

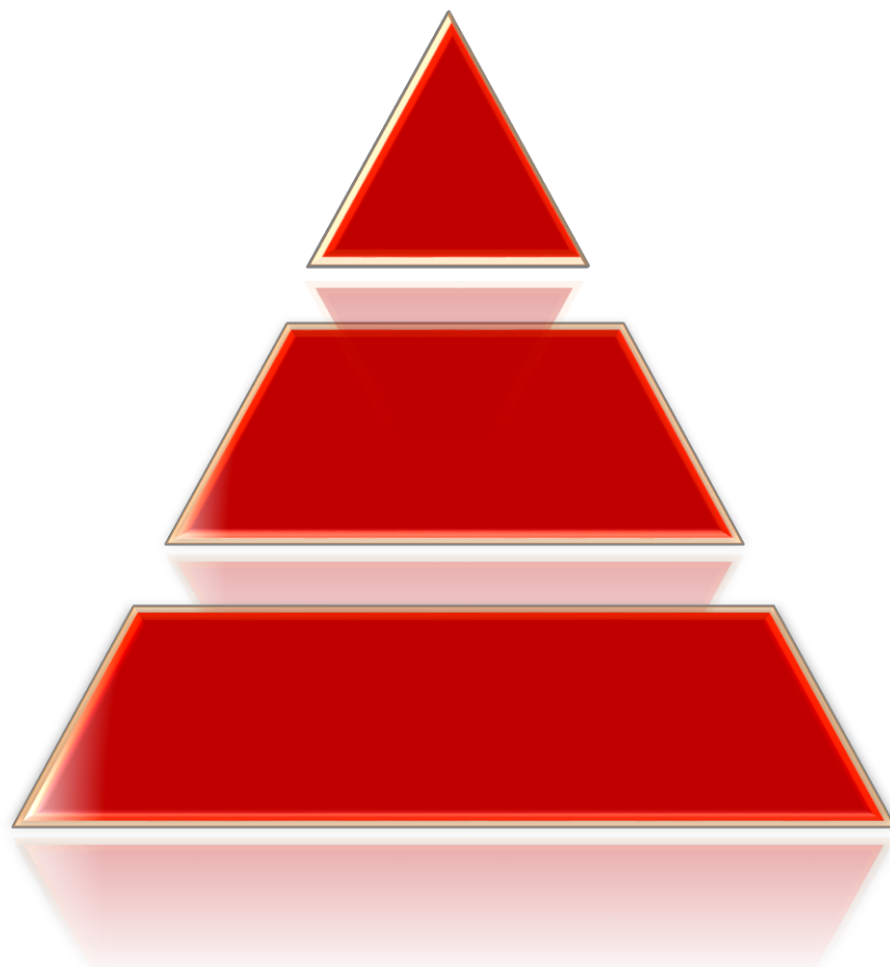
The background of the slide is a photograph of an elderly couple standing in a field of tall, golden grass at sunset. The man, with white hair, is wearing a teal t-shirt and has his arm around the woman. The woman, with short blonde hair, is wearing a white t-shirt. The sun is low on the horizon, creating a warm, golden glow and lens flare effects. A white geometric wireframe pattern is overlaid on the image, resembling a molecular structure or a network diagram.

Idera Pharmaceuticals 36th Annual J.P. Morgan Healthcare Conference

Forward Looking Statements and Other Important Cautions

- This presentation contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements, other than statements of historical fact, included or incorporated in this presentation, including statements regarding our strategy, future operations, collaborations, intellectual property, cash resources, financial position, future revenues, projected costs, prospects, plans, and objectives of management, are forward-looking statements. The words "believes," "anticipates," "estimates," "plans," "expects," "intends," "may," "could," "should," "potential," "likely," "projects," "continue," "will," and "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we will actually achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on these forward-looking statements. There are a number of important factors that could cause our actual results to differ materially from those indicated or implied by our forward-looking statements. Factors that may cause such a difference include: whether interim results from a clinical trial will be predictive of the final results of the trial, whether results obtained in preclinical studies and clinical trials will be indicative of the results that will be generated in future clinical trials, including in clinical trials in different disease indications; whether products based on our technology will advance into or through the clinical trial process on a timely basis or at all and receive approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; whether, if our products receive approval, they will be successfully distributed and marketed; and such other important factors as are set forth under the caption "Risk Factors" in the Company's Annual Report and on Form 10-K for the period ended December 31, 2016. 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.

Applying Oligonucleotide Expertise to Generate and Develop Therapeutics for Rare/Unmet Diseases



Advancing development pipeline

Focused on serious unmet needs in Cancers & Rare Diseases

Committed to advancing patient care



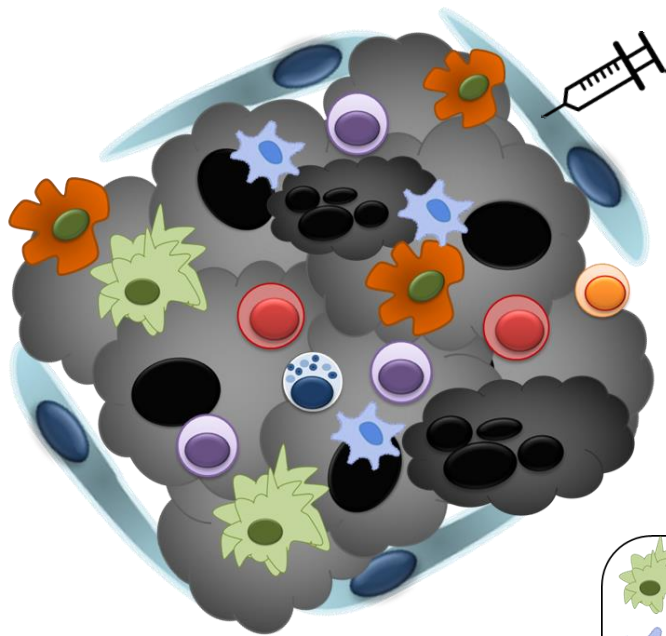
Injecting a New Approach to Advancing Cancer Immunotherapy

