Data Highlights from Incyte's Adenosine Program from AACR 2021

APRIL 12, 2021

FORWARD-LOOKING STATEMENTS

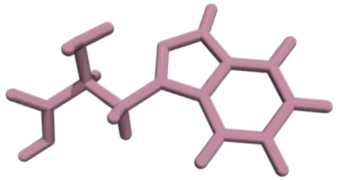
Except for the historical information set forth herein, the matters set forth in this presentation contain predictions, estimates and other forward-looking statements, including without limitation statements regarding: our expectations regarding our multiple opportunities for next generation immune-oncology therapies and the efficacy of our drug candidates and potential combination therapies; our development strategy for our immune-oncology drug candidates and potential combination therapies; and the expected timing of results from, and start dates for clinical trials of, our drug candidates, including INCB106385, INCA00186 and combination trials involving those drug candidates. These forward-looking statements are based on our current expectations and are 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; determinations made by the FDA; the ability to identify patients for our potential targeted therapies; the acceptance of our products and the products of our collaboration partners in the marketplace; risks associated with market competition; risks associated with manufacturing; and other risks detailed from time to time in our reports filed with the U.S. Securities and Exchange Commission, including our annual report on Form 10-K for the year ended December 31, 2021. We disclaim any intent or obligation to update these forward-looking statements.

INCYTE'S KEY IMMUNO-ONCOLOGY PIPELINE

Bi-specific Antibodies

PD-L1xCD137
(MCLA-145)[1]

Small Molecules

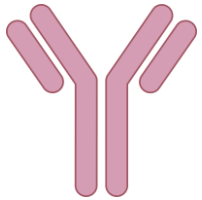


A_{2A}/A_{2B}
(INCB106385)

PD-L1
(INCB86550)

AXL/MER
(INCB81776)

Monoclonal Antibodies



PD-1
(retifanlimab)

CD73
(INCA00186)

LAG-3
(INCAGN2385)[2]

TIM-3
(INCAGN2390)[2]

1. MCLA-145 development in collaboration with Merus
2. INCAGN2385 and INCAGN2390 in discovery collaboration with Agenus

INCYTE'S NEXT GENERATION IO THERAPIES

~15% of cancer patients benefit from PD-(L)1 therapies

PD-L1 (INCB86550)

PD-1 (retifanlimab)

~85% of cancer patients DO NOT benefit from PD-(L)1 therapies

T-cell Exhaustion/Redundant Immune Checkpoints

PD-L1xCD137 (MCLA-145)[1]

LAG-3 (INCAGN2385)[2]

TIM-3 (INCAGN2390)[2]

Immunosuppressive Cells

AXL/MER (INCB81776)

Immunosuppressive Metabolites

A_{2A}/A_{2B} (INCB106385)

CD73 (INCA00186)

Haslam A. and Prasad V. JAMA Netw Open, 2019,; 2(5): 3192535

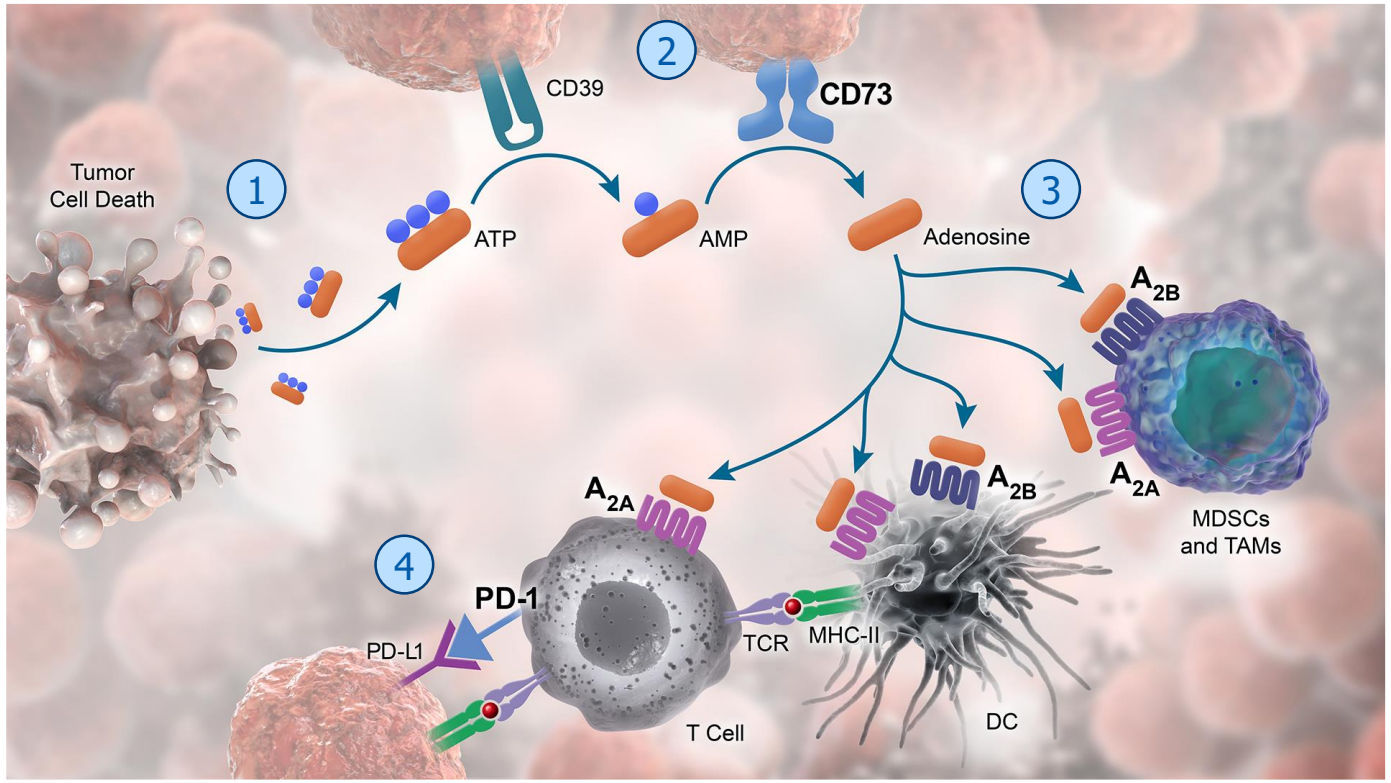
1. MCLA-145 development in collaboration with Merus
2. INCAGN2385 and INCAGN2390 in discovery collaboration with Agenus

