



# ***October 2019 Corporate Overview***



# Forward-Looking Statements & Other Important Cautions

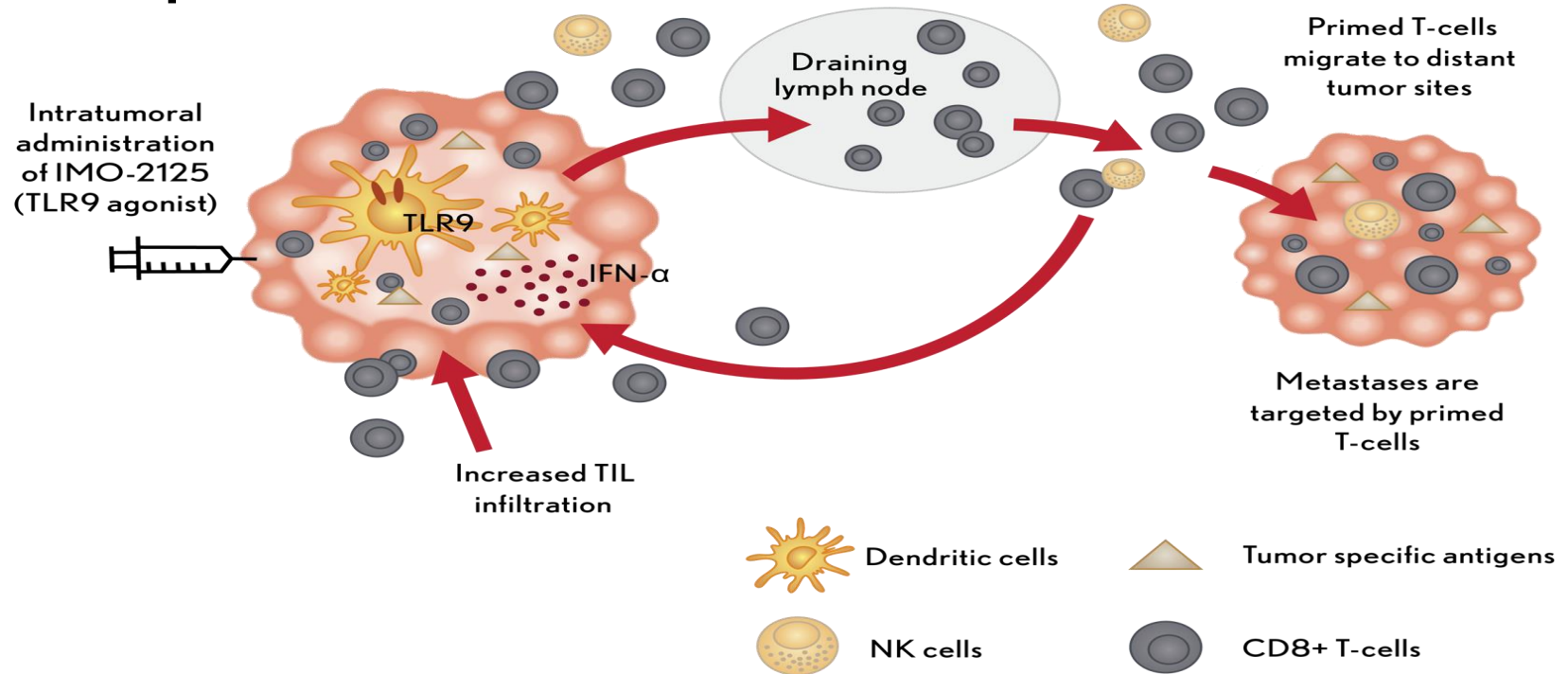
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# **Injecting a New Solution to Advance Cancer Immunotherapy**

## **Near Term Value Growth Driven by Tilsotolimod**

- Phase 3 Trial 75% Enrolled
- Encouraging Clinical Outcomes
- Studies of Tumors Beyond Melanoma Underway
- Collaborations with BMS and AbbVie
- Strengthened Exclusivity Proposition

# Designed to Stimulate the Immune System Locally to Potentially Lead to Better Systemic Patient Outcomes with Checkpoint Inhibitors





**Randomized Phase 3 Study of Tilsotolimod in Combination With Ipilimumab Compared With Ipilimumab Alone in Patients With Advanced Melanoma Following Progression On or After Anti-PD-1 Therapy**

# High unmet medical need in metastatic melanoma for patients who progress after PD-1 inhibitors

Historical Data of 321 Patients Suggest ORR Range of 4-16%\*

N=	ORR	References
97	13%	Long, et al., Presentation at Society for Melanoma Research 2016 Congress, 2016 (post-hoc analysis of KEYNOTE-006 patients who received ipilimumab monotherapy following failure of pembrolizumab)
60	4%	Fujisawa, et al., Retrospective study of advanced melanoma patients treated with ipilimumab after nivolumab: Analysis of 60 Japanese patients, J. Dermatol. Sci. 2018 Jan ; 89(1): 60-66
47	4%	Weichenthal, et al., Presentation at the 2019 ASCO Annual Meeting, Salvage Therapy after Failure From Anti PD-1 Single Agent Treatment, A Study by the German ADOReg Melanoma Registry
47	16%	Zimmer, et al., Ipilimumab alone or in combination with nivolumab after progression on anti PD-1 therapy in advanced melanoma, Eur. J. Cancer 2017; 75:47-55
40	10%	Bowyer, et al., Efficacy and toxicity of treatment with the anti-CTLA-4 antibody ipilimumab in patients with metastatic melanoma after prior anti-PD-1 therapy. Br. J. Cancer. 2016;114(10):1084–1089.
30	7%	Muto, et al., Investigation of clinical factors associated with longer overall survival in advanced melanoma patients treated with sequential ipilimumab, J. Dermatology, 2019; 46; 498-506

\* There are three additional studies of n=9, n=8, n=7 respectively: Aya, et al., Future Oncol. 2016; 12(23):2683-2688 (ORR=22%); Jacobsoone-Ulrich et al., Melanoma Research 2016, 26:2 (2016) (ORR=50%); Saijo, et al., Tohoku J. Exp. Med., 2019, 248, 37-43 (ORR=0%)



# ILLUMINATE-301 – Trial Design

## PD-1 Refractory Metastatic Melanoma

### Patient Stratification

- Duration of prior anti-PD-1 therapy (<12 or ≥12 weeks)
- Metastasis stage (M1c or other)
- BRAF mutation status and prior targeted therapy  
BRAF wild type, mutation positive with, or without prior targeted

#### Key Inclusion Criteria:

- Age ≥ 18 years
- Stage III or Stage IV melanoma
- ≥ 1 measurable lesion accessible for injection
- ECOG PS ≤ 1
- Adequate organ function