Activating the Immune Response with TLR9 Agonist

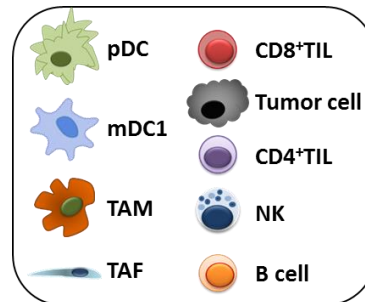
Current State of Immunotherapy in Melanoma

- Anti-PD-1 therapy is standard of care in all patients in 1L metastatic setting, and moving into adjuvant
- Treatment options following failure of first line anti-PD-1 therapy in melanoma are very limited
- The overall response rate (ORR) to ipilimumab following progression on pembrolizumab is only 13%, and not all responses are durable (Long, 2016)
- In presence of liver metastasis, pembrolizumab was associated with reduced response and shortened PFS (Tumeh, 2017)

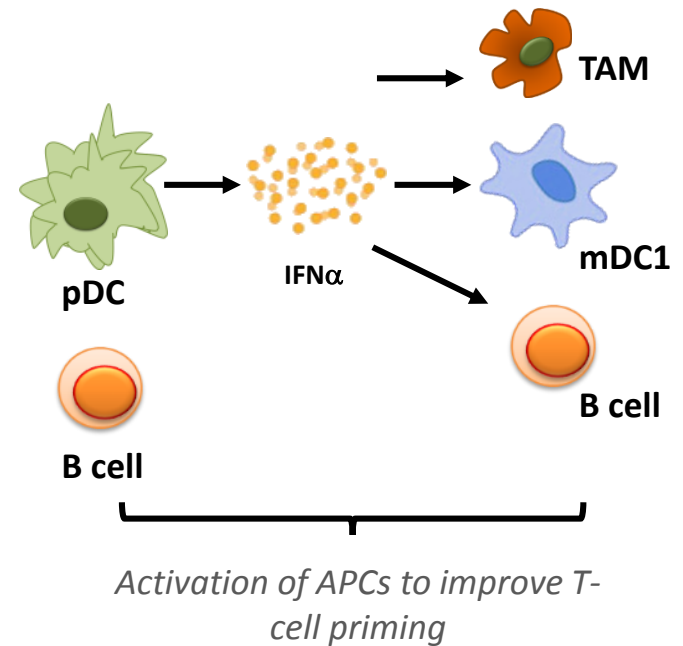
Tumor Microenvironment Modulation Potential Key to Significantly Advancing I/O Outcomes



