SOLVE ON.

ORAL PD-L1 PROGRAM:

- INCB86550
- INCB99280
- INCB99318

NOVEMBER 13, 2021

FORWARD LOOKING STATEMENTS

Except for the historical information set forth herein, the matters set forth in this presentation contain predictions, estimates, and other forward-looking statements, such as statements regarding Incyte's expectations with respect to its oral PD-L1 franchise, including the potential for market growth and the potential treatment benefits and Incyte's expectations regarding ongoing clinical trials and clinical trials to be initiated for INCB86550, INCB99280, and INCB99318.

These forward-looking statements are based on the Company's current expectations and subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments in and risks related to: further research and development and the results of clinical trials possibly being unsuccessful or insufficient to meet applicable regulatory standards or warrant continued development; the ability to enroll sufficient numbers of subjects in clinical trials and the ability to enroll subjects in accordance with planned schedules; the effects of the COVID 19 pandemic and measures to address the pandemic on the Company's clinical trials, supply chain and other third-party providers, sales and marketing efforts and business, development and discovery operations; determinations made by the FDA, FTC and other regulatory agencies both inside and outside of the United States; the Company's dependence on its relationships with and changes in the plans of its collaboration partners; the efficacy or safety of the Company's products and the products of the Company's collaboration partners; the acceptance of the Company's products and the products of the Company's collaboration partners in the marketplace; market competition; unexpected variations in the demand for the Company's products and the products of the Company's collaboration partners; the effects of announced or unexpected price regulation or limitations on reimbursement or coverage for the Company's products and the products of the Company's collaboration partners; sales, marketing, manufacturing and distribution requirements, including the Company's and its collaboration partners' ability to successfully commercialize and build commercial infrastructure for newly approved products and any additional products that become approved; greater than expected expenses, including expenses relating to litigation or strategic activities; and other risks detailed from time to time in the Company's reports filed with the Securities and Exchange Commission, including its quarterly report on Form 10 Q for the quarter ended September 30, 2021. The Company disclaims any intent or obligation to update these forward-looking statements.

HERVÉ HOPPENOT

CHIEF EXECUTIVE OFFICER, INCYTE

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ORAL PD-L1 FRANCHISE OVERVIEW

- Portfolio of three oral PD-L1 inhibitors in clinical trials
- INCB86550 is the first oral PD-L1 inhibitor to demonstrate clinical efficacy
- Parallel development of three compounds to identify best candidates for full development
  - Dosing schedule optimization and phase 2 study of INCB86550 is underway
  - INCB99280 and INCB99318 in dose escalation
- Unique attributes of an oral PD-L1 inhibitor create a significant opportunity

STEVEN STEIN

CHIEF MEDICAL OFFICER

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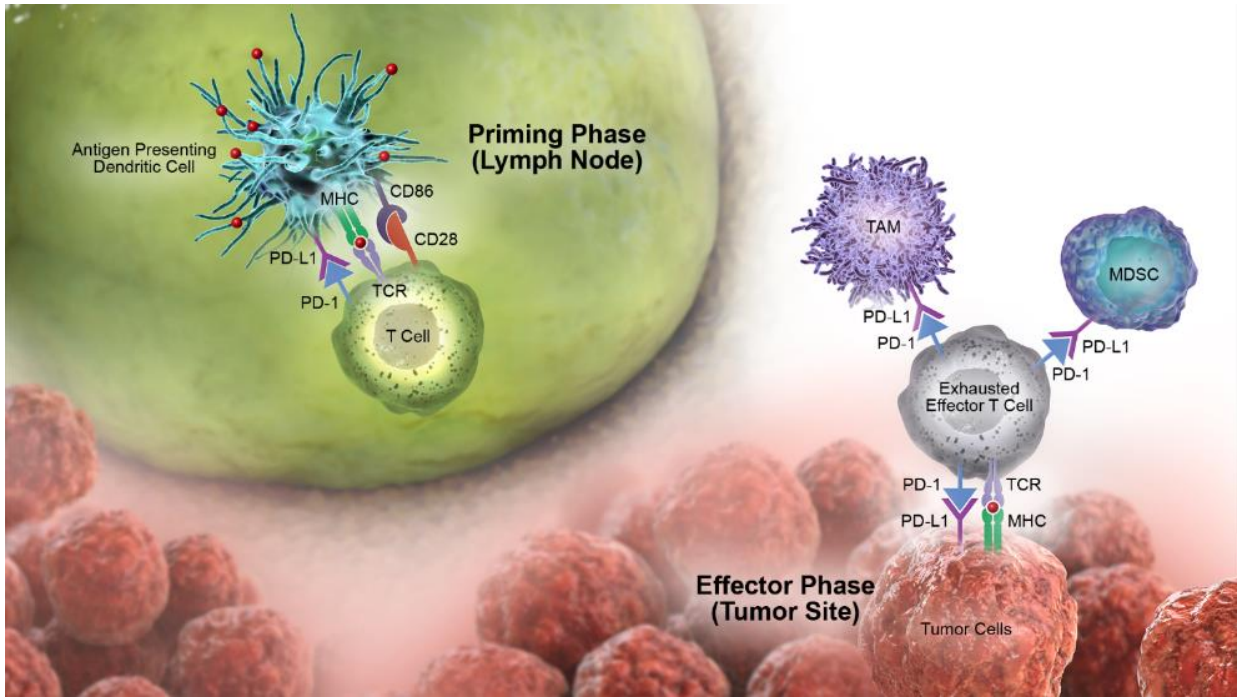
SMALL-MOLECULE PD-L1 INHIBITORS, A DIFFERENTIATED APPROACH TO CANCER THERAPY

