpoint inhibitors and improve outcomes for cancer patients

• **Rare disease programs** focus on serious unmet medical needs in collaboration with strong advocacy communities

• **Enhanced executive management team** has track record of success and expertise to build the business