Targeting Multiple Nodes of the Adenosine Pathway

A_{2A}/A_{2B} and CD73

ADENOSINE SIGNALING IS A KEY IMMUNOSUPPRESSIVE CHECKPOINT IN THE TUMOR MICROENVIRONMENT

1. Cell destruction results in release of high levels of ATP, triggering inflammation
2. CD39 and CD73 catalyze the conversion of ATP into adenosine
3. Adenosine signalling via A_{2A} and A_{2B} receptors within the TME results in immunosuppression
4. High levels of adenosine in the TME may limit effectiveness of PD-1/PD-L1 inhibitors



AMP, adenosine monophosphate; ATP, adenosine triphosphate; DC, dendritic cell; MDSC, myeloid-derived suppressor cells; MHC-II, major histocompatibility class 2; TAM, tumor-associated macrophage; TCR, T-cell receptor; TME, tumor microenvironment.

INCYTE'S COMBINATION APPROACH TO MAXIMIZE ADENOSINE PATHWAY INHIBITION

INCA00186 (anti-CD73 mAb)

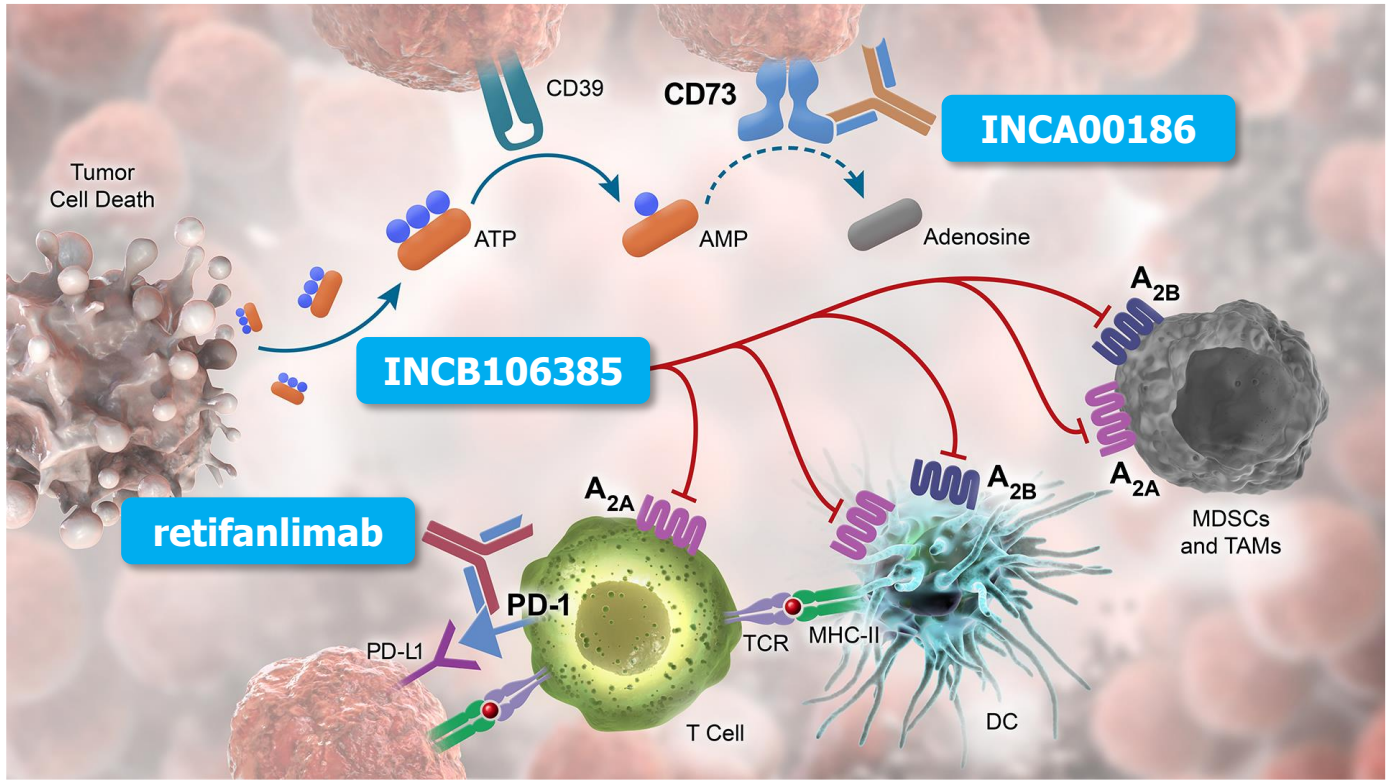
- Antagonizes CD73 function preventing conversion of AMP to adenosine