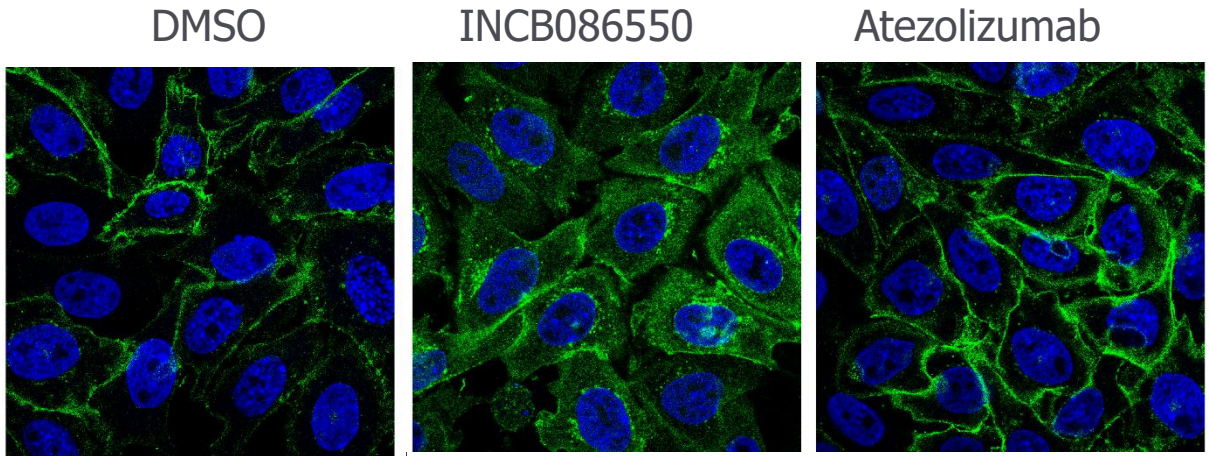
- Blocking PD-1/PD-L1 interaction is effective in reversing immune suppression by tumor cells[1,2]
- Monoclonal antibodies against PD-L1 or PD-1 have been approved for the treatment of multiple tumor histologies[1,2]
- Oral, small-molecule PD-L1 inhibitors
  - Are potent and selective
  - Induce PD-L1 internalization
  - Exhibit antitumor efficacy as single agent

PD-1/PD-L1 interaction reduces T-cell function



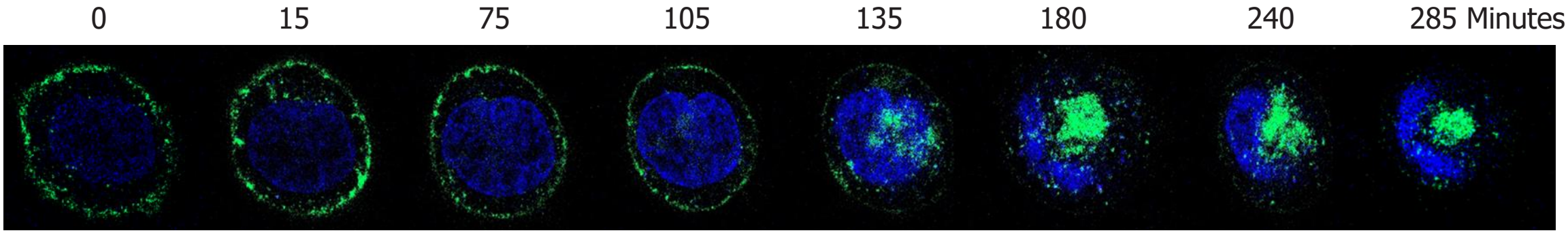
1. Ribas A and Wolchok JD. Science. 2018;359:1350–55.
2. Sharpe AH and Pauken KE. Nat Rev Immunol. 2018;18:153–67.