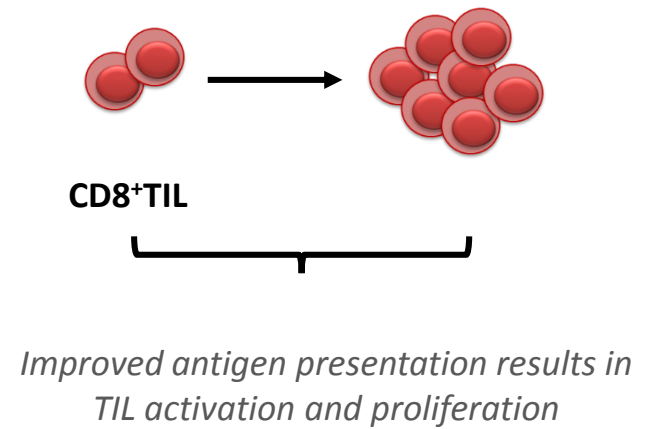
Intratumoral
administration
of IMO-2125



1. TLR9 induction of IFN α and APC maturation

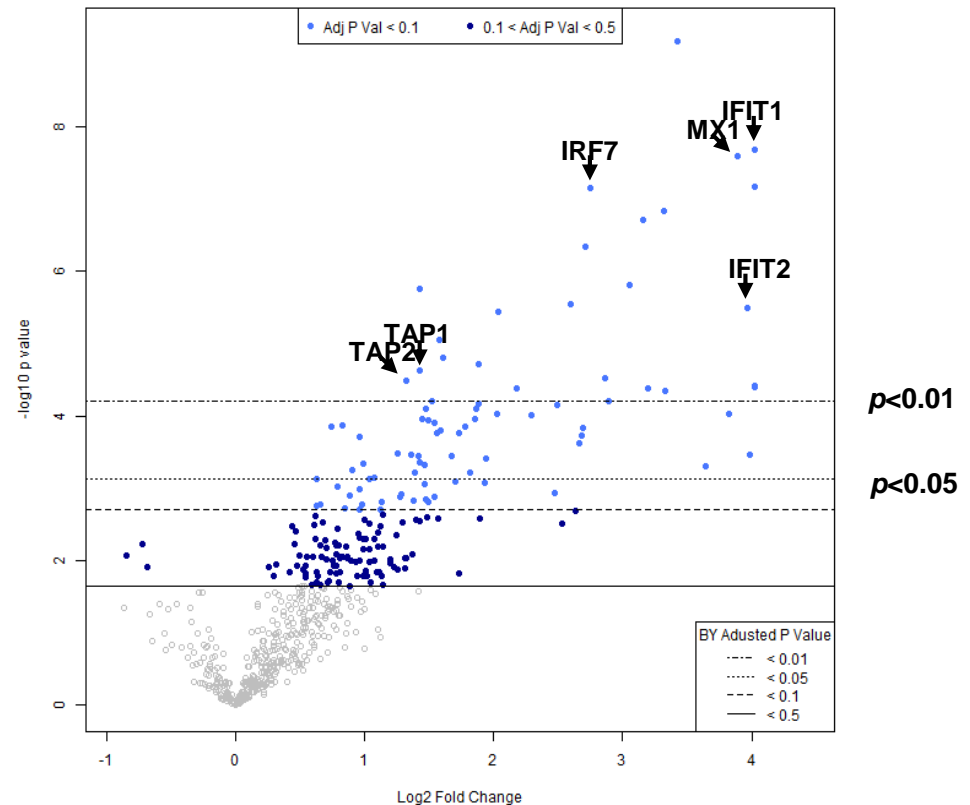
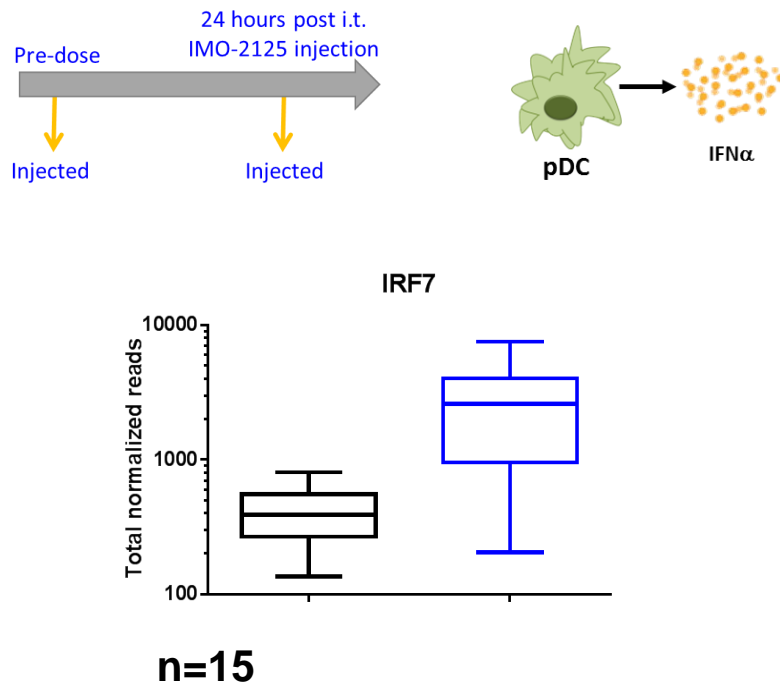


2. TIL Activation and Proliferation



Induction of IFN α -response gene signature after i.t. IMO-2125

IMO-2125 is a synthetic phosphorothioate oligonucleotide that acts as a direct agonist of TLR9 to stimulate the innate and adaptive immune systems. Activation of TLR9 by IMO-2125 induces high levels of IFN- α from dendritic cells (DCs) (Haymaker, SITC 2017).



Key Attributes of IMO-2125

- Stimulator of innate and adaptive immunity
- Convenient administration:
 - Non-infectious
 - No need for a device (e.g. electroporation)
- Can be administered to deep lesions or viscera (with radiology guidance)
 - Key for refractory patients
- Single site of injection
 - Total duration of Rx is 6 months for IMO + ipilimumab combination





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IMO-2125 Clinical Trials

FDA Fast Track Designation in anti PD-refractory melanoma, with ipilimumab

Study	IMO-2125	Indication	Ph 1	Ph 2	Ph 3
204	+ ipilimumab	PD-1 R/R melanoma	→		
204	+ pembrolizumab	PD-1 R/R melanoma	→		
301*	+ ipilimumab	PD-1 R/R melanoma	→		
RST-001	Single agent	Refractory solid tumors	→		
MST-205*	+ CPI	CPI approved tumors	→		