#### Key Exclusion Criteria:

- Prior TLR agonists
- Prior ipilimumab
- CNS disease

Randomization

1:1  
N≈454

#### Arm A

- Ipilimumab 3 mg/kg (4 doses: weeks 1, 4, 7, and 10)
- Treatment Duration: 10 weeks

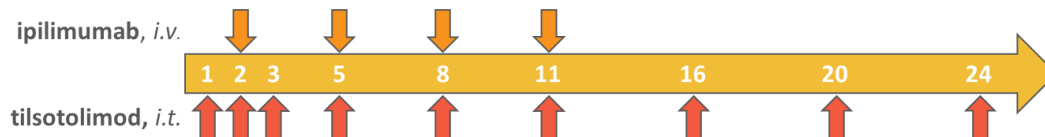
No crossover

#### Arm B

- Ipilimumab 3 mg/kg (4 doses: weeks 2, 5, 8, and 11) +
- Intratumoral tilsotolimod 8 mg (9 doses: weeks 1, 2, 3, 5, 8, 11, 16, 20, and 24)
- Treatment Duration: 24 weeks

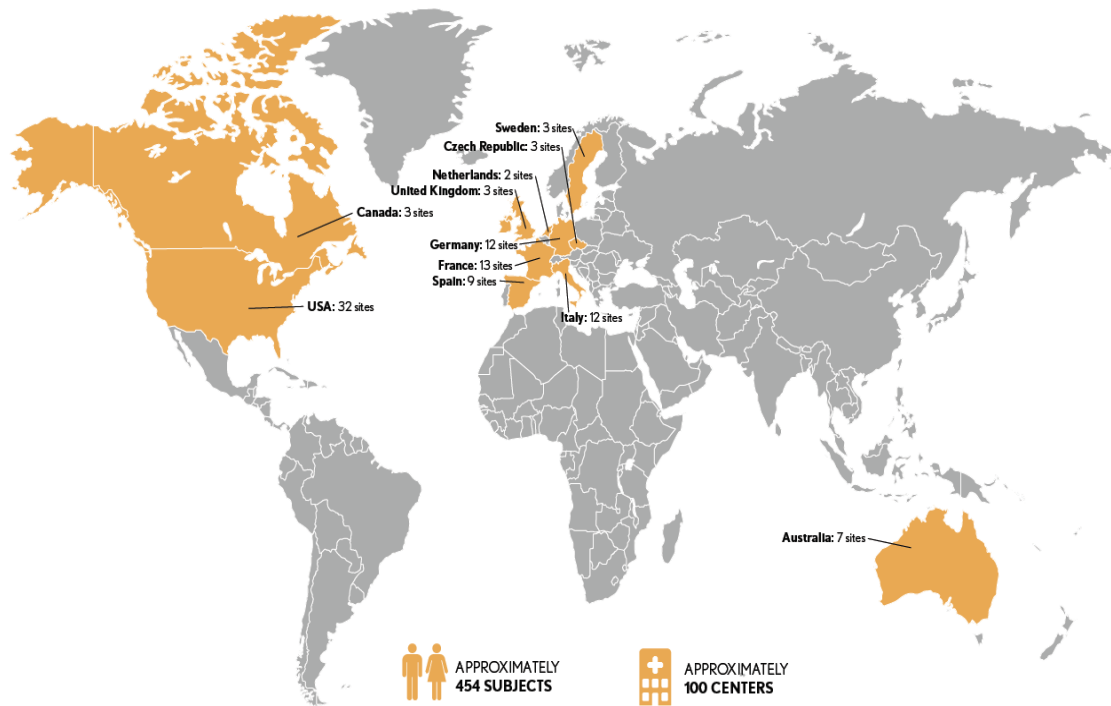
### Endpoints

- Primary endpoint family
- ORR by independent review per RECIST v1.1
  - OS
- Key secondary endpoints
- Durable response rate
  - Time to response
  - Progression-free survival
  - Patient-reported outcomes
  - Safety



i.v., intravenous; i.t., intratumoral; ORR, overall response rate; OS, overall survival,

# ILLUMINATE-301 Global Registration Trial



- **342 patients enrolled;**
- **Enrollment completion expected 1H 2020**

*\* Enrollment Update as of 10/23/2019*

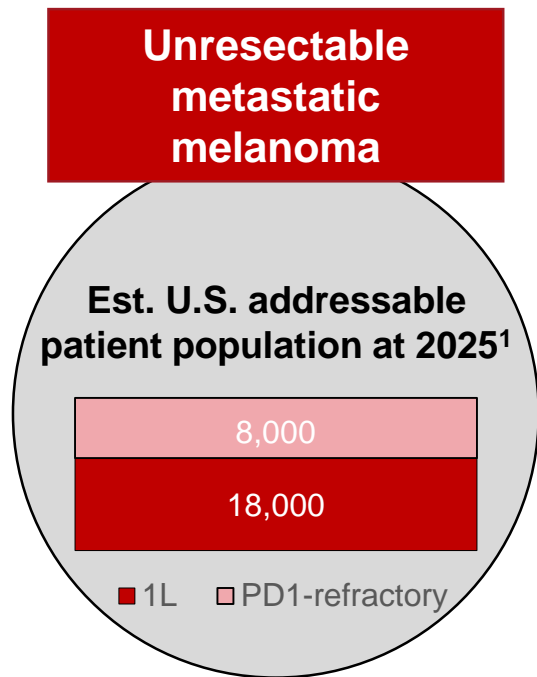


# Exclusivity

## Three Sources of Exclusivity for Tilsotolimod

- Composition of Matter Patent Exclusivity
  - Provides exclusivity until 2030 (estimated), inclusive of patent term extension
- Method-of-Use Patent
  - Covers certain melanoma treatments in combination with therapies targeting CTLA-4, PD-1, or PD-L1
  - Estimated expiration in September 2037
- Orphan Drug Designation
  - Granted *“for treatment of melanoma Stages IIb to IV.”*

# 1<sup>st</sup> Indication Commercial Opportunity



- High unmet need in anti-PD1-refractory patients
- **U.S. Peak year sales estimate > \$500 million,<sup>2</sup> if approved**

<sup>1</sup> Proprietary Idera Commercial Research

<sup>2</sup> Based on current company forecast through 2030



# Reasons to Believe

- Encouraging Clinical Data
- Translational Data



# ILLUMINATE-204



## A Phase 1/2 Study to Assess the Safety and Efficacy of Intratumoral Tilsotolimod in Combination with Ipilimumab or Pembrolizumab in Patients with Metastatic Melanoma

- Primary objectives
  - Phase 1: to determine the recommended phase 2 dose
  - Phase 2: to assess preliminary clinical activity of tilsotolimod in combination with ipilimumab at the recommended phase 2 dose in patients with metastatic melanoma that is not responsive to PD-1 inhibitor therapy, using RECIST v1.1
- Secondary objectives include:
  - Phase 2: to further assess the safety and tolerability of tilsotolimod in combination with ipilimumab or pembrolizumab (pembrolizumab combination not studied in this phase)