INHIBITOR-INDUCED INTERNALIZATION OF PD-L1



- Internalization starts within 1 hour and increases over time
- Co-localization observed with markers of the early endosome

Live cell imaging



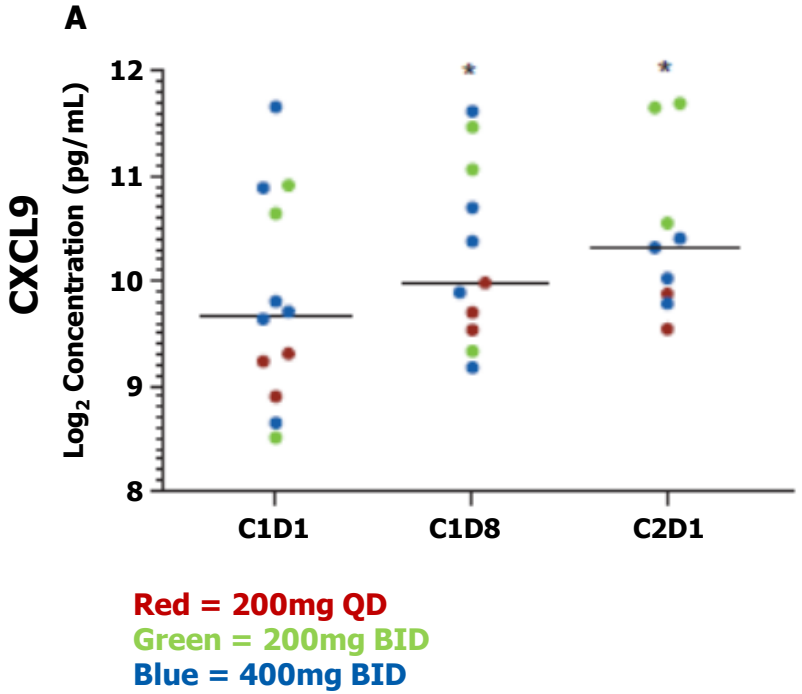
Anti-PD-L1–AF488 (Green)
Nuclei – Hoechst (Blue)

Liu, et al AACR 2019.

INCB86550: PHARMACODYNAMIC ACTIVITY

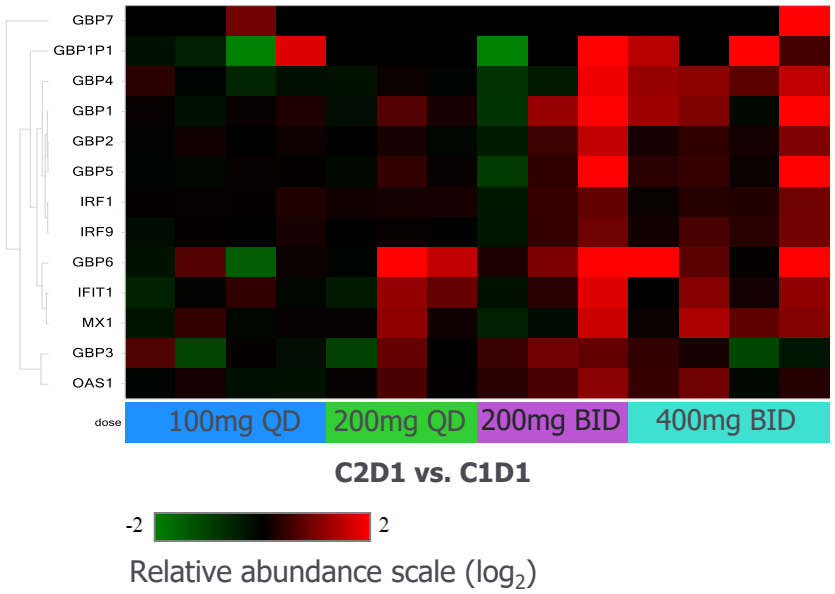
- **Pharmacodynamic biomarkers demonstrate T-cell activation in patients treated with INCB86550**

Circulating Cytokines[1]

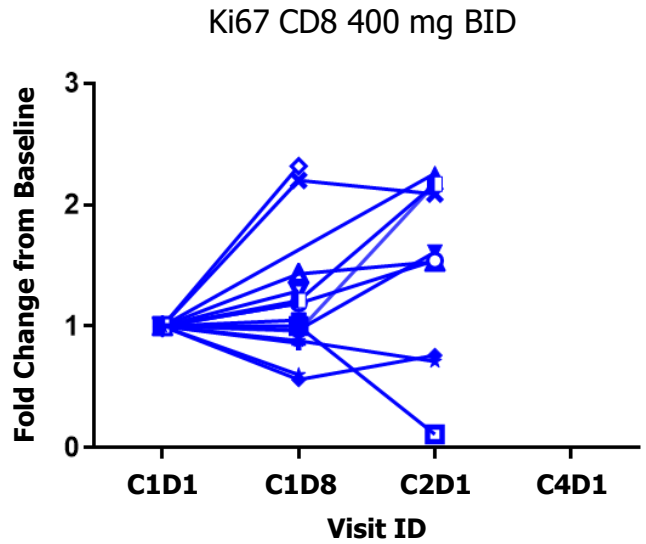


Red = 200mg QD
Green = 200mg BID
Blue = 400mg BID

Interferon-Related Gene Expression in Blood[1]