* Planned for 2018 initiation

Phase 1/2 Study in Anti-PD-1 Refractory Melanoma

Phase 2 Expansion with Ipilimumab Enrolling

RP2D of IMO-2125 is 8mg

Dose-finding:
IMO-2125 + ipilimumab
SAFETY ASSESSMENT COMPLETED



Phase 2
IMO-2125 + ipilimumab
OPEN

N ~ 80

Dose-finding:
IMO-2125 + pembrolizumab
ONGOING



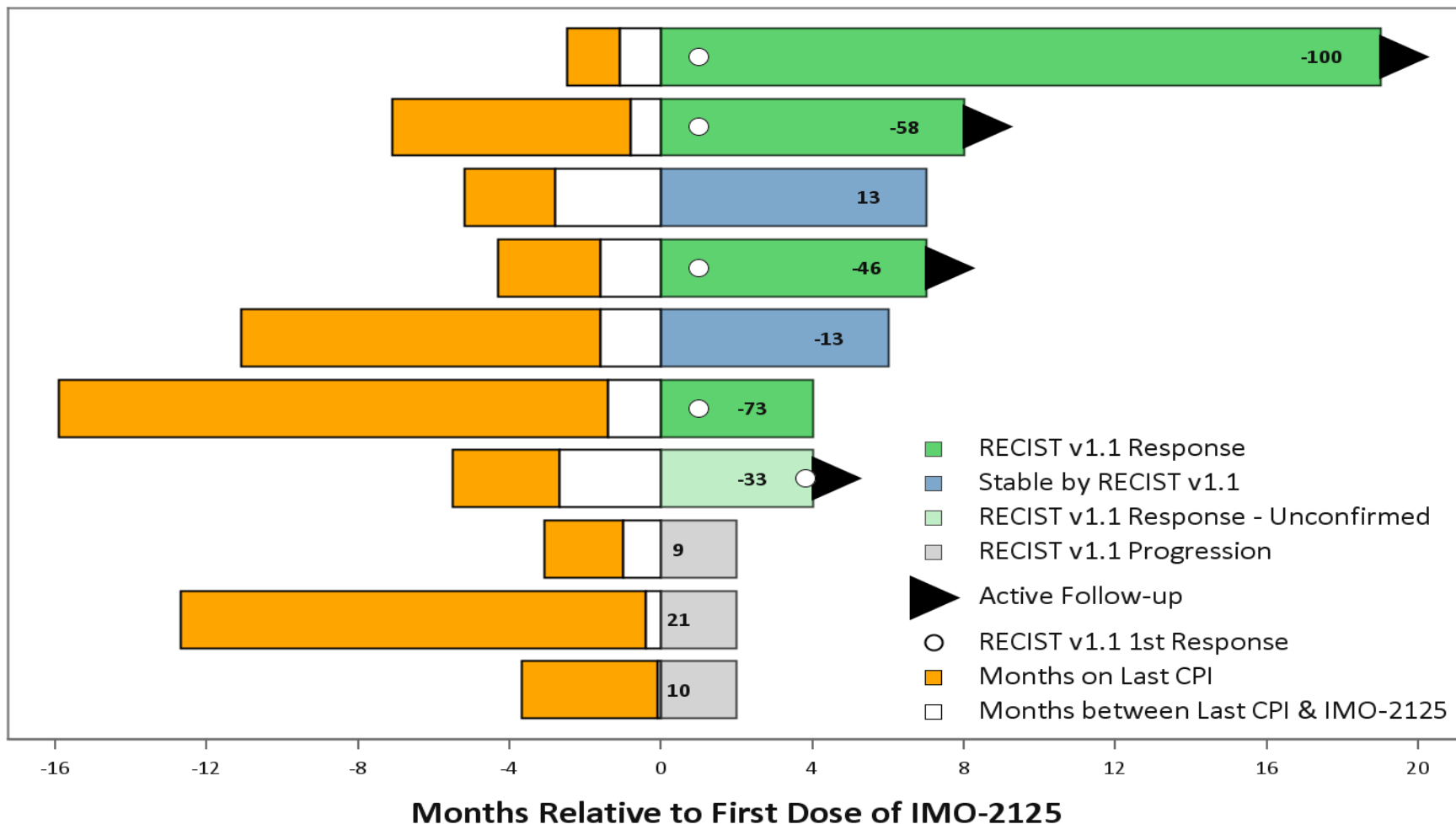
Phase 2
IMO-2125 + pembrolizumab
PLANNED

N ~ 30

Dosing:

IMO-2125 is given as a single intratumoral agent week 1,2,3,5,8,11,15,19,23
Ipilimumab and pembrolizumab are administered per label beginning week 2
Deep injections are permitted with interventional radiology guidance
No need for infectious precautions

Time on Study: Best RECIST v1.1 Response and Largest Percentage Decrease in Target Lesions (8mg subjects)