# ILLUMINATE-204 Results to Date Imply Potential for Clinically Meaningful Benefit

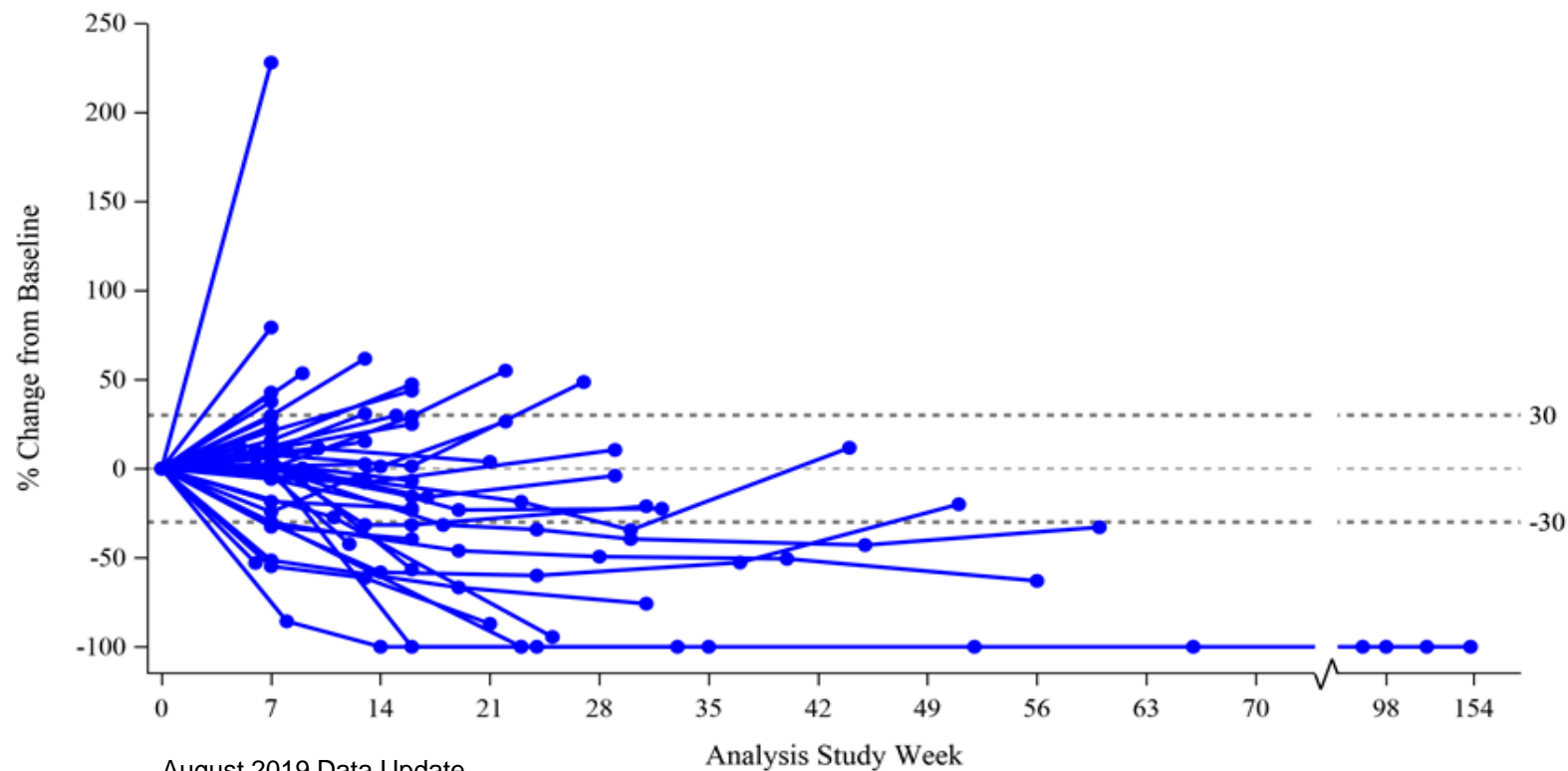
Best Overall Response	tilsotolimod + ipilimumab (N=49) <sup>1</sup>	ipilimumab monotherapy post PD-1 (N=321) <sup>2</sup> (pooled post-hoc analysis of six studies)
Overall Response Rate (CR or PR)	24% (12)	4-16%
Disease Control Rate (CR, PR, or SD)	71% (35)	17-45%

- 11 of 12 responses confirmed per RECIST v1.1
  - 3 Confirmed Complete Responses (CR)
- 5 of 10 RECIST v1.1 responses evaluable for durability (>6 mos.) to date
- Median OS (overall survival) not yet reached (min/max: 1.6 – 35 mos.)
- Safety profile observed consistent with previously reported results

<sup>1</sup> 49 of 53 subjects had at least 1 post-baseline disease assessment at time of October 2019 data update

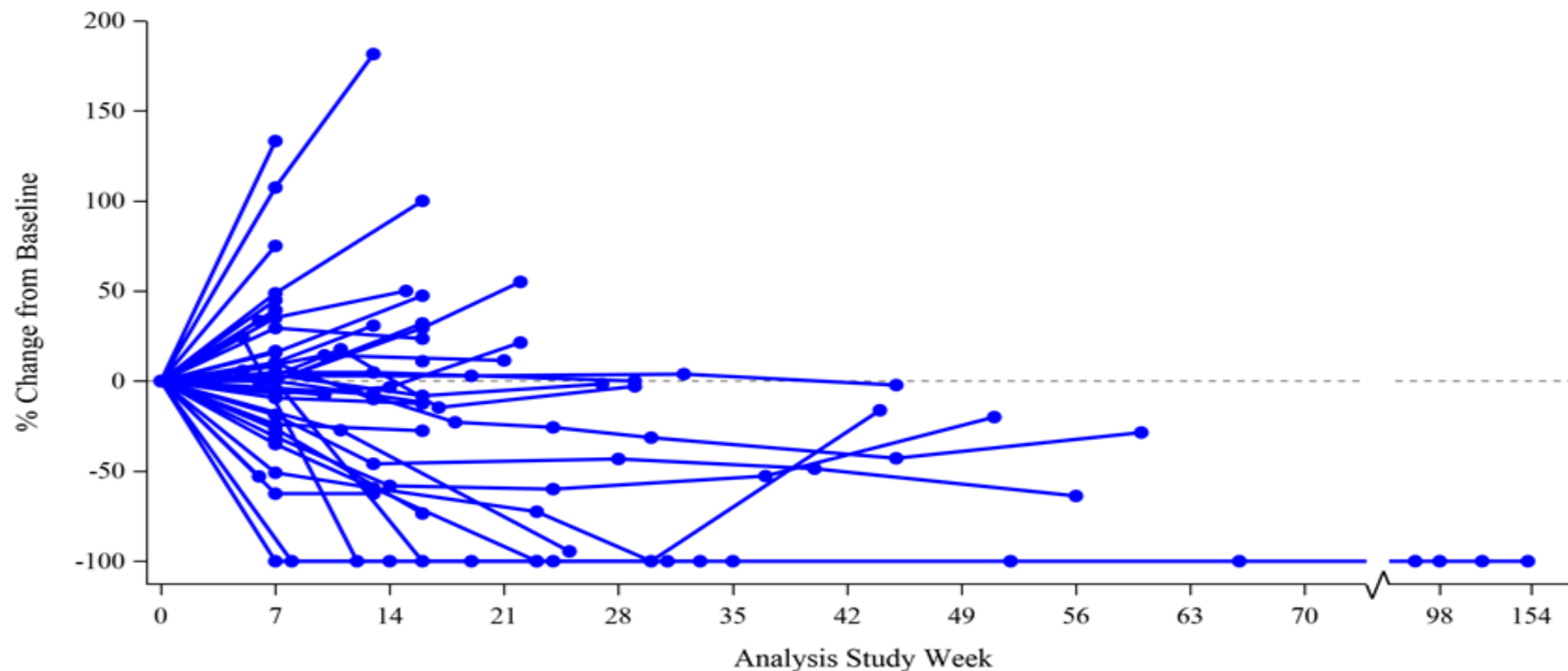
<sup>2</sup> References available on Slide 7