T-cell Proliferation[2]



1. Piha-Paul SA, et al. SITC 2020. 2. Data on file.

INCB86550: EARLY DEVELOPMENT

Dose Escalation

Part 1

- **3 + 3 design**
- **100mg QD to 800mg BID**

Key Inclusion Criteria
- Age ≥ 18 years
- Advanced solid tumors
- Measurable lesions per RECIST v1.1 or RANO
- Disease progression after standard available therapy* or intolerant of or ineligible for standard treatment
- ECOG score 0–1
- Mandatory baseline tumor biopsy

Dose Expansion

Part 2 Expansion

- n≤15 / dose level at PADs
- Dose not exceeding MTD

Cohort 2A: I/O experienced
- n=5 / dose level
- Confirmed progression on anti-PD-1 mAb

Cohort 2B: I/O naïve
- n=10 / dose level
- Select solid tumors

Part 3 Expansion

- MSI-H or dMMR solid tumors
- I/O naive

n≤60 at PADs

Part 4 Expansion

- HPV+ solid tumors
- Prior standard therapy

n≤60 at PADs

Cohort 2B Expansion
- n≤20 per tumor type†

Primary Endpoints
- Safety and tolerability
- Identification of a PAD and/or MTD
- Identification of the RP2D

Secondary Endpoints
- PK, PD
- Preliminary efficacy including ORR, DCR, and DOR

BID, twice daily; DCR, disease control rate; dMMR, mismatch repair deficient; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; HPV, human papilloma virus; MSI-H, microsatellite instability–high; MTD, maximum tolerated dose; ORR, objective response rate; PADs, pharmacologically active doses; PD, pharmacodynamics; PK, pharmacokinetics; QD, once daily; RANO, response assessment in neuro-oncology; RECIST, Response Evaluation Criteria in Solid Tumors; RP2D, Recommended Phase 2 Dose.
* There was no limit to the number of prior treatment regimens. † If preliminary responses are observed, further expansion in ≤3 tumor types may be undertaken.

INCB86550: PATIENT DEMOGRAPHICS

Characteristic	Total (N=79)
Age, y	
Mean (SD)	64.0 (11.2)
Median (range)	65.0 (31.0–84.0)
Female, n (%)	45 (57.0)
Race, n (%)	
White	71 (89.9)
Black	3 (3.8)
Asian	2 (2.5)
Other	3 (3.8)
ECOG status, n (%)	
0	29 (36.7)
1	50 (63.3)
Previous lines of therapy, n (%)	
0	6 (7.6)
1	24 (30.4)
≥2	49 (62.0)
Previous IO treatment	13 (16.5)

- 79 patients received treatment in study parts 1-3 before data cutoff (April 9, 2021)
  - Dose escalation: 27 (34.2%) patients
  - Dose expansion: 52 (65.8%) patients
    - Part 2A, I/O experienced: 10 patients
    - Part 2B, IO naïve: 33 patients
    - Part 3, IO naïve, MSI-H or dMMR tumors: 9 patients
- 49 (62.0%) patients had ≥2 lines of prior therapy
- 13 (16.5%) patients had previous IO treatment

IO = immuno-oncology.

INCB86550: NUMBER OF PATIENTS PER DOSE LEVEL

Dose Level, n (%)	Total (N=79)
100 mg QD	6 (7.6)
200 mg QD	3 (3.8)
200 mg BID	24 (30.4)
400 mg QD	4 (5.1)
400 mg BID	32 (40.5)
800 mg QD	1 (1.3)
800 mg BID	6 (7.6)
400 mg BID 1 week; 100 mg QD 1 week; repeat	1 (1.3)
400 mg BID 2 weeks; 100 mg QD 2 weeks; repeat	2 (2.5)

Tumor types in the study included adrenal, anal, anal canal, angiosarcoma, basal cell, breast, cancer of unknown primary, carcinoma of parotid gland, castrate-resistant prostate cancer, cervical, cholangiocarcinoma, colorectal, endometrial, esophageal, fallopian, gall bladder, gastric, gastroesophageal junction, glioblastoma, hepatocellular, melanoma, mesothelioma, myoepithelial, neuroendocrine, ovarian, pancreatic, penile, pleomorphic sarcoma, prostate, prostate adenocarcinoma with neuroendocrine differentiation, renal cell, salivary gland, sarcoma, small cell lung cancer, squamous cell carcinoma of the head and neck, urothelial, vaginal, and well-differentiated liposarcoma