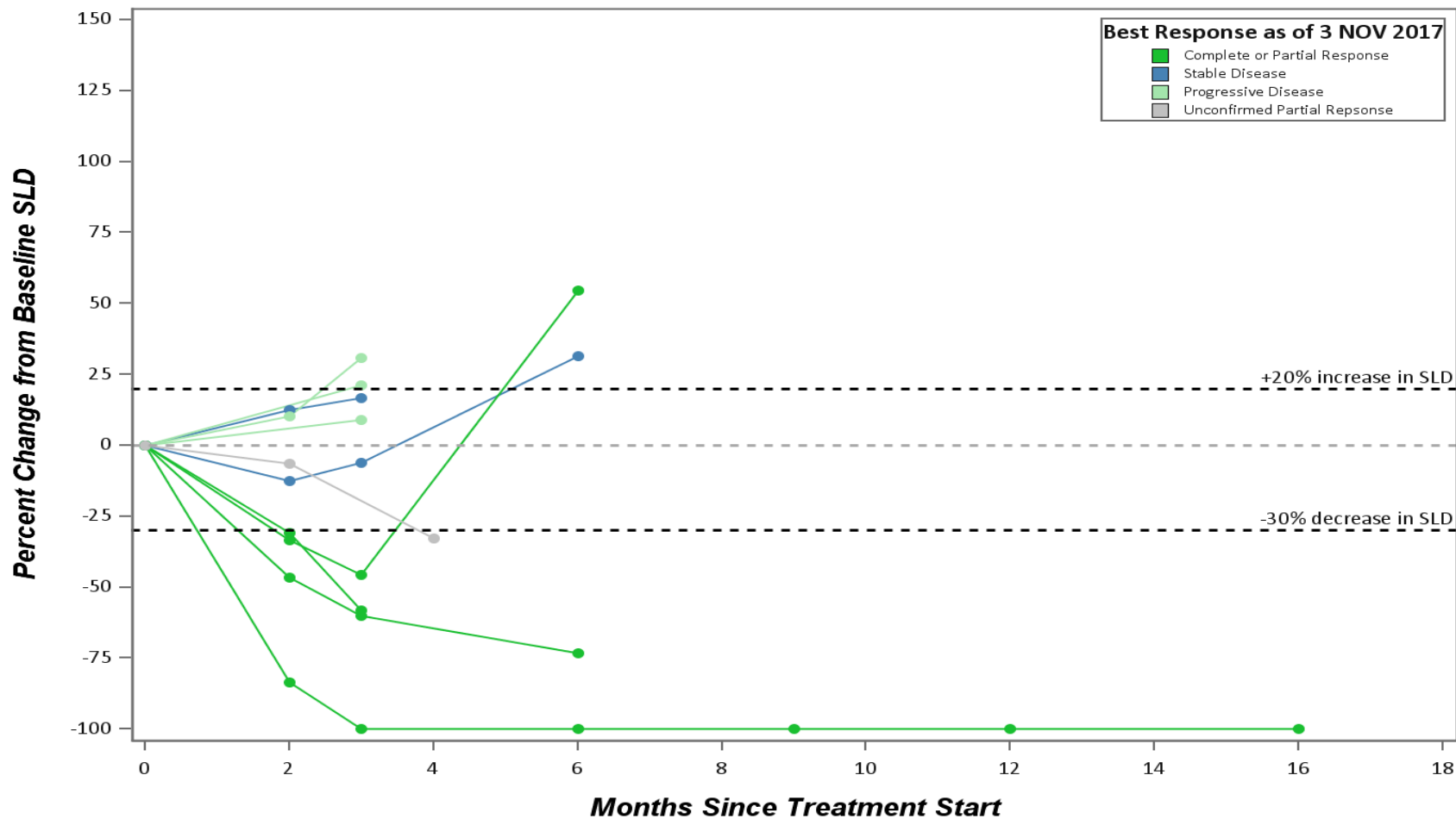
Time on study ends at RECIST v1.1 PD (including death & start of anti-cancer therapy) or withdrawal for any reason.

Subjects treated with IMO-2125 8mg + Ipilimumab with at least 1 post-baseline disease evaluation. Some CPI start and stop dates have been imputed.

Data cut-off date: 03NOV2017

Produced on 11DEC2017

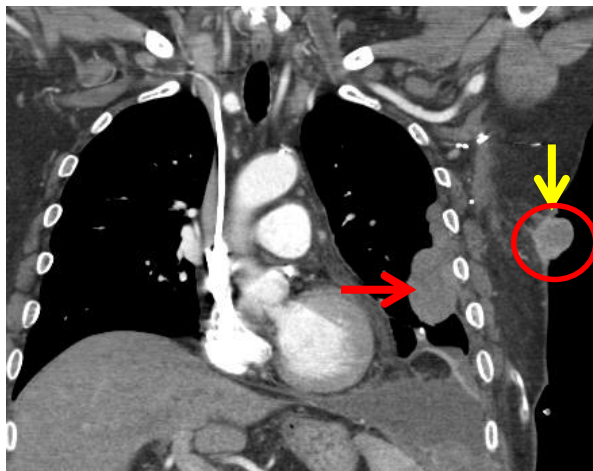
Percent Change from Baseline Sum of Longest Diameters by RECIST v1.1 (8mg subjects)



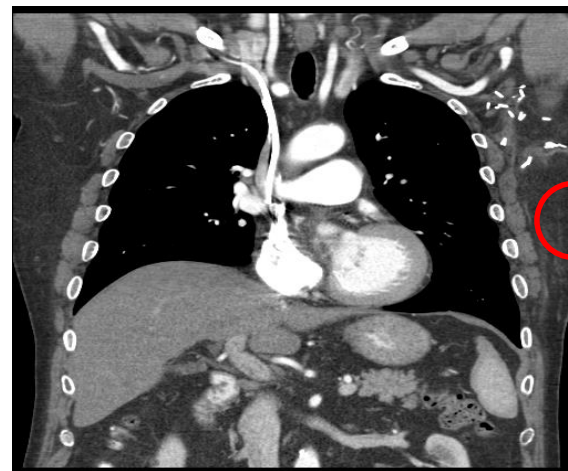
Data cut-off date: 03NOV2017

Produced on 03JAN2018

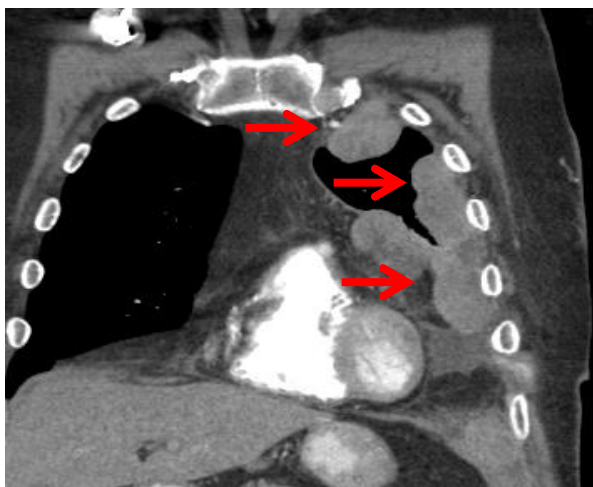
Patient 004 Remains a CR since May 2016



**Pre-Therapy
03/2016**

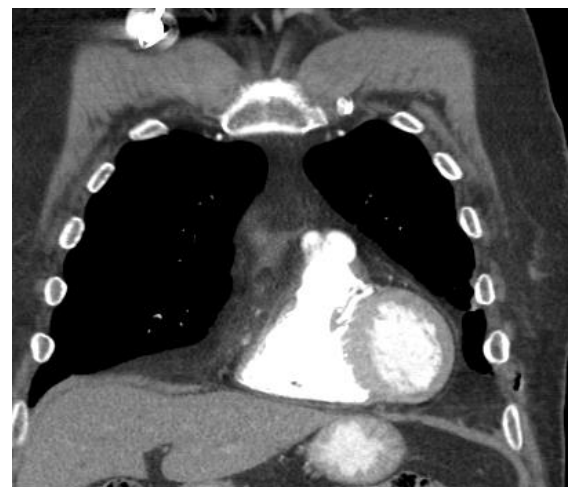


**Post-Therapy
08/2016**



Injected Lesion 

Distant Lesions 



Phase 1 Conclusions

- The combination of IMO-2125 with ipilimumab was tolerable at all dose levels studied;
- Dendritic cell activation, detectable within 24 hours of the first IMO-2125 injection, is evidence for target acquisition at the Recommended Phase 2 Dose (8mg);
- IMO-2125 with ipilimumab showed clinical activity at the RP2D of 8mg in anti-PD-1 refractory melanoma;
 - 5 of 10 (50%) responded;
 - 7 of 10 (70%) experiencing disease control; and
 - An additional PR of >1year has been reported at 4mg
- Dose finding for IMO-2125 with pembrolizumab is ongoing, and one partial response (PR) has been seen.

- Ipilimumab Combination Phase 2 Trial Expansion – Targeting approximately 60 patients with PD-1 refractory metastatic melanoma treated with 8mg
 - 21 patients enrolled
 - 10 Centers (5 sites currently enrolling)
 - MD Anderson, Roswell Park, Vanderbilt, Huntsman, Uni. of Arizona
 - Efficacy populations for future reporting
 - Primary Ipilimumab + IMO-2125 Efficacy Evaluable (PIIEE)
Population: all patients who are ipilimumab-naïve on study entry
 - Secondary Ipilimumab + IMO-2125 Efficacy Evaluable (SIIEE)
Population: all patients who are not ipilimumab-naïve on study entry
 - Open label design
 - Allows for periodic data updates
 - Opportunistic engagements with regulatory authorities



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IMO-2125 Clinical Trials

2125-MEL-301

Phase 3 Trial Design

Unresectable or metastatic melanoma w/ confirmed radiologic progression on or after a PD-1 inhibitor:

- ≥ 21 d from most recent aPD-1 and no intervening systemic Tx
- No prior ipi (except adjuvant)
- Ocular melanoma excluded

N~300

Ipilimumab 3 mg/kg Q3wks for 4 doses

No cross-over

Ipilimumab (same, beginning wk 2)
+
intratumoral IMO-2125,
wks 1, 2, 3, 5, 8, 11, 16, 20, 24

1^o endpoint family:

- OS
- ORR (RECIST v1.1)



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IMO-2125 Clinical Trials

2125-MEL-301

Phase 3 Readiness (FPFV 1Q18)

- Agreement with FDA and MHRA on design and path forward for regular and accelerated approval (one study)
- Fast Track Designation Granted by U.S. FDA in Q4 2017
- Global trial (US, Can, EU, Aus)
 - ~300 patients
 - ~70 sites planned
- CMC work on track for 1Q18 start
 - Commercial presentation of IMO-2125 will be used
- Regulatory filings underway
 - Open U.S. IND
 - CTA filings on track



- Cohort 1 (8 mg) enrollment complete
 - All subjects dosed (N=11) completed the 21 day DLT period.
 - No DLTs or safety concerns have occurred.
- Cohort 1 (8 mg) diseases under study include
 - pancreatic cancer (6), ocular melanoma (1), colorectal cancer (1), metastatic chondrosarcoma (1), metastatic breast cancer (1), metastatic esophageal cancer (1)
- 8 subjects included injections of liver lesions
- Cohort 2 (16 mg) enrolling



- Three subjects in cohort 1 (8 mg) continue IMO-2125 monotherapy on the RST study.
- Initial investigator assessments indicate stable disease (SD) in 2 (pancreatic, colorectal) of these subjects, and 1 irSD (pancreatic) in the third.
- While these are preliminary data, we are hopeful for these subjects and their ongoing care and upcoming disease assessments.

INTRODUCE

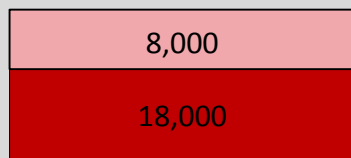
EXPAND

TRANSFORM

Unresectable metastatic melanoma

- High unmet need in anti-PD1-refractory patients
- Peak year sales estimate > \$500 million

Est. U.S. addressable patient population at 2025¹

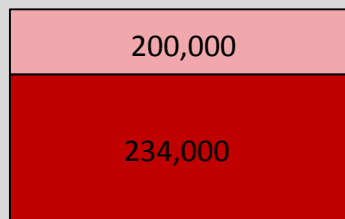


■ 1L ■ PD1-refractory

Emerging I/O addressable tumors

- Moderate response to cornerstone anti-PD1
- Increasing number of approved settings

Est. U.S. addressable patient population at 2025^{1,2}



■ 1L ■ PD1-refractory

“Cold” tumors unaddressable with current I/O

- Significant opportunity in tumors with:
 - Low mutation load
 - Low dendritic cell infiltration
- Bioinformatics research ongoing to identify attractive tumor targets

¹ Proprietary Idera Commercial Research

² NSCLC, head and neck, colorectal, bladder and gastric



Developing a Targeted Treatment Option for Dermatomyositis with IMO-8400

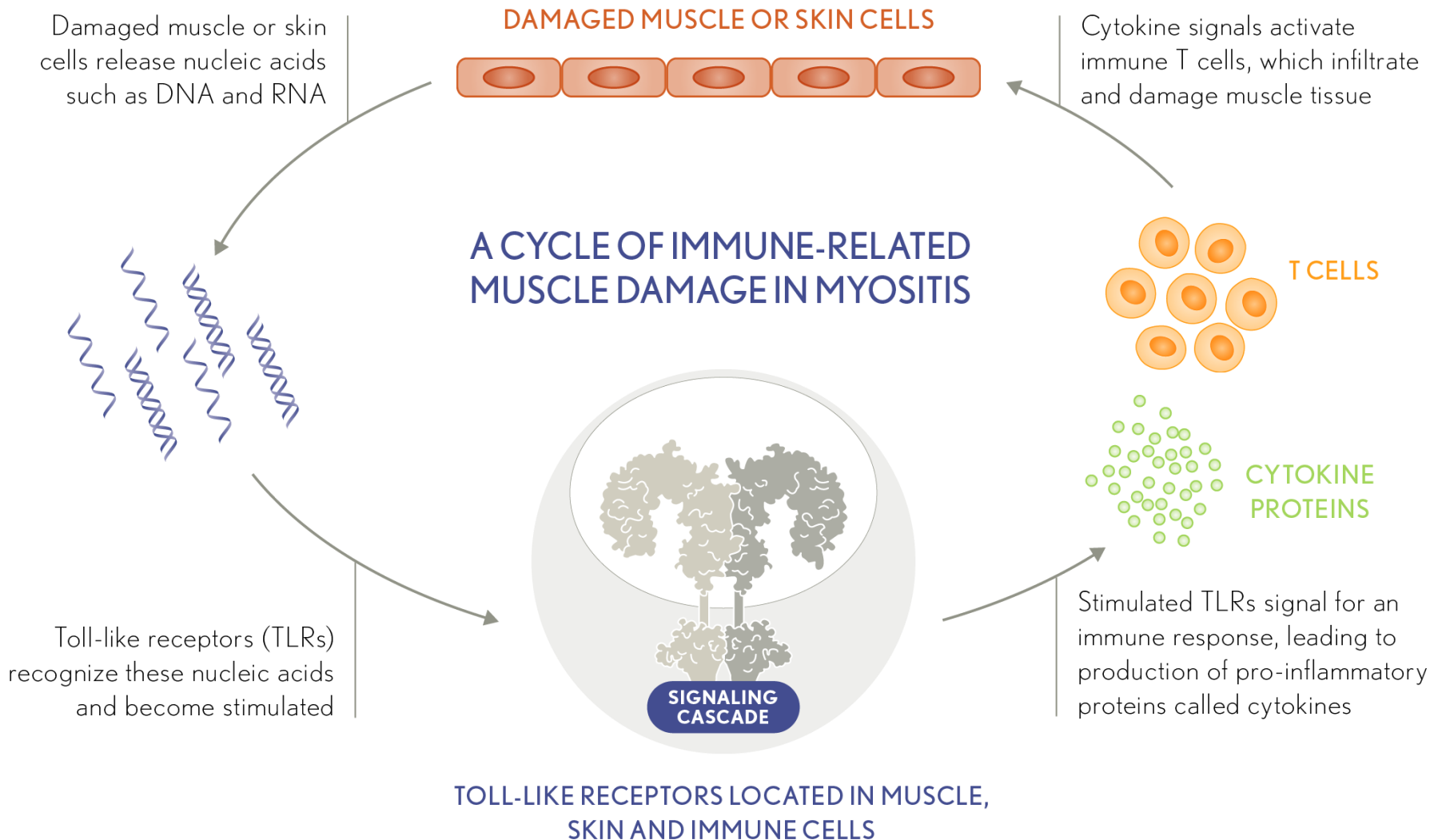


Dermatomyositis (DM)



- Rare, debilitating, inflammatory condition associated with increased risk of pre-mature death
- Multisystem disorder affecting both skin and muscle
- Twice as common in women as men
- Affects roughly 25K adults in the U.S.
- Current treatments have limited efficacy and serious side effects

Toll-like Receptors in Dermatomyositis



The Role of Toll-like Receptors in DM

TLR Activation

- Certain TLRs are over-expressed in the muscles of patients with dermatomyositis

Cytokine Expression

- Expression of certain TLRs has been correlated to the expression of certain cytokines, which are proteins involved in immune signaling¹

Disease Activity

- Cytokine expression has been correlated to changes in disease activity, including the IMACS physician global assessment²

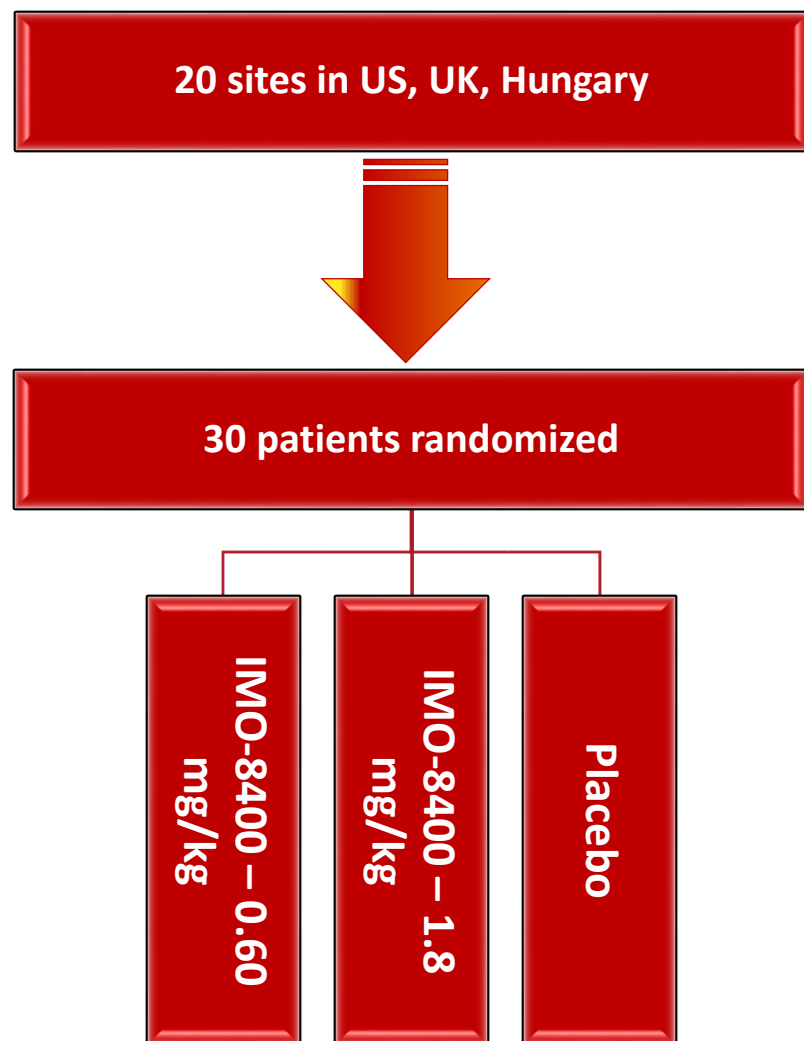
¹Kim, et al. Clin Rheumatol, 2010.

²Reed, et al. Arthritis & Rheumatism, 2012.

IMO-8400

- IMO-8400 is a synthetic oligonucleotide-based antagonist of Toll-like receptors (TLRs) 7,8 and 9
 - IMO-8400 is designed to inhibit, or antagonize, specific TLR activity
 - Treatment is administered subcutaneously
- Clinical proof of concept previously demonstrated in clinical trial in Psoriasis
- To date, IMO-8400 has been studied in over 100 patients and has been generally well-tolerated

Trial Data Expected Q2 2018



PIONEER

A PHASE 2 STUDY OF IMO-8400
IN DERMATOMYOSITIS

- ▶ **PIONEER** is a Phase 2, double-blind, placebo-controlled study for adults with dermatomyositis currently experiencing symptoms of active skin disease
- ▶ **Enrollment:** 30 patients through approximately 20 sites in US, UK, and Hungary
- ▶ **Objectives:** Investigate impact of IMO-8400 on skin and muscle symptoms of disease, as well as safety and tolerability, antibody profiling, and identifying dose for further development
- ▶ **Dosing:** 1x/week, via subcutaneous injection, up to 24 weeks



Gene Silencing Oligonucleotide Technology



First Gene Silencing Oligo (GSO) Candidate Selected for Pre-clinical evaluation

- Apolipoprotein C-III (APOC-III) target selected for development
 - Available established pre-clinical animal models
 - Well-known clinical endpoints in Familial Chylomicronemia Syndrome (FCS) and Familial Partial Lipodystrophy (FPL)
 - Potential for broad and rare disease applications
- IDRA-008 comparable in-vivo potency to Volanesorsen (IONS)*
- Design of IDRA 008 to balance liver tissue accumulation (safety/tolerability) and PD effect (efficacy) confirmed in multiple murine models (surrogate oligo in mouse model; clinical asset in Tg mouse model)
- Pre-clinical safety package supports Phase 1 clinical development strategy and plan*
- Head to head study on-going in non-human primates to inform probability of success to be superior to that asset; anticipate IDRA-008 design may be safer in long term studies, but no opportunity to predict that outcome in absence of large/long clinical trial that in absence of superiority in NHP model warrants that investment
- Development decision to be made in 1Q 2018 based on totality of the head to head data with Volanesorsen

* IDRA Internal Pre-Clinical Study

Evolving Gene Silencing Oligonucleotide Strategy

- Utilize a variety tools including our proprietary algorithm for selecting unique target sequences and custom oligonucleotide chemistries to produce potent and selective gene silencing candidates
- Target selections process:

Rare Disease(s) → Competition → Targets → **Oligo Therapeutic**

- Unmet medical need
- Clinical development
- Registration path

- All modalities
- Stage of development
- Learnings to leverage?

- Amenable to gene silencing

- Full toolbox of oligo technologies



Near-term Expected Deliverables

- ILLUMINATE 204 Data Updates Throughout 2018
 - Next planned data update ASCO 2018
- Q1 2018 – Initiation of ILLUMINATE 301 – Phase 3 Trial of IMO-2125 in combination with Ipilimumab in Anti-PD-1 refractory metastatic melanoma
- 1Q 2018 – IDRA-008 Pre-clinical Cyno Model comparator study data available
 - Go-forward decision point
- 2Q 2018 – Data available from Phase 2 IMO-8400 clinical trial in Dermatomyositis