# ILLUMINATE 204: Percent (%) Change from Baseline in All Target Tumors



August 2019 Data Update

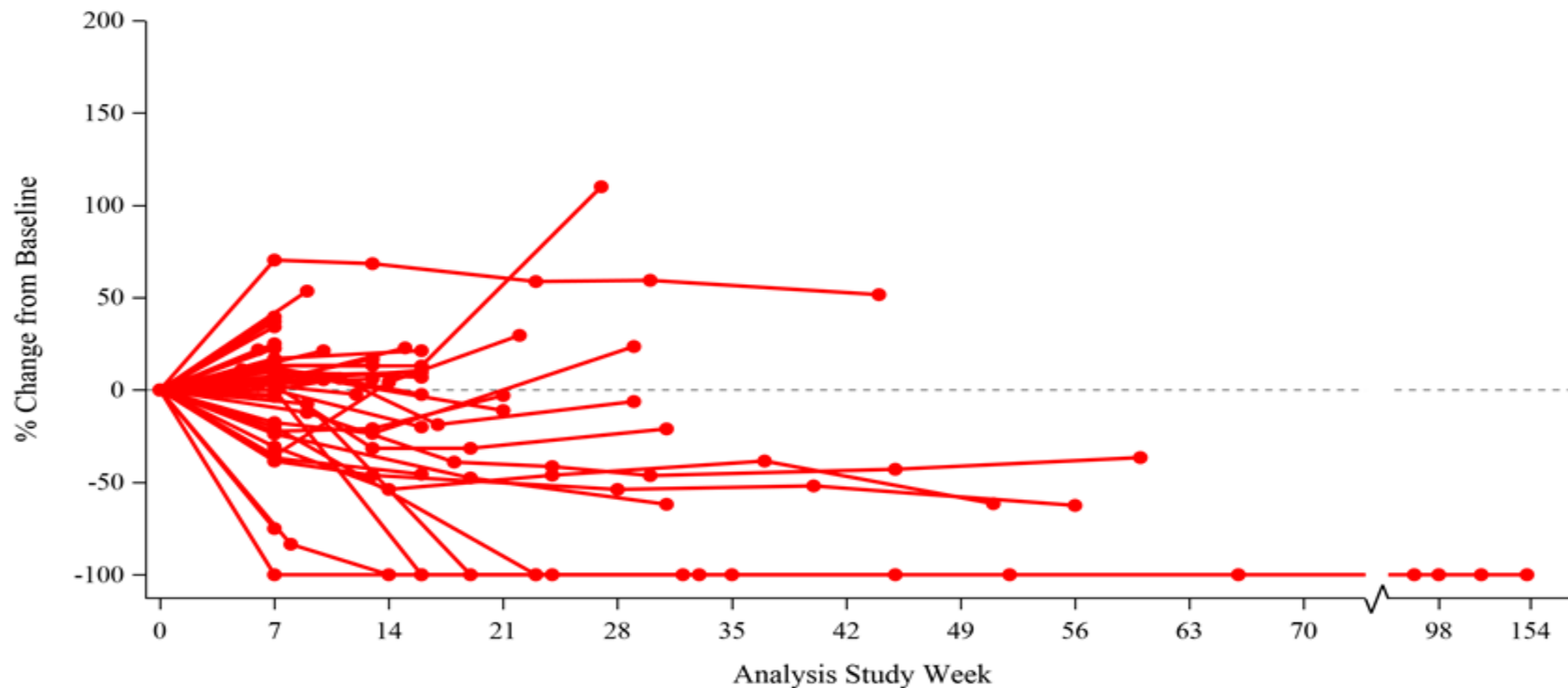
# ILLUMINATE 204: Percent (%) Change from Baseline in Injected Tumors



August 2019 Data Update



# ILLUMINATE-204: Percent (%) Change from Baseline Uninjected Tumors Demonstrating Abscopal Effect



# ILLUMINATE-204 – Safety Analysis

	N=72	%
Subjects with at least one AE	71	98.6
Subjects with at least one SAE	27	37.5
Subjects with at least one $\geq 3$ AE	36	50.0
Subjects with an AE leading to Study drug withdrawn	8	11.1
Subjects with an AE leading to Study discontinuation	1	1.4
Subjects with Death related to AE	0	0.0

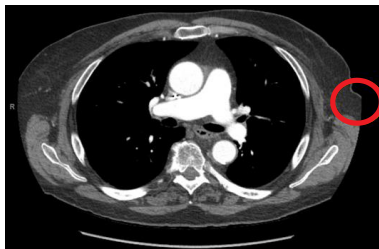
Maximum Severity	N=72	%
Grade 1	14	19.4
Grade 2	21	29.2
Grade 3	29	40.3
Grade 4	7	9.7
Grade 5	0	0.0

# ILLUMINATE-204 Case Studies

## Complete response (68 years old)



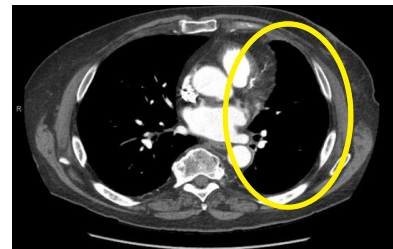
Pretreatment  
Injected tumor



Posttreatment 24 weeks  
Injected tumor



Pretreatment  
Uninjected tumor



Posttreatment 24 weeks  
Uninjected tumor

# ILLUMINATE-204 Case Studies

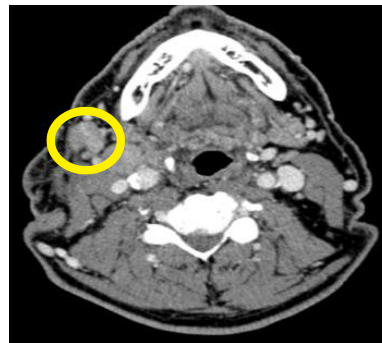
## Partial response (62 years old)



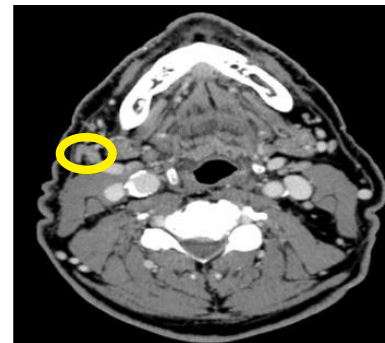
Pretreatment  
Injected tumor



Posttreatment 56 weeks  
Injected tumor



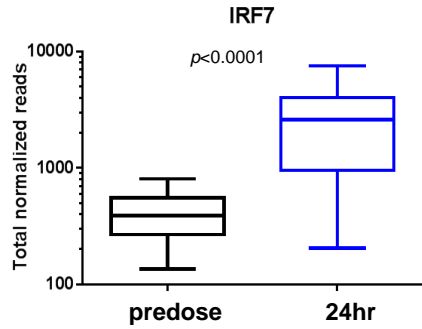
Pretreatment  
Uninjected tumor



Posttreatment 56 weeks  
Uninjected tumor

# Tilsotolimod activates local IFN $\alpha$ -response gene signature and combination with ipilimumab therapy induces proliferation of T-cells in distant lesion

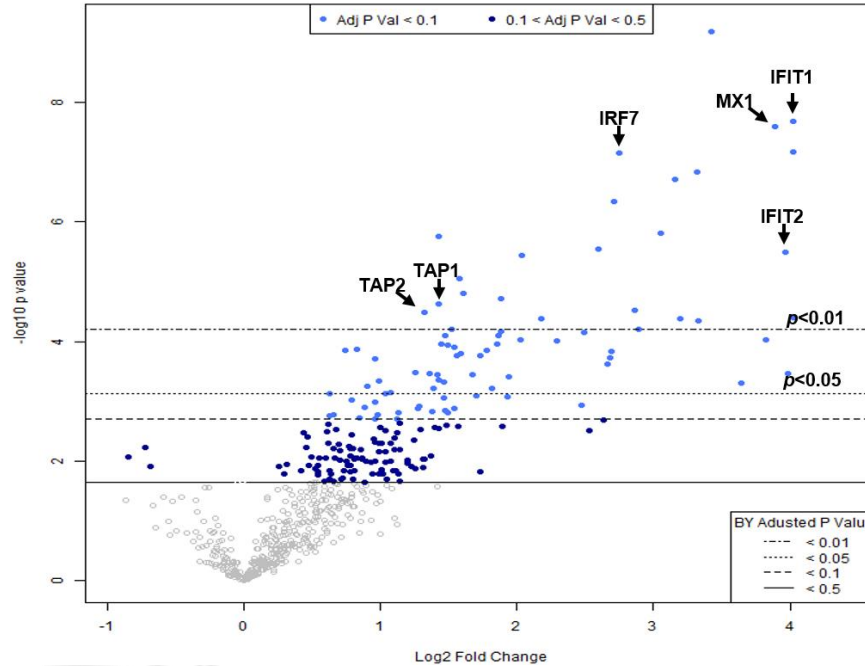
**tilsotolimod only  
(prior to ipilimumab)**



**n=15**

**Injected Lesion**

**tilsotolimod only  
(prior to ipilimumab)**

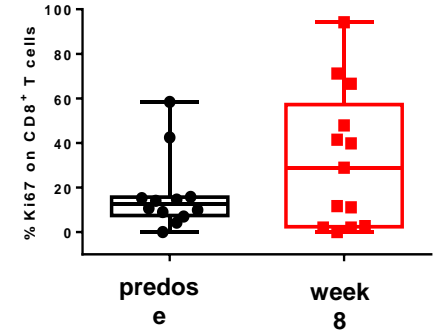


**Injected Lesion**

**20**

**n=15**

**tilsotolimod + ipilimumab**

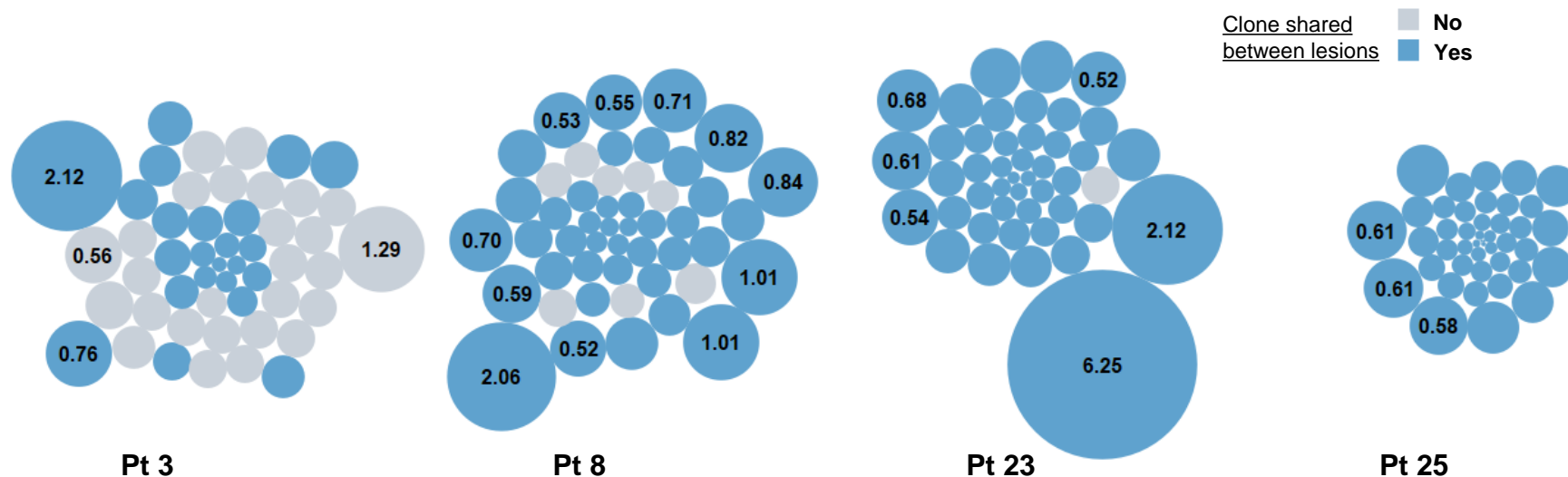


**n=12**

**Distant Lesion**

# Expanding Clones in the Distant Lesion are Shared with the Injected Lesion

Top 50 clones in the distant lesion at C3W8 of responding patients



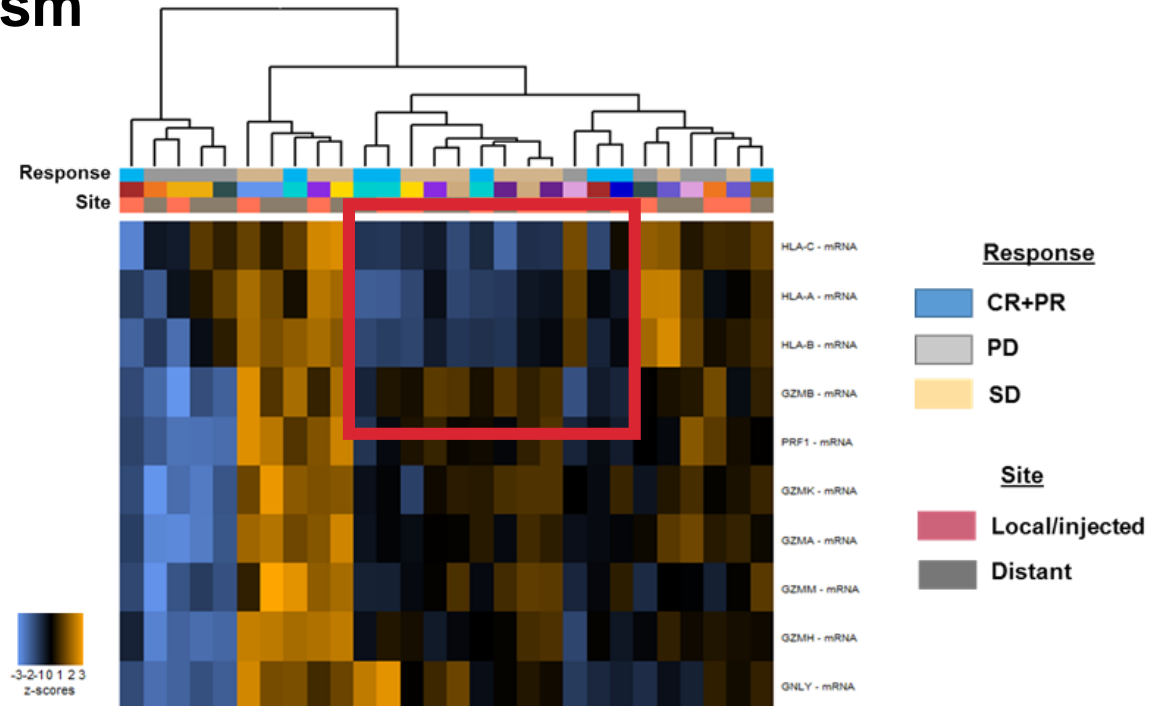
Number = clonal specific change in frequency (C3W8 – predose)  
Circle size reflects the frequency of the clone relative to the other clones present

Source: SITC 2017

# Demonstrated Potential of Tilsotolimod to Overcome CTLA-4 (Cytotoxic T-Lymphocyte Antigen) Resistance Mechanism

Responses seen  
in HLA-ABC\* low  
tumors at  
baseline  
(red box)

\* HLA-ABC: human leucocyte antigen; ABC refers to three genes part of MHC class 1





# ILLUMINATE 204 Summary

*Final data planned for major medical meeting 1H 2020*

- Established the recommended Phase 2 dose (RP2D) of 8mg tilsotolimod
- Provided proof of mechanism for tilsotolimod based on translational work from Phase 1
  - Rapid, within 24 hours, induction of IFN $\alpha$
  - Responses in tumors not expected to respond to ipilimumab alone based on HLA-ABC low baseline expression
- Clinical responses rates (ORR/DCR) greater than historical control and median overall survival (OS) not yet reached



# Tilsotolimod Expansion Strategy



# ILLUMINATE-101

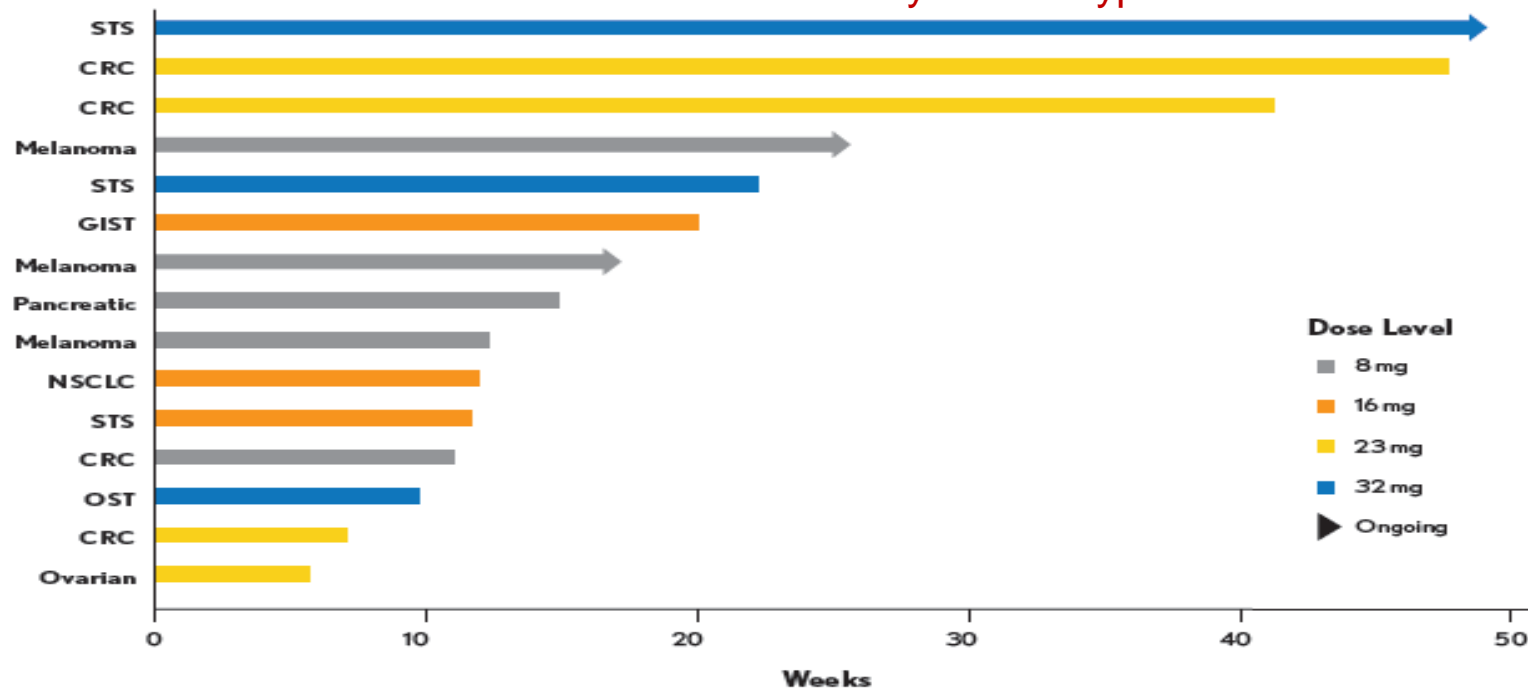


## A Phase 1B Study of Intratumoral Tilsotolimod (IMO-2125) in Patients with Refractory Solid Tumors (Data as of July 1, 2019)

- Dose-escalation cohort objectives
  - Primary: safety
  - Secondary: establish RP2D; assess clinical activity and pharmacokinetics
  - Exploratory: evaluate immunologic activity
- Dose-expansion cohort objectives
  - Primary: clinical activity of overall response rate via RECIST v1.1
  - Secondary: safety, other measures of clinical benefit, and pharmacokinetics
  - Exploratory: evaluate biomarkers for immunologic assessment and assess antidrug antibody formation

# ILLUMINATE-101 Efficacy

## Duration of Stable Disease By Tumor Type



CRC, colorectal cancer; GIST, gasotrointestinal stromal tumor; NSCLC, non-small cell lung cancer; OST, osteosarcoma; STS, soft tissue sarcoma.

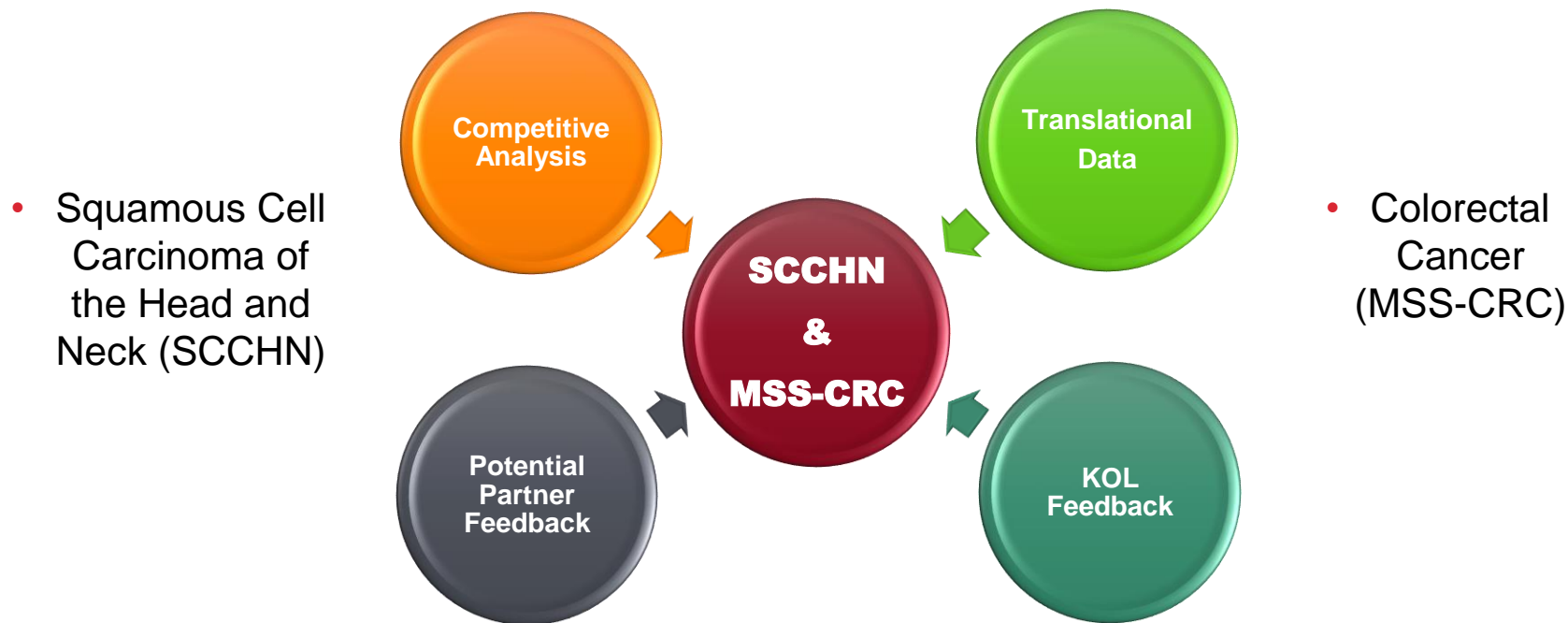
# ILLUMINATE-101 - Summary



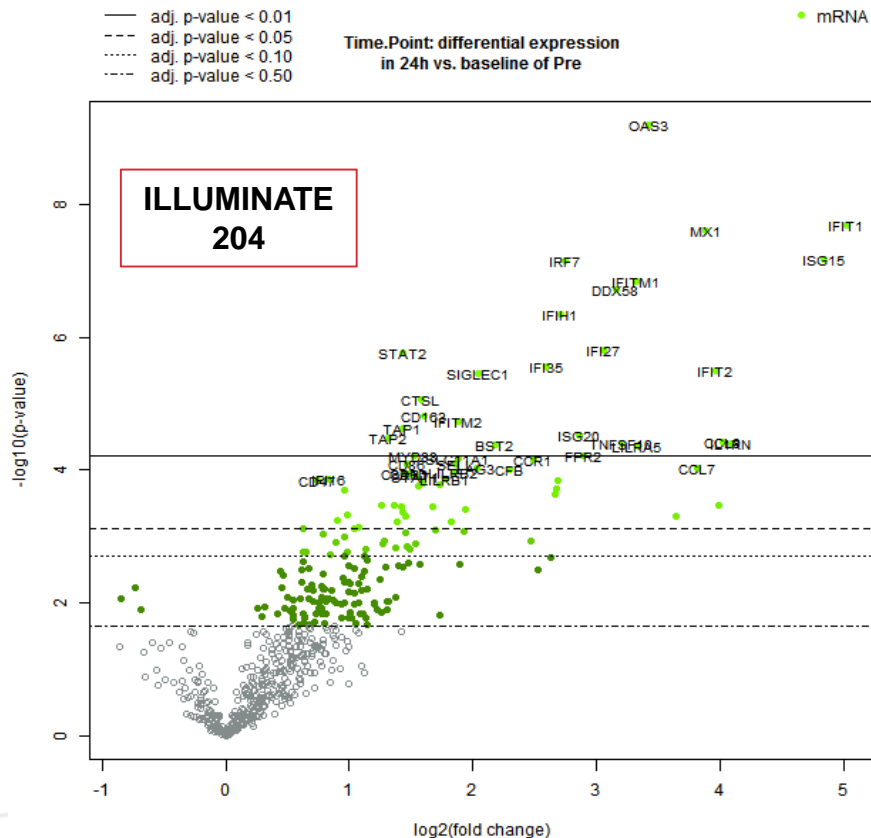
- Intratumoral injection of single-agent tilsotolimod is generally well-tolerated; preliminary evidence of clinical activity across multiple solid tumors include those traditionally unresponsive to immunotherapy
- Uninjected lesions respond similarly to injected lesions, suggesting a potential abscopal-like effect
- Tilsotolimod rapidly increases dendritic cell activation, upregulation of MHC class II, and upregulation of IFN- $\alpha$  signaling, is suggesting improved antigen presentation
- Tilsotolimod-induced upregulation of antigen presentation is observed across multiple tumor types; changes are consistent with those observed in a previous phase 1/2 clinical trial of patients with metastatic melanoma

# ILLUMINATE 206 Initial Expansion Beyond Melanoma

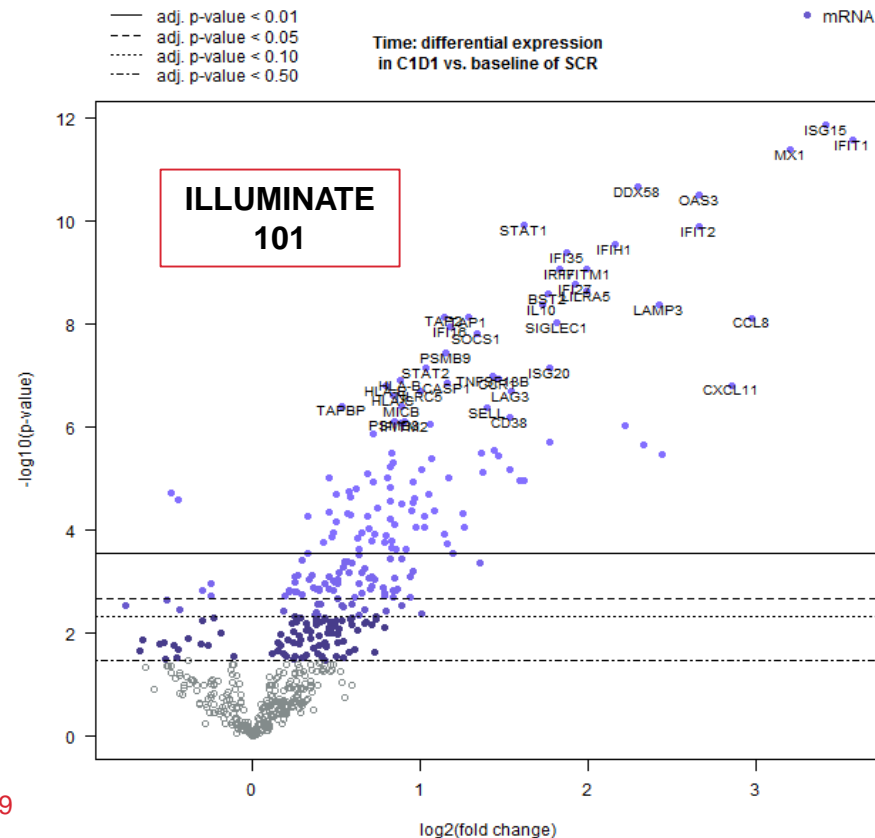
Broad Effort to Determine Appropriate First Tumor Types for Expansion



# Tilsotolimod Induces Rapid Gene Expression in the Tumor Microenvironment, Regardless of Tumor Type



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# Recently Announced Clinical Collaboration with AbbVie Broadens Expansion Efforts



## **Idera Pharmaceuticals Announces Immuno-Oncology Clinical Research Collaboration with AbbVie**

**Exton, PA. September 4, 2019** —Idera Pharmaceuticals, Inc. (NASDAQ: IDRA) announced today that they have entered into an immuno-oncology clinical research collaboration with AbbVie, a global, research-based biopharmaceutical company. The purpose of the collaboration is to conduct a clinical study evaluating whether combinations of an OX40 agonist (ABBV-368), a TLR-9 agonist (tilsotolimod), chemotherapy (nab-paclitaxel) and/or an anti-programmed cell death 1 (PD-1) antagonist (ABBV-181) stimulate the immune system resulting in anti-tumor responses.

This Phase 1b, multi-center, open-label study is designed to determine the safety, tolerability, pharmacokinetics and preliminary efficacy of combinations of ABBV-368 plus tilsotolimod in subjects with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC).

The study will test three separate treatment arms:

- ABBV-368 plus tilsotolimod;
- ABBV-368 plus tilsotolimod and nab-paclitaxel; and
- ABBV-368 plus tilsotolimod, nab-paclitaxel and ABBV-181.

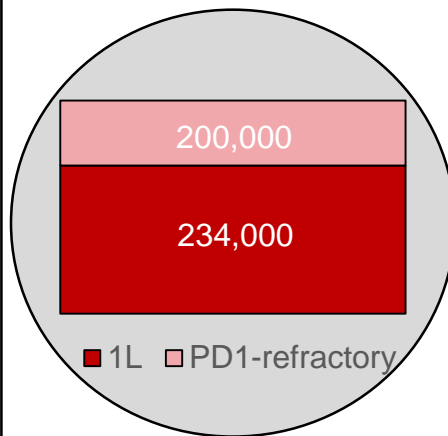
Under the terms of the agreement, Idera will provide clinical trial supply of tilsotolimod to AbbVie and AbbVie will be responsible for conduct of the study.

# Expanding Potential Growth Opportunities

## Emerging I/O addressable tumors

- Moderate response to cornerstone anti-PD1
- Goal to increase number of approved settings

Est. U.S. addressable patient population at 2025<sup>1,2</sup>



## “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

<sup>1</sup> Proprietary Idera Commercial Research

<sup>2</sup> NSCLC, head and neck, colorectal, bladder and gastric

# Financials and Capital Structure Updates

- Completed Q2 2019 with \$52.4M cash
- Expected cash runway into Q2 2020
- Approximately 29M shares outstanding
- \$35M Common Stock Purchase Agreement with Lincoln Park Capital
- \$50M ATM in place

# Key Milestones

- Completion of ILLUMINATE-301 Enrollment – 1H 2020
- Topline Data from ILLUMINATE-204 – 1H 2020
- Interim Data from ILLUMINATE-206 - 2020
- ORR Data from ILLUMINATE-301 – 1H 2021