INCB86550: TREATMENT-RELATED TEAEs (in ≥5% of patients)

Treatment-Related TEAEs, n (%)	Any Related (N=79)	Grade ≥3 Related (N=79)	Serious Related (N=79)
Any	46 (58.2)	10 (12.7)	6 (7.6)
Most common†			
Nausea	13 (16.5)	0	0
Fatigue	8 (10.1)	1 (1.3)	0
Decreased appetite	7 (8.9)	0	0
Vomiting	7 (8.9)	1 (1.3)	1 (1.3)
Diarrhea	6 (7.6)	0	0
Lipase increased	6 (7.6)	0	0
Headache	5 (6.3)	0	0
Peripheral sensory neuropathy	5 (6.3)	2 (2.5)	1 (1.3)
Pruritus	5 (6.3)	1 (1.3)	0
Rash	5 (6.3)	1 (1.3)	0

- TEAEs consistent with mAbs, with the exception of the rate of peripheral neuropathy at higher doses

TEAE, treatment-emergent adverse event.
† Occurring in ≥5% of patients.

INCB86550: IMMUNE-RELATED TEAEs AND MANAGEMENT

- Immune-related TEAEs (irTEAEs) occurred in 15 patients (19.0%)
  - 2/24 patients at 200mg BID had irTEAEs (Grade 2 peripheral neuropathy, Grade 2 pruritis)
  - 13/40 patients at ≥400mg BID had irTEAEs
- 10 patients (12.7%) had irTEAEs of peripheral neuropathy; all were Grade ≤3
  - All Grade 2 or 3 TEAEs of peripheral neuropathy resolved or improved

			Management§ (N=79)		
Immune-Related TEAEs, n (%)	**Any Related (N=79)**	**Grade ≥3 Related (N=79)**	**Dose Interruption / Reduction**	**Discontinuation**	**Corticosteroid Treatment**
Any	15 (19.0)	7 (8.9)	6 (7.6)	3 (3.8)	6 (7.6)
Most common*					
Peripheral neuropathy†	10 (12.7)	4 (5.1)	3 (3.8)	2 (2.5)	4 (5.1)
Pruritus	3 (3.8)	1 (1.3)	1 (1.3)	0	2 (2.5)
Rash‡	3 (3.8)	1 (1.3)	1 (1.3)	0	2 (2.5)

* Occurring in >1 patient.
† TEAEs of peripheral neuropathy included peripheral sensory neuropathy (n=5), immune-mediated neuropathy (n=2), peripheral motor neuropathy (n=2), Bell's palsy (n=1), paresthesia (n=1), peripheral neuropathy (n=1), polyneuropathy (n=1), and sensory loss (n=1).
‡ TEAEs of rash included rash (n=1), rash maculopapular (n=1), and rash pruritic (n=1).
§ Patients may have been counted in multiple management categories.

INCB86550: EFFICACY RESULTS

Best Overall Response,*† n	Efficacy-Evaluable Population‡ (n=68)	Part 2B IO Treatment-Naive Expansion 400 mg BID (n=14)	Part 3 MSI-H/dMMR IO Treatment-Naive Expansion 400 mg BID (n=5)
CR+PR§	8	3	3
CR	1	1	0
PR	7	2	3
DCR (CR+PR+SD ≥12 weeks)	13	5	3
SD (≥12 weeks)	5	2	0
PD	39	7	2
Not evaluable¶ / Not assessed‖	16	2	0

First oral PD-L1 inhibitor to demonstrate clinical responses

*Assessed by RECIST v1.1 or RANO;. † 1 patient with GBM was assessed by RANO and had best overall response of progressive disease. ‡ The efficacy-evaluable population included all solid tumor participants enrolled in the study who received at least 1 dose of INCB086550, completed a baseline scan, and met at least 1 of the following criteria: ≥1 postbaseline scan, participant had been on the study for a minimum of 63 days of follow-up, or participant had discontinued from treatment. § No objective responses were observed below 400 mg BID. ¶ "Not evaluable" indicates participants in the efficacy-evaluable population that did not have valid postbaseline overall response assessments by RECIST or RANO. ‖ "Not assessed" indicates participants in the efficacy-evaluable population that did not have any postbaseline overall response assessments by RECIST or RANO.

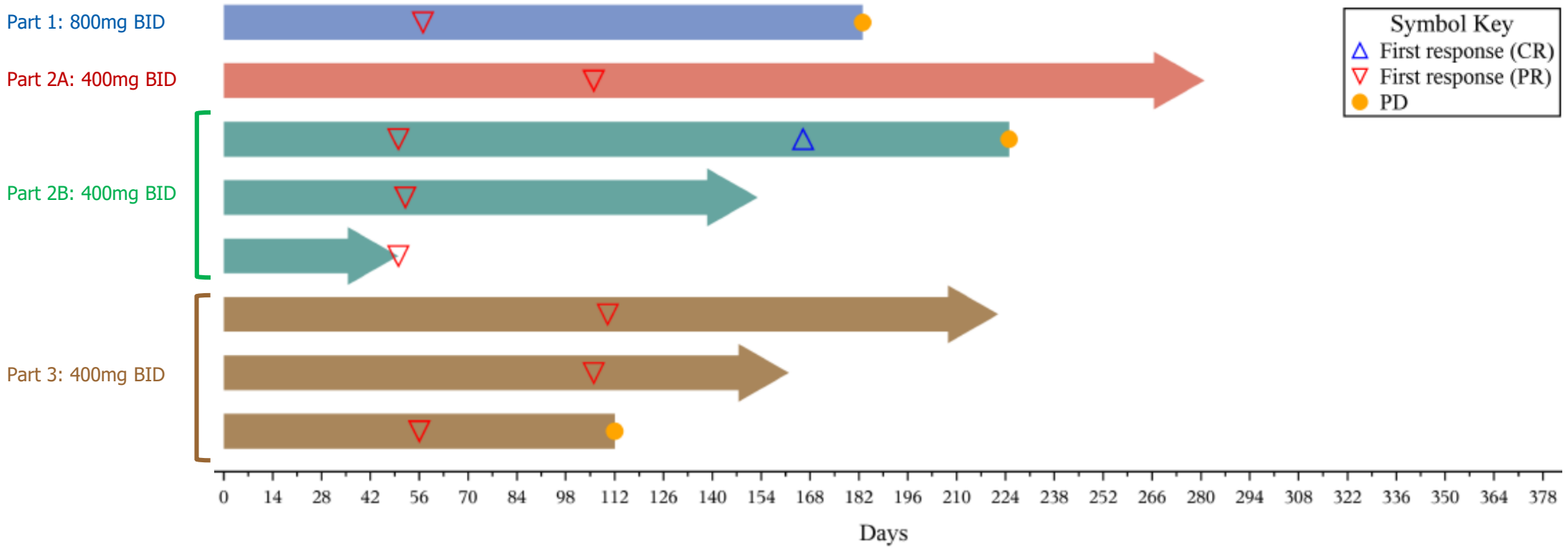
INCB86550: RESPONSE BY HISTOLOGY AND MSI STATUS

Tumor Type	IO Treatment -Naive	Dose	Best Overall Response	Duration of Response (Months)
Squamous cell anal cancer	Yes	800 mg BID	PR	4.17
Squamous cell anal cancer	Yes	400 mg BID	CR	5.78
MSI-H colon adenocarcinoma	No	400 mg BID	PR	5.78+
Clear cell ovarian cancer	Yes	400 mg BID	PR	3.35+
MSI-H colon adenocarcinoma	Yes	400 mg BID	PR	3.71+
dMMR gastric cancer	Yes	400 mg BID	PR	1.87+
MSI-H neuroendocrine colon cancer	Yes	400 mg BID	PR	1.87
Squamous cell vaginal cancer	Yes	400 mg BID	PR	0.03+

+ Ongoing response

INCB86550: TIME TO FIRST RESPONSE AND DURATION OF RESPONSE

TREATMENT



Data on file.

INCB86550: SUMMARY OF RESULTS & DOSE OPTIMIZATION

- Efficacy seen in tumor types known to be responsive to anti-PD-(L)1 mAb therapy
- Immune-related AEs observed in phase 1 are consistent with those seen with mAb immune checkpoint inhibitors, with the exception of an increased rate of peripheral neuropathy
  - All Grade 2 or 3 TEAEs of peripheral neuropathy resolved or improved

Dose schedule optimization underway

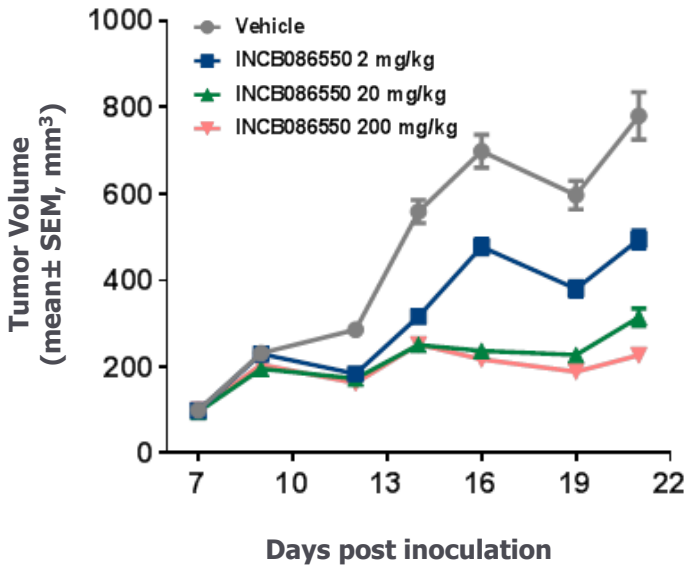
- Optimization of dosing schedule to maximize response and minimize toxicity
  - 400 mg BID x 1 week, Off x 1 week
  - 200 mg BID (MSI-h/dMMR patients only)

THREE ORAL PD-L1 INHIBITORS IN THE CLINIC

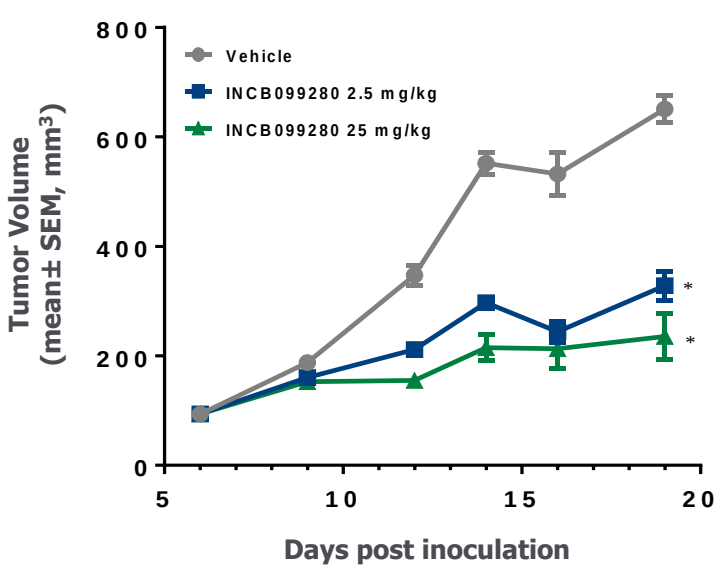
	INCB86550	INCB99280	INCB99318
Similarities	➢ Similar mechanism of action resulting in dimerization and internalization of PD-L1 ➢ Potently and selectively binds the target ➢ Preclinical profile ➢ Clinical PD expected to be achievable based on dose projections and early PK		
Differences	➢ Structurally distinct compound (‘318) ➢ Different PK profile in the clinic		

SIMILAR ANTI-TUMOR ACTIVITY OF ORAL PD-L1 SMALL MOLECULES IN HUMANIZED MOUSE MODEL

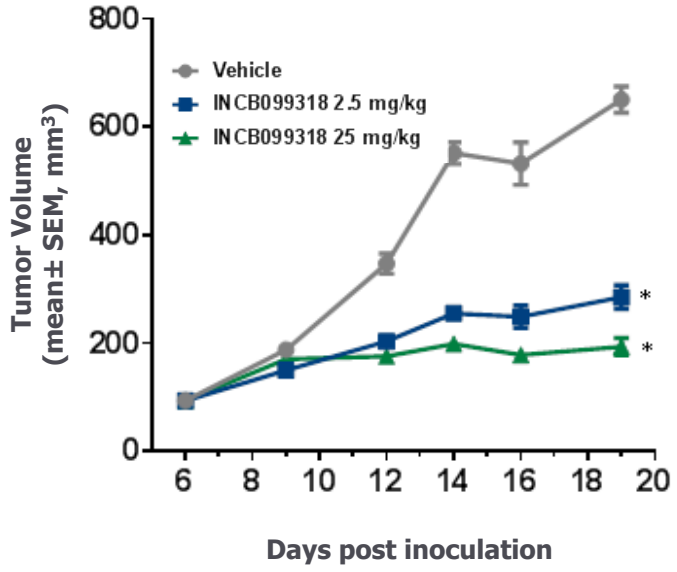
INCB86550



INCB99280



INCB99318



Early clinical data from '280 and '318

- Tumor shrinkage observed
- Thus far, no evidence of peripheral neuropathy

MC38 human PD-L1 mouse model

CURRENT STATUS AND NEXT STEPS

INCB86550

Dosing schedule optimization

Phase 2:

- CPI-naïve with selected solid tumors

INCB99280

Dose escalation:

- Select solid tumors / I/O-naïve
- MSI-H or dMMR tumors / I/O-naïve
- Progression of any solid tumor treated w/approved anti-PD-1

INCB99318

Dose escalation:

- Select solid tumors / I/O-naïve
- MSI-H or dMMR tumors / I/O-naïve
- Progression of any solid tumor treated w/approved anti-PD-1

2022 planned updates:

- Data readout
- Selection of lead program(s)
- Indications for development based on clinical profile