INCB106385 (A_{2A}/A_{2B} antagonist)

- Blocks adenosine signalling via A_{2A} and A_{2B} receptors

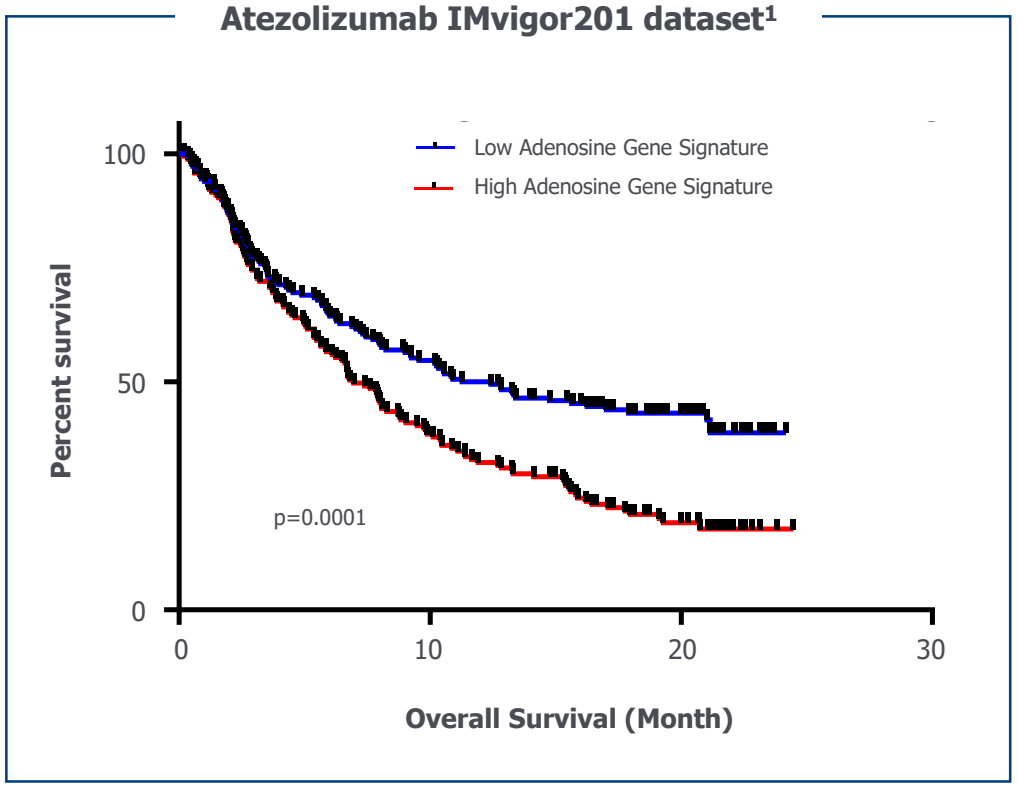
retifanlimab (anti-PD-1 mAb)

- Activates exhausted tumor-infiltrating lymphomocytes (TILs) by inhibiting PD-1/PD-L1



INCYTE'S ADENOSINE GENE SIGNATURE IN TUMORS IS ASSOCIATED WITH RESISTANCE TO ANTI-PD-(L)1 THERAPY

- Incyte-derived gene signature for adenosine pathway activation identifies patients with poor outcomes to anti-PD-(L)1 therapies
- Internal datasets show similar association in multiple tumors including in:
  - head and neck cancer (~60% with adenosine signature)
  - non-small cell lung cancer (40-60% with adenosine signature)
- Provides an opportunity to select patients of high unmet need and adenosine-mediated immunosuppression

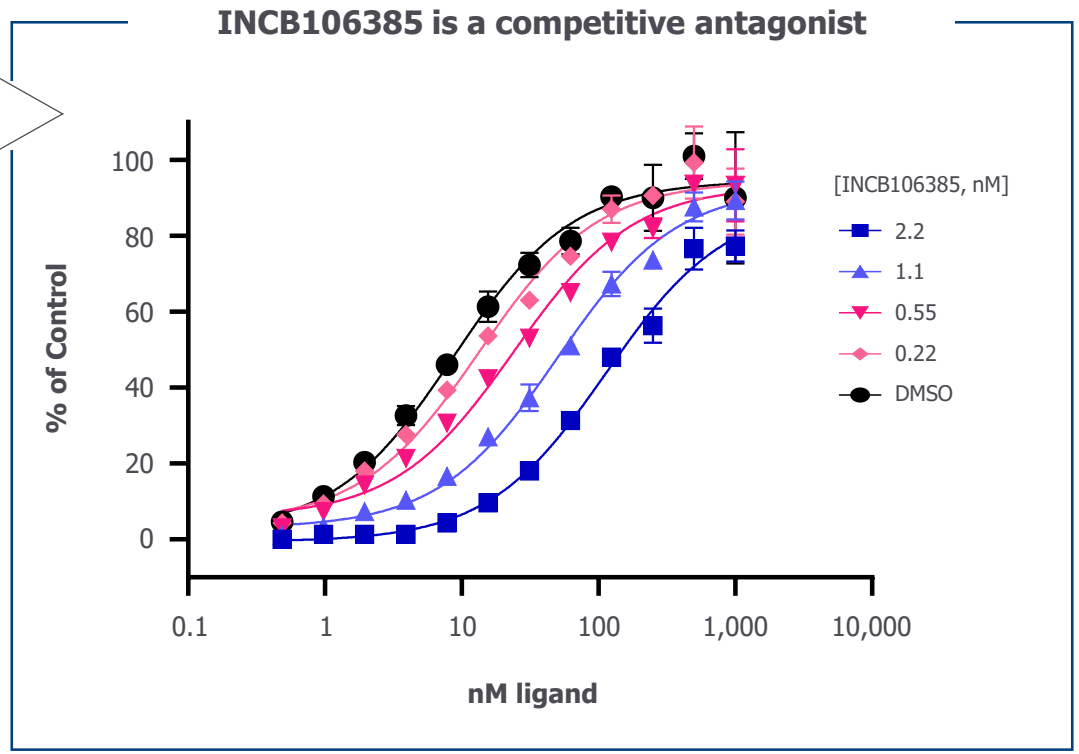


1. Mariathasan S et. al. Nature 2018.

INCB106385 and INCA00186

INCB106385: A POTENT, SELECTIVE A2A/A2B ANTAGONIST

- ✓ A potent and competitive antagonist of A_{2A} and A_{2B} receptors
- ✓ Orally bioavailable with excellent ADME profile
- ✓ Highly accessible to tumor cells
  - ➢ Tumor/plasma ratio >1
- ✓ Minimal brain penetration (<1%)
  - ➢ Significantly limits A1 and A3 targeting and CNS effects



ADME = absorption, distribution, metabolism and excretion; nM = nanomolar.

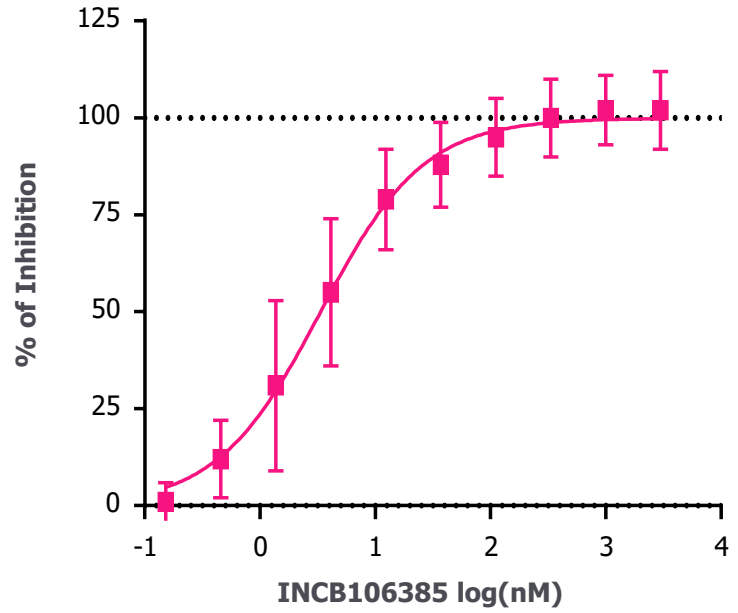
OPTIMAL A2A/A2B RECEPTOR ANTAGONIST

Superior drug-like properties

- Potent inhibition of receptor signaling under physiological conditions
- Dual inhibition of A_{2A} and A_{2B} receptors targets immunosuppressive myeloid cells

Compound	WB pCREB (IC_{50}, nM)	Potent Inhibition of A_{2B}
INCB106385	**4.3**	**YES**
AB928[1]	80	YES
CPI-444[1]	>3000	NO
AZD4635[1]	2600	NO

INCB106385 inhibits pCREB in T cells in human whole blood



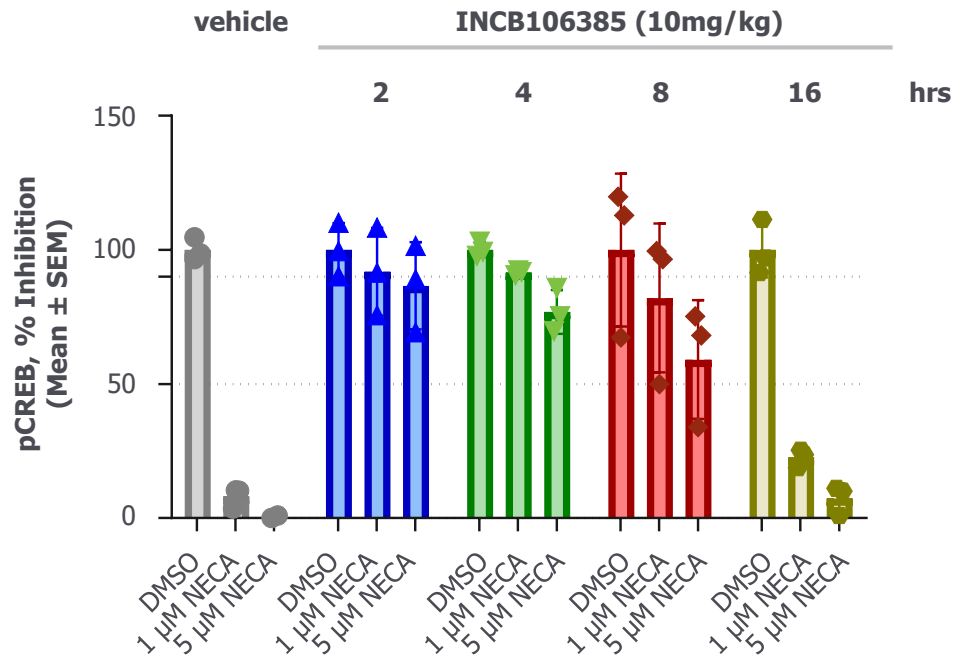
WB assay in presence of 5 µM NECA

1. Arcus Corporation update (2020)

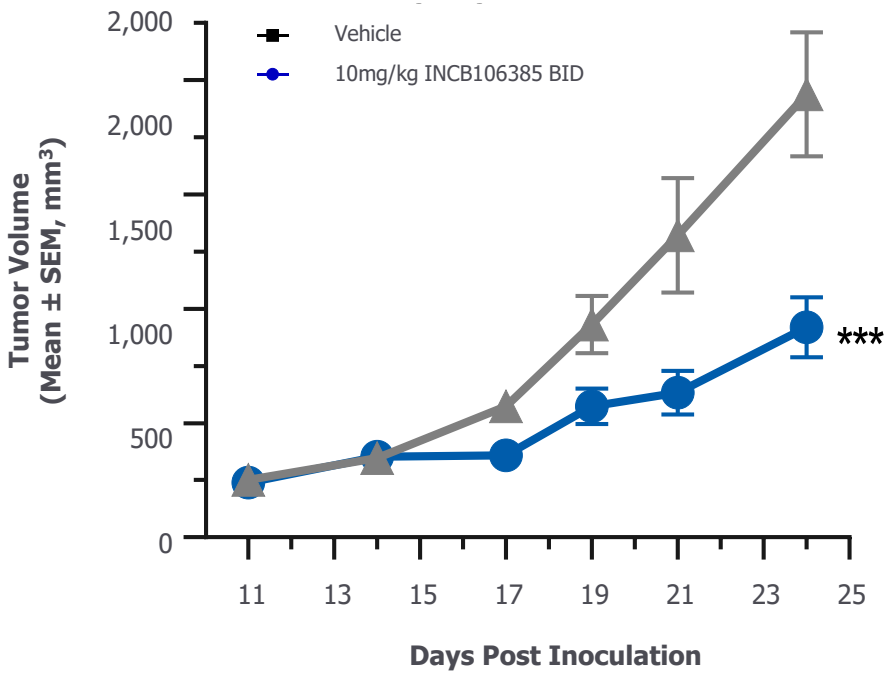
pCREB = phosphorylated cAMP Response Element Binding protein. AMP = adenosine monophosphate.

SIGNIFICANT ON-TARGET MONOTHERAPY ACTIVITY IN VIVO

Achieving maximum coverage in vivo[1]



INCB106385 10mg/kg BID demonstrates monotherapy activity in tumors[2]



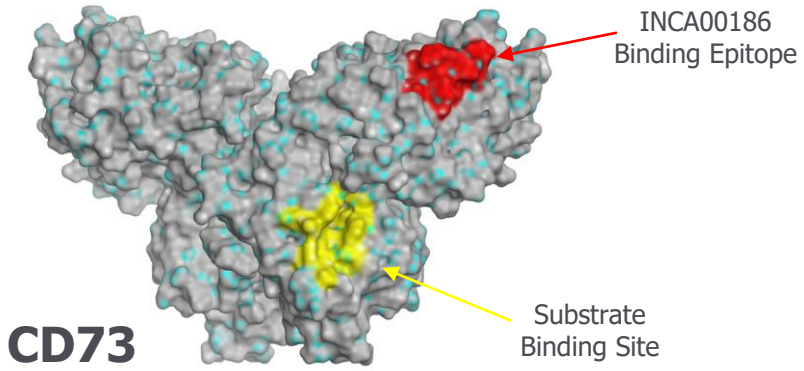
1. Phospho-CREB in CD8+ T cells at indicated time points were measured by flow cytometry after ex vivo NECA treatment.
2. CT26 syngeneic model.

INCA00186: A POTENT, ALLOSTERIC CD73 ANTAGONIST

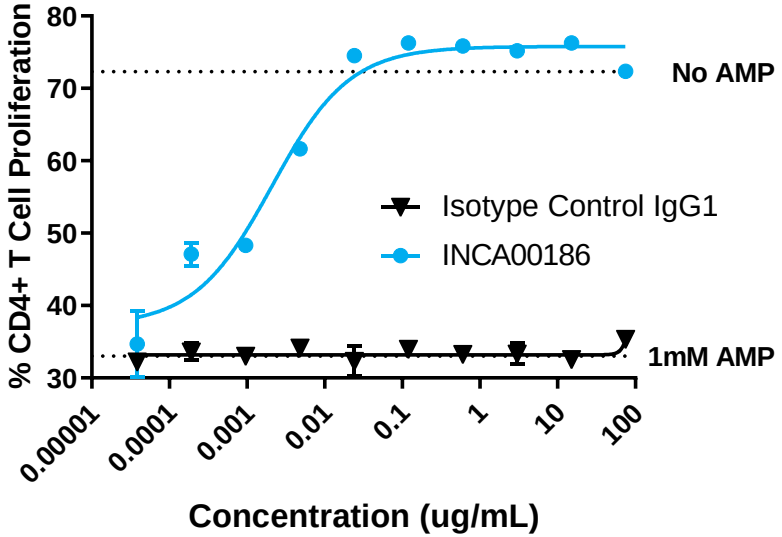
POTENTIAL FOR DIFFERENTIATED PROFILE

- Selective binding to CD73 with picomolar affinity
- Allosteric, non-competitive binding with substrate (AMP)
  - Functions at high AMP concentrations within TME
- Includes downregulation of cell surface CD73 upon binding

INCA00186 is a non-competitive inhibitor[1]



AMP-mediated T cell suppression reversed by INCA00186 treatment[2]

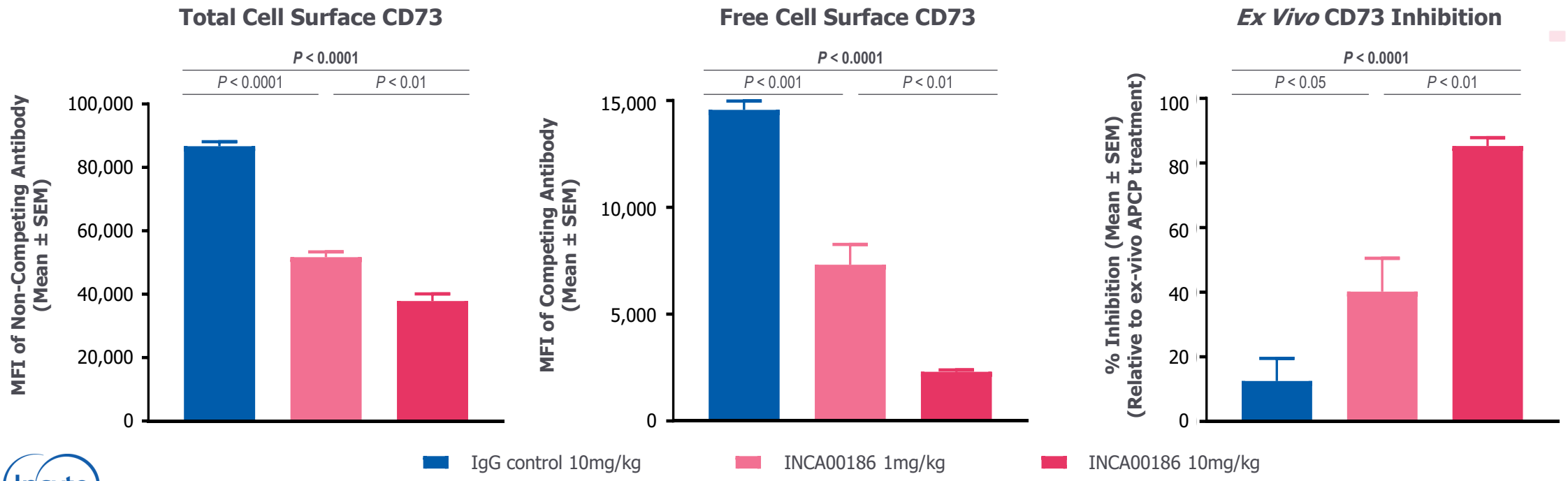


1. Epitope binding site determined by HDX, Hydrogen/deuterium exchange, liquid chromatography mass spectrometry
2. Ex vivo culture from representative human healthy donors.

INCA00186 ANTAGONIZES CD73 FUNCTION IN TUMORS

Treatment with INCA00186 leads to:

- Decreased total cell surface CD73 levels
- High receptor occupancy of remaining cell surface CD73
- Decreased CD73 activity

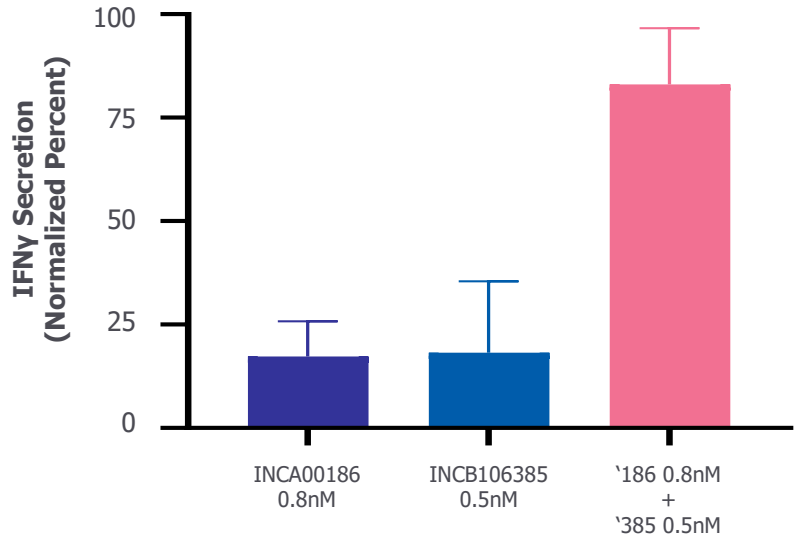


Human A375 melanoma tumor model in CD34+ humanized NSG mice.

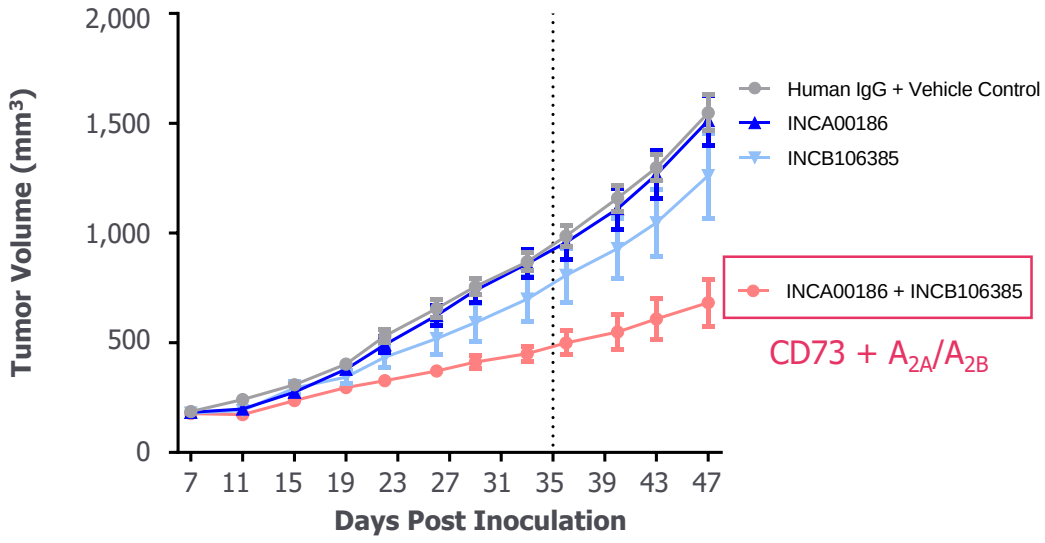
DUAL INHIBITION OF A2A/A2B AND CD73 OVERCOMES HIGH AMP-MEDIATED IMMUNOSUPPRESSION IN THE TME

- Very high adenosine levels (~100μM)[1] and adenosine signaling[2] have been reported in human solid tumors
- INCA00186 synergizes with INCB106385 to restore T-cell activity in high AMP conditions
- INCA00186 in combination with INCB106385 enhances anti-tumor efficacy in a model with high CD73

Dual inhibition has antitumor effect in high AMP conditions as found in TME



INCA00186 + INCB106385 significantly inhibits tumor growth in MDA-MB-231 tumors with high CD73

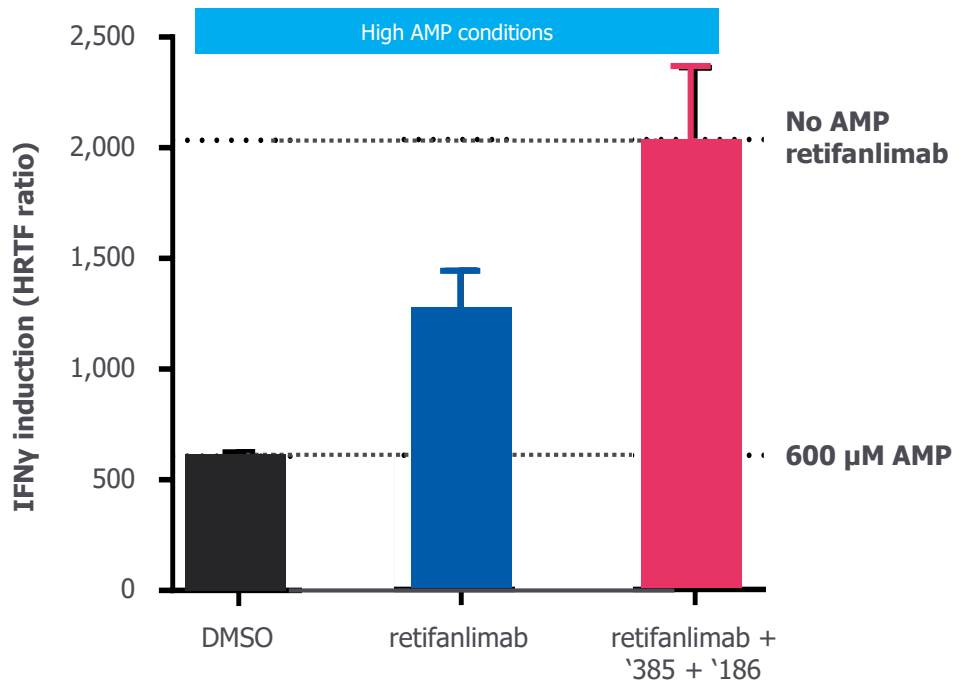


1. Houthuys E et. al. Keystone Symposia 2018
2. Sidders B et. al. Clin. Cancer Res. 2020

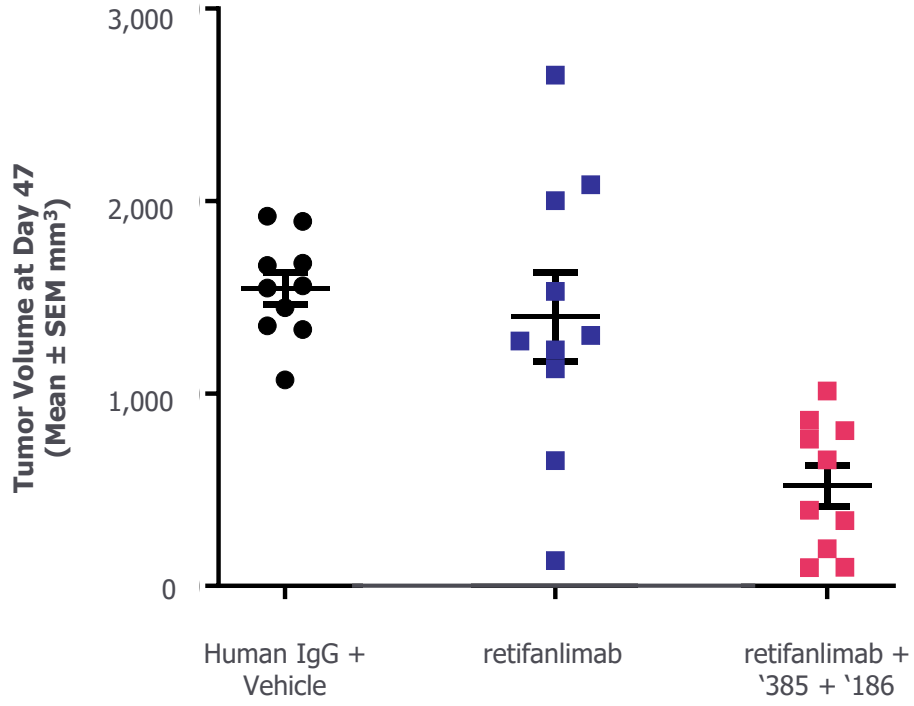
‘186 = INCA00186 (CD73); ‘385 = INCB106385 (A2A/A2B).

TRIPLET THERAPY OVERCOMES ADENOSINE MEDIATED PD-1 RESISTANCE

INCA00186 + INCB106385 rescues anti-PD-1 activity in high AMP conditions



Superior efficacy with triple combination versus others



‘186 = INCA00186 (CD73); ‘385 = INCB106385 (A2A/A2B). Dose of retifanlimab = 10mg/kg IP Q5D.

SUMMARY

- High levels of adenosine in the TME create an immunosuppressive TME
- **INCB106385** is a potential best-in-class A_{2A}/A_{2B} receptor antagonist
- **INCA00186** is a potent, allosteric CD73 antagonist
- Triple combination of **INCB106385**, **INCA00186** and **retifanlimab** (PD-1) overcomes adenosine mediated PD-1 suppression
- Compelling rationale to develop further INCB106385, INCA00186 and retifanlimab as combination immunotherapy for cancer patients

PLANNED STUDIES FOR THE ADENOSINE PROGRAM

Incyte's Proprietary Adenosine Gene Signature and Biomarker Strategy to Guide Development

	Status	Combination
INCB106385 (A_{2A}/A_{2B})	**Dose escalation/ expansion** ➢ Solid tumors ➢ Progressed on prior SOC, including PD-L1	**INCB106385** (A_{2A}/A_{2B}) + **retifanlimab** