2017 JP Morgan Healthcare Conference
January 11, 2017

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Happy New Year!!!!

2016 Achievements -

- **Completed Enrollment in Phase 1 Dose Escalation IMO-2125 Trial – IPI Arm**
- **Commenced Dosing Phase 1 Dose Escalation IMO-2125/Pembro Arm**
- **Presented Clinical and Translational Data at SITC**
- **Designed clinical program to approval in PD-1 Refractory Melanoma**
- **Planned additional IMO-2125 trials beyond PD-1 refractory melanoma**
- **Opened IMO-8400 Phase 2 Trial in Dermatomyositis – 20 Sites initiated and enrollment underway**
- **Increased number of 3GA compounds to 22 gene targets for potential development**
- **Executed out-licensing agreement for IMO-9200 to Vivelix**
- **Strengthened company balance sheet extending cash runway through next 18 months**

- Leading to Pivotal 2017

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Addressing Immuno-Oncology's Unmet Need

- Intra-tumoral IMO-2125

Tumor Microenvironment is Key to Improving Treatment Outcomes

- Despite success of checkpoint inhibitor (CPI) therapy, a significant proportion of patients do not benefit
- Combination of CPIs offers modest improvement juxtaposed by increased toxicity
- Limited options after failure of anti PD-1 therapy
  - Ipilimumab provides 13% ORR[1]
  - Provides path to regulatory approval
- Melanoma is the fastest-increasing tumor worldwide[2] - significant unmet medical need remains

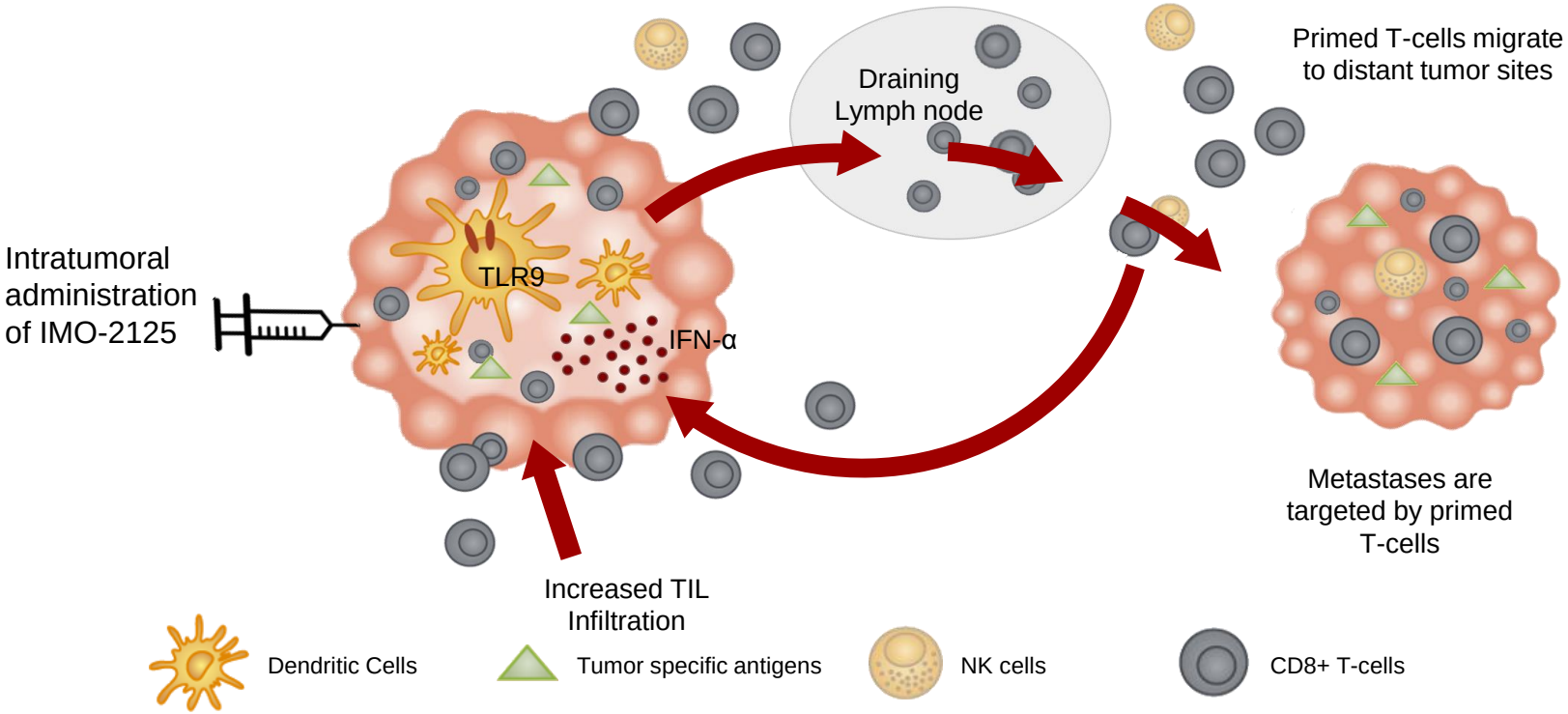
IMO-2125 Initial Development/Commercialization Target is PD-1 Refractory Melanoma

[1] Long GV, SMR, 2016

[2] Weinstock MA. Epidemiology, Etiology, and Control of Melanoma. Med Health R I. 2001;84(7):234-236

Intra-tumoral IMO-2125 Mechanism of Action

Immune Activation in Local Tumor has been Observed to Lead to Systemic Effect in both Animal and Human Trials



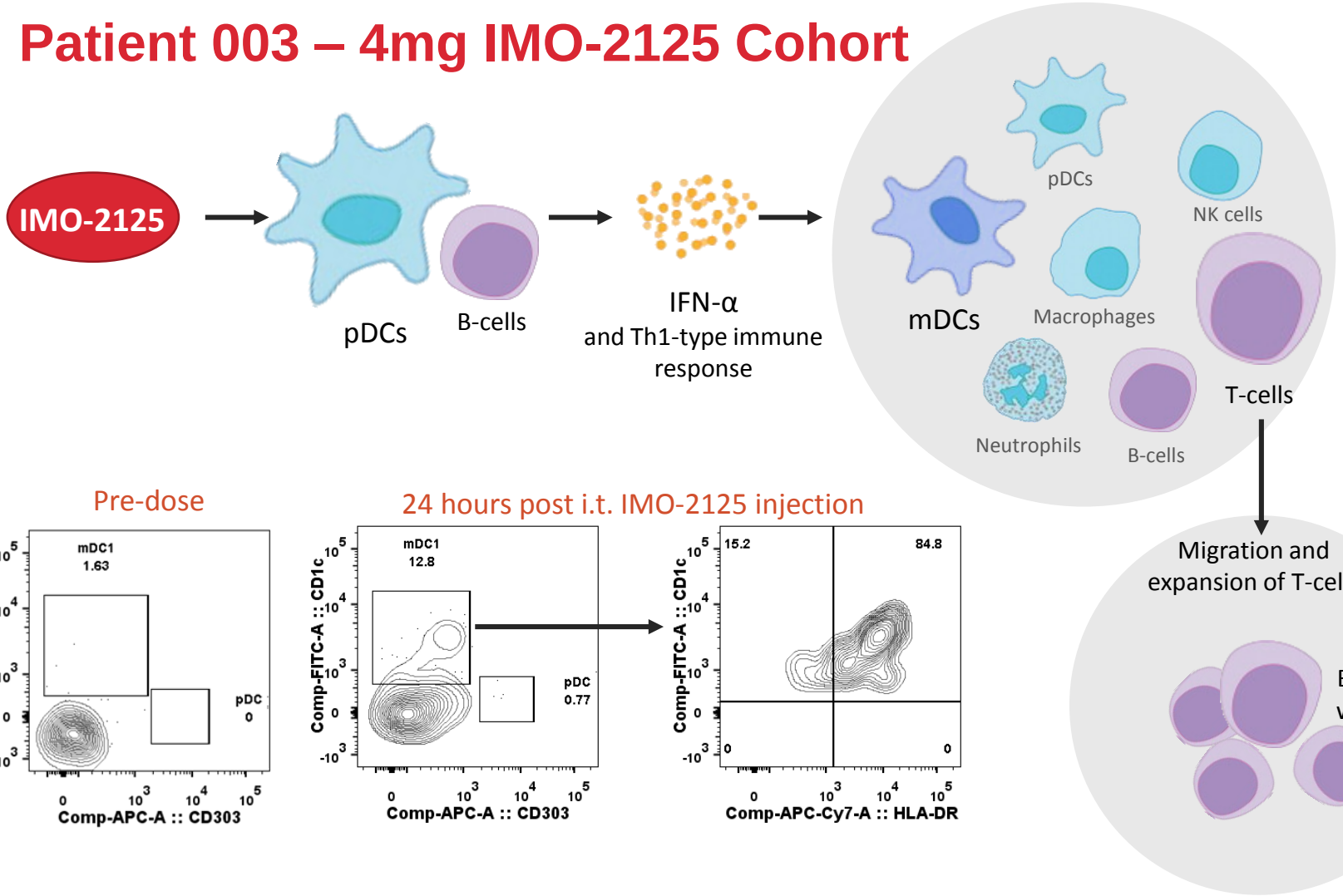
Demonstration of Clinical and Translational Responder

Patient 003 – 4mg IMO-2125 Cohort

- 58 y/o WM with BRAF wild-type melanoma originating base of penis
  - Metastases to inguinal lymph nodes and liver
- Rapid progression on nivolumab (4 cycles) prior to enrollment
- Received 6 doses IMO and 3 doses ipi (last one held for hypophysitis)
  - Well-known AE deemed related to ipi

DC Maturation in the Injected Tumor

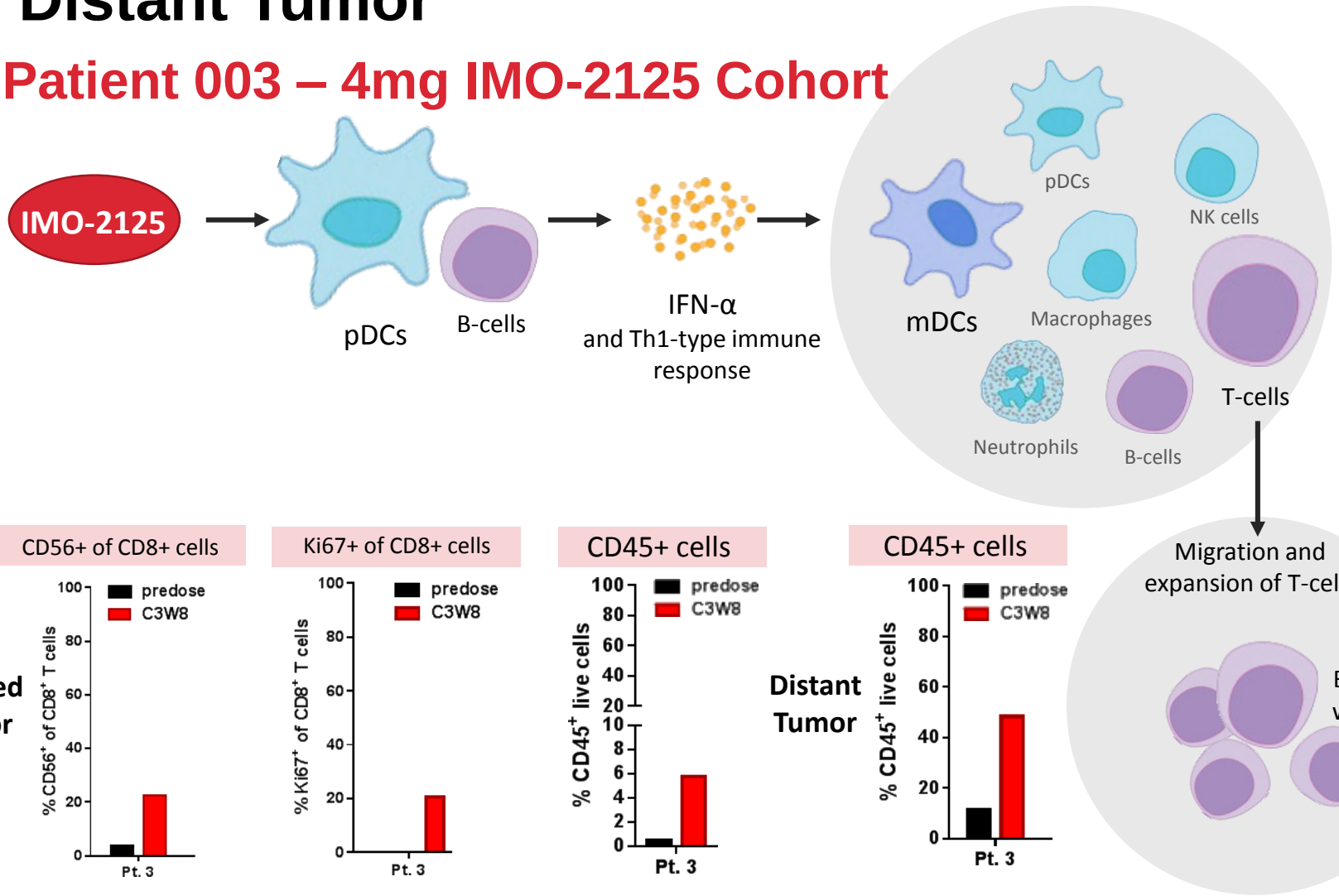
Patient 003 – 4mg IMO-2125 Cohort



Graphical representation

T-cell Activation Occurring in the Injected and Distant Tumor

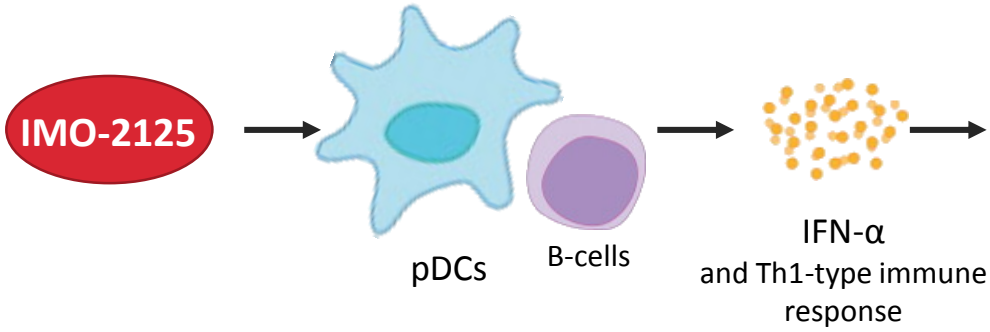
Patient 003 – 4mg IMO-2125 Cohort

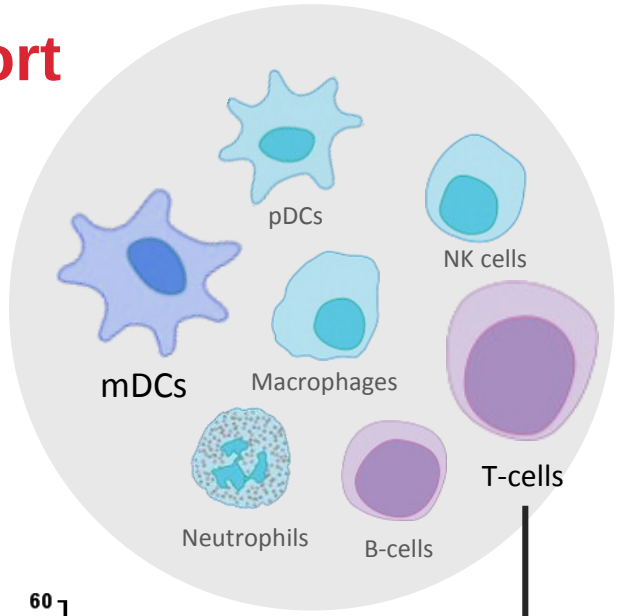


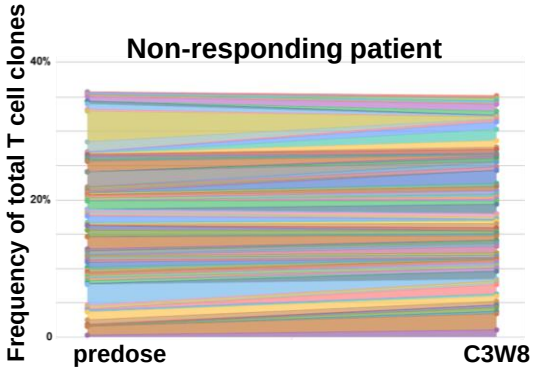
Graphical representation

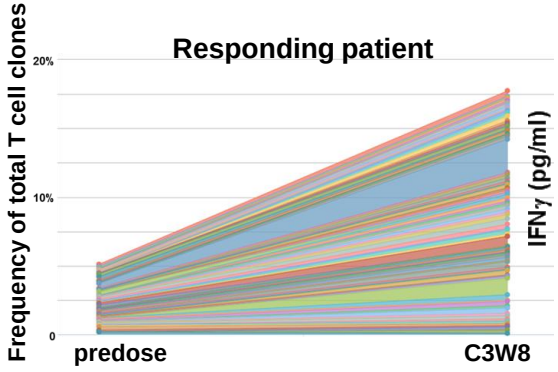
Expansion of top T-cell clones in the distant lesions, induction of IFN-γ

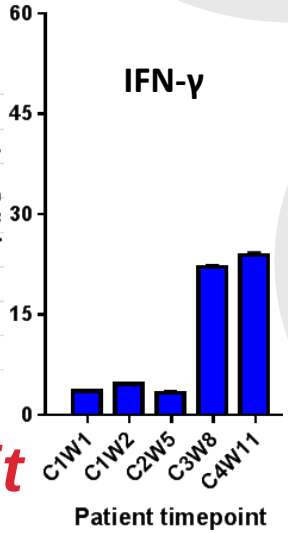
Patient 003 – 4mg IMO-2125 Cohort

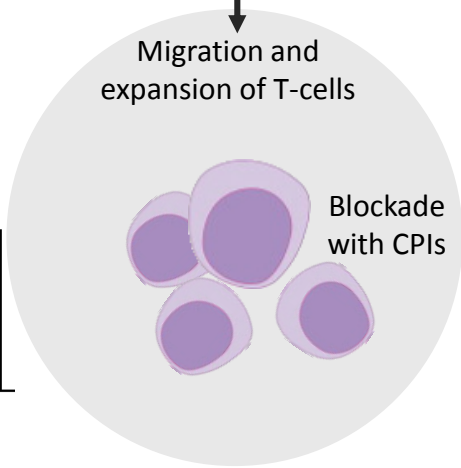












Patient 003 Remains PR at 6 Mos. Visit

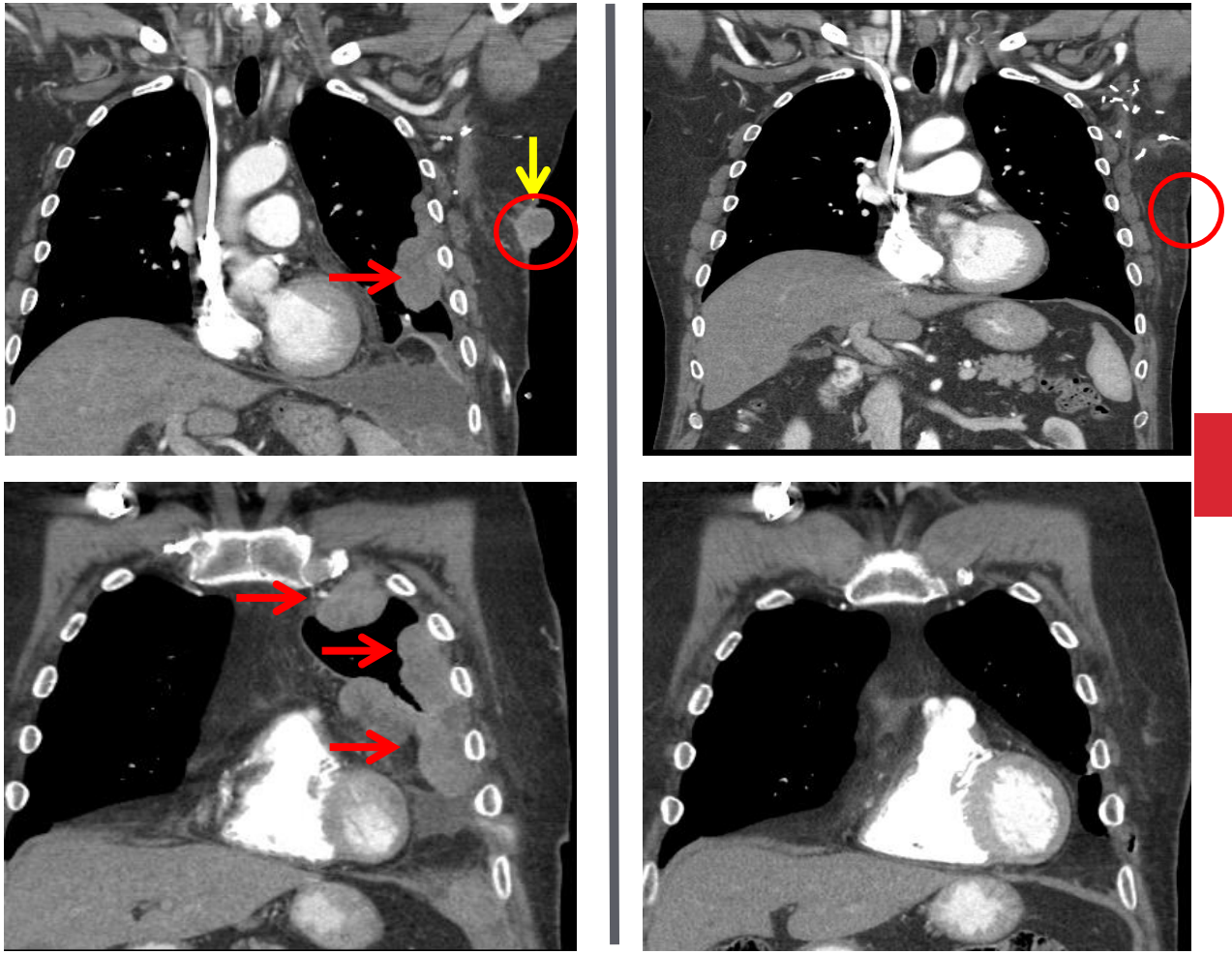
Additional Clinical Responder Case Study

Patient 004 – 8mg IMO-2125 Cohort

- 68 y/o male with BRAF wt melanoma, metastatic to lung (bulky), pleura, LN, widespread soft tissue
- Marked progression on Nivo + Urelumab (anti-4-1BB)
  - Marked progression w/ severe dyspnea
  - Referred to hospice
- Pleural effusion drained, then begun on study treatment
- Received 6 doses IMO + 4 doses ipi
- Dramatic response after 6 wks of therapy
- Investigator-assessed CR at 5 months

Tumor Imaging: Patient 004 Remains a CR at 6 Months Visit

Ipilimumab 3mg plus i.t. IMO-2125 8 mg



Pre-Therapy 03/2016

Post-Therapy 08/2016

Injected Lesion

Distant Lesions

IMO-2125-ipilimumab Combination Development

Additional sites are being added in 1H17 for Phase 2

Enrollment Completed	Ongoing	Planned

Cohort 1
(IMO 4 mg + ipi 3 mg/kg)

Cohort 2
(IMO 8 mg + ipi 3 mg/kg)

Cohort 3
(IMO 16 mg + ipi 3 mg/kg)

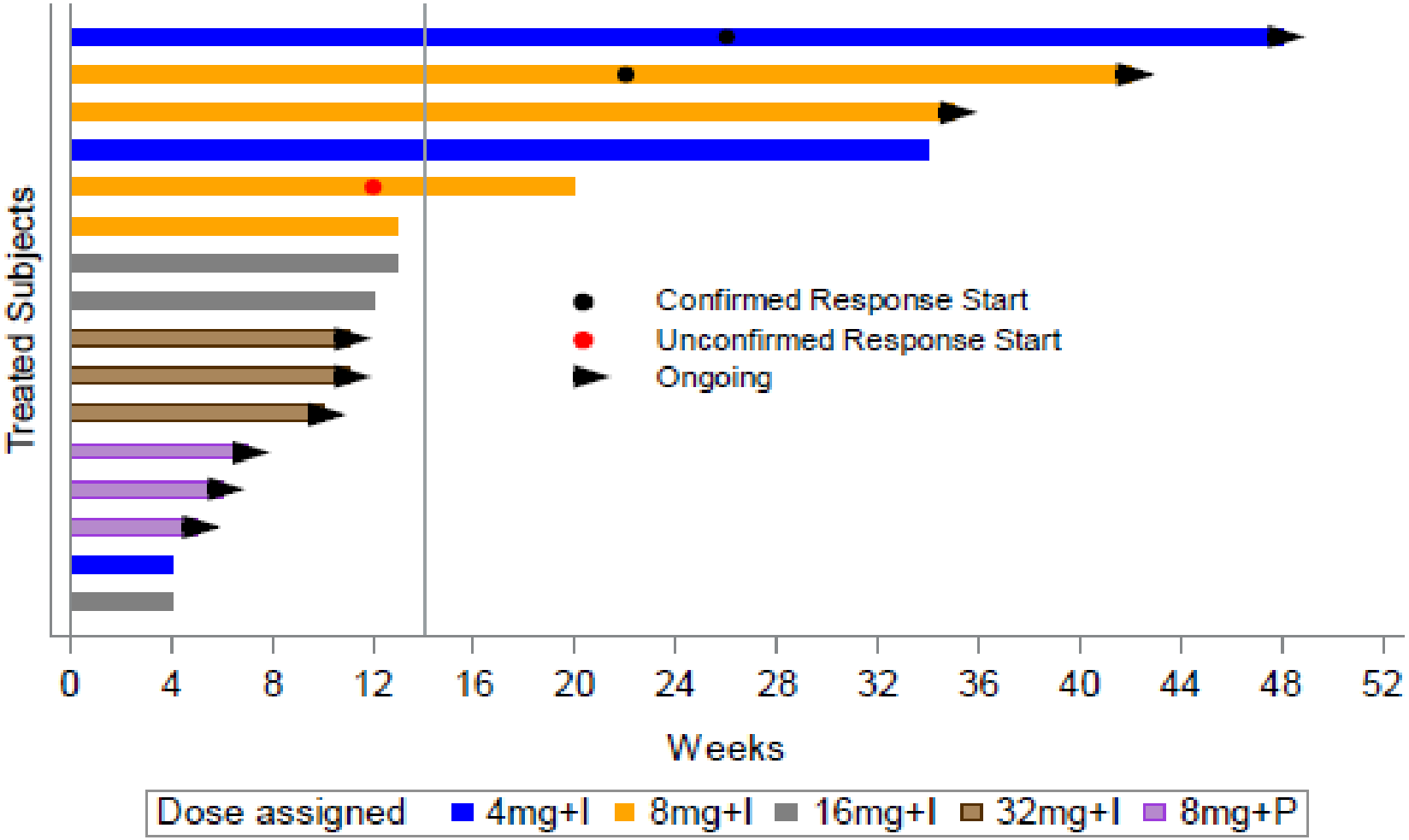
Cohort 4
(IMO 32 mg + ipi 3 mg/kg)

Phase 2 (N=21)

Cohort 5 (Backfill)
(IMO 8 mg + ipi 3 mg/kg)

Cohort 6 (Backfill if needed)
(IMO tbd + ipi 3 mg/kg)

Durable Responses with Prolonged Stabilization of Disease



Data cut-off date: 05JAN2017

IMO-2125 in PD1 Refractory Melanoma Path Forward

- January data-cut for Q1 2017
  - EOP1 FDA Meeting
- Phase 2 Dose selection anticipated by end of Q2 2017
  - Seamless initiation of Phase 2 portion (N=21)
- Phase 3 design to be finalized post FDA meeting

IMO-2125 Beyond Melanoma

Mechanism of Action Supports Broader Expansion

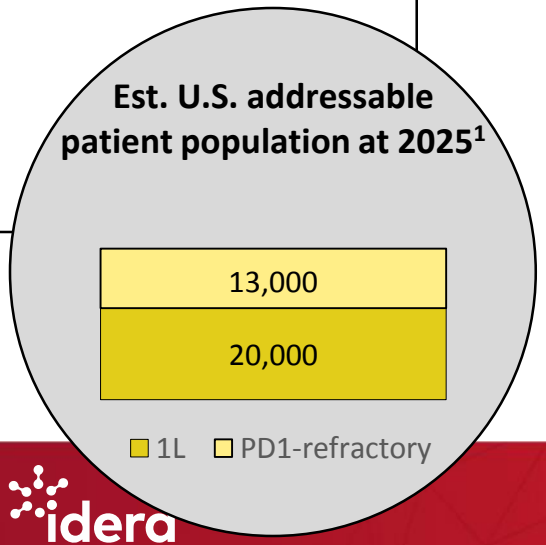
- To further capitalize in 2017 we plan to:
  - Initiate Phase 1 Multi-tumor type Monotherapy Trial – Q1
    - Critical for registration and exploratory purposes
  - Initiate Phase 2 combo basket study – 2H
    - Multiple CPI combos, multiple tumor types
- Multiple discussions underway for potential clinical development partnerships

Long-term Expansion Opportunity Significant

INTRODUCE

Unresectable metastatic melanoma

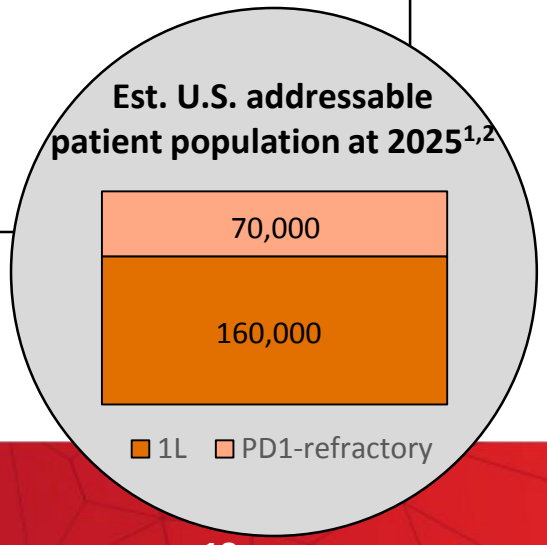
- Maturing I/O market primed for combo
- High unmet need in anti-PD1-refractory patients



EXPAND

Emerging I/O addressable tumors

- Moderate response to cornerstone anti-PD1
- PD-L1 expression guided treatment is restrictive



TRANSFORM

"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, RCC and bladder only

Providing Hope for a Serious Rare Condition

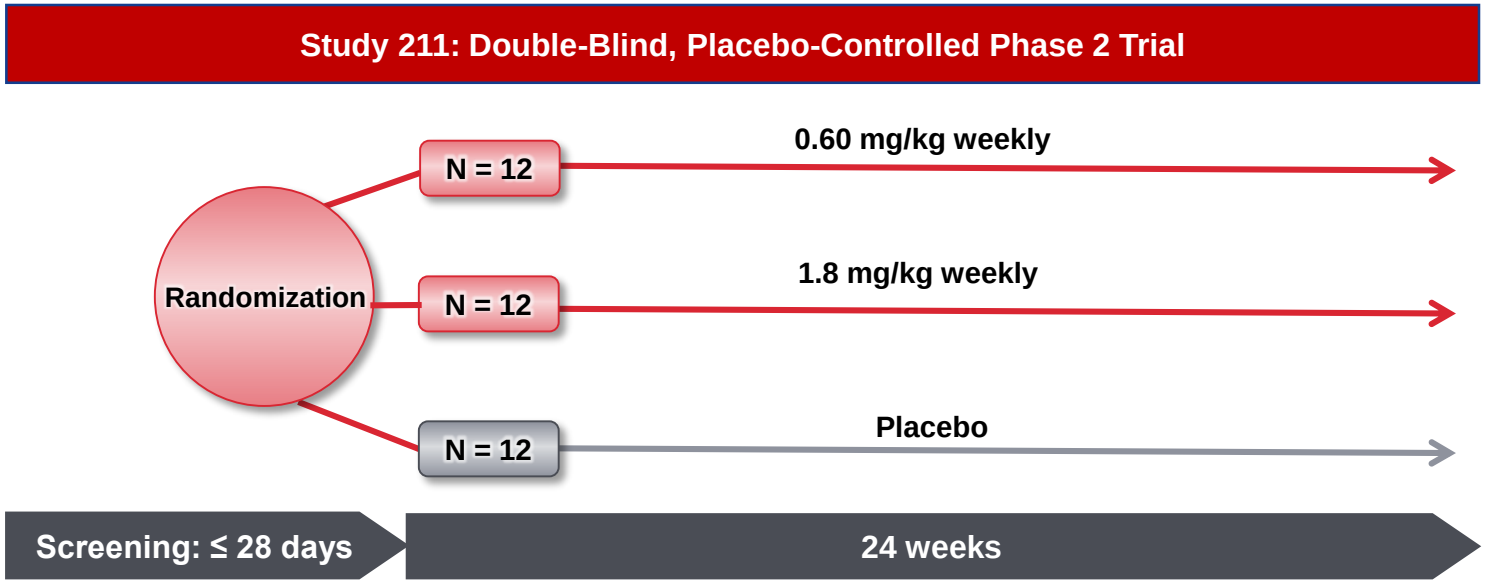
- IMO-8400 to Treat Dermatomyositis

Dermatomyositis

- 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
- TLR antagonism may disrupt autoimmune cycle of tissue damage to improve disease symptoms

Phase 2 Trial Enrollment Underway

Phase 2 Data Expected in 2018



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

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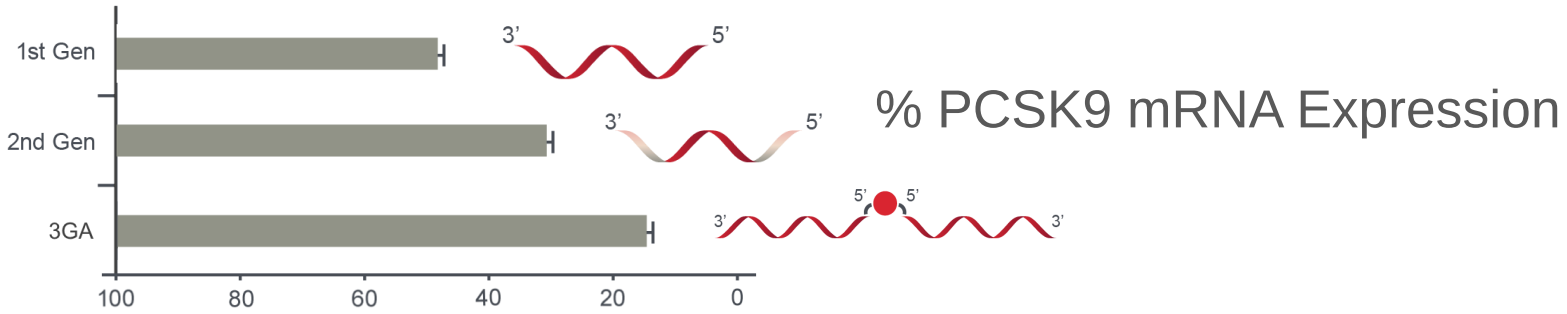
Platform of Unlimited Possibilities

- Demonstrating the Potential of 3GA

Why is a better RNA-directed technology needed ?

Current RNA-focused Platform Technologies Remain Flawed

- 3GA may realize the full potential of antisense technology for the treatment of diverse diseases
- 3GA designed to overcome the limitations of the first and second generation antisense technology:
  - Immunotoxicities
  - Therapeutic Index



Assays were conducted with antisense constructs in Hepa 1-6 cells; RNA levels were quantified by qPCR

3GA Development to Date

22 3GA Compounds Developed to Specific Gene Targets Across Wide Variety of Therapeutic Areas

- Therapeutic areas range across:
  - Rare diseases, oncology, autoimmune disorders, metabolic conditions, single-point mutations, etc.
- Ongoing activity ranges from cell culture through IND-enabling toxicology
- Current portfolio feeds potential for both internal development candidates and partnering opportunities

1st Clinical Candidate for Idera Development Selected

First 3GA Candidate Selected to Enter Clinic

Opportunity to Validate Technology Platform / Advance Into Late Stage Development

- For strategic and competitive purposes, Idera to withhold naming selected target until 2H 2017
  - Well-established liver Target
  - Available pre-clinical animal models
  - Well-known clinical endpoints
  - Potential for broad and rare disease applications
- Potential Value Drivers
  - Establishment of human proof of concept for platform in 2018
  - Differentiation from other RNA-based therapeutic platforms (Improved safety/efficacy)

PROGRAM	MECHANISM	INDICATION	COMMERCIAL RIGHTS	DISCOVERY	PHASE 1	PHASE 2	PIVOTAL
IMMUNO-ONCOLOGY	TLR9 Agonist	IMO-2125 Refractory PD-1 Metastatic Melanoma / CPI Comb.	idera				
		IMO-2125 Monotherapy Additional Tumor Types					
		IMO-2125 Combo Additional Tumor Types – CPI Comb.					
RARE DISEASES	TLR 7,8,9 Antagonist	IMO-8400 Dermatomyositis	idera				
	3GA-NLRP3	3GA Undisclosed Indication					
	3GA-DUX4	3GA Undisclosed Indication					
PARTNERED PROGRAMS	3GA	3GA Renal Diseases	gsk				
	TLR 7,8,9 Antagonist	IMO-9200 Autoimmune Diseases	Vivelix				
Partnering Opportunities – Idera-Sponsored Clinical Development Suspended	TLR 7,8,9 Antagonist	IMO-8400 B-Cell Lymphoma	idera				

Near Term Expected Deliverables

- IMO-2125 Data Updates and Major Medical Meetings Throughout 2017
- Feb 2017 – IMO-2125 Melanoma Study Phase 1 Clinical Data (ASCO-SITC)
- Q1 2017 – Initiate Phase 1 IMO-2125 Monotherapy in Multiple Refractory Solid Tumors Clinical Trial
- 2H 2017 – Enroll IMO-2125 Phase 2 Expansion in Ongoing Clinical Trial
- 2H 2017 – Initiate Phase 2 IMO-2125 Combination Trial in Multiple Refractory Solid Tumors Clinical Trial
- 2H 2017 – Complete Enrollment of IMO-8400 Dermatomyositis Trial
- 2H 2017 – Announce Undisclosed 3GA Development Target and Plan
- Q1 2018 – File IND for First 3GA Compound
- Q1 2018 – Initiate and Enroll First 3GA Clinical Trial

Anticipated R&D Day in 2H 2017

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Thank You