CPI = checkpoint inhibitor

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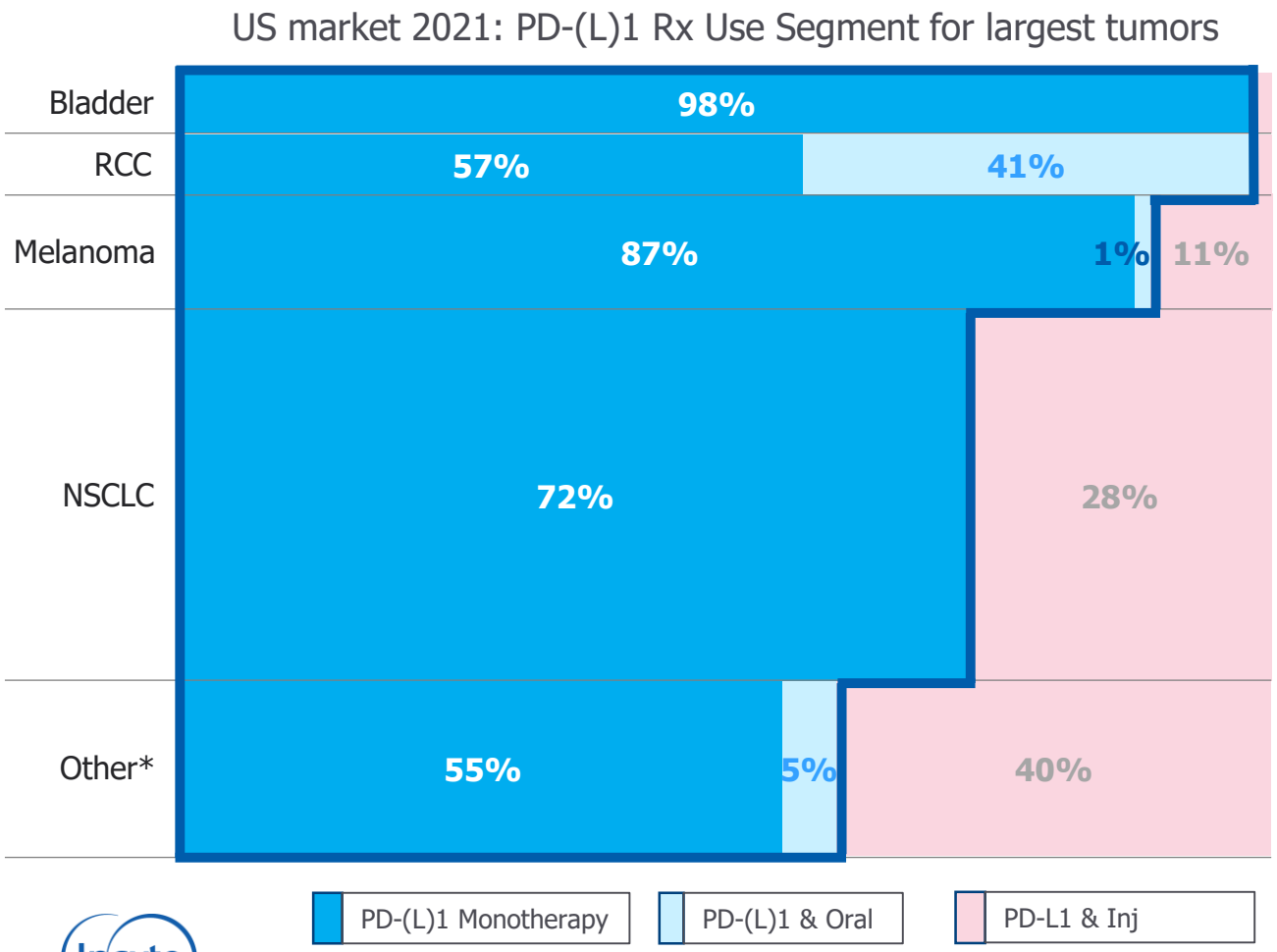
US PD-(L)1 MARKET MOSTLY COMPRISED OF MONOTHERAPY AND PD-(L)1 ORAL COMBOS



~80% of current US PD-(L)1 market is amenable to an oral agent targeting the PD-(L)1 axis

* Includes SCCHN, HCC, Gastric, CRC, Endometrial, Breast, CSCC, SCLC and other Source: PrecisionIQ (Sep 2020 – Aug 2021)

DIFFERENTIATION OF AN ORAL PD-L1

Potential Benefit	US	Ex-US	I/O Combo	Targeted Combo	Monotherapy
Ease of dosing / no need for in-office visit	✓	✓		✓	✓
No administration cost for IV infusion		✓		✓	✓
Oral-oral combinations	✓	✓		✓	
Rapid titration for better management of irAEs	✓	✓	✓	✓	✓

Potential for increased tumor penetration ➢ Increased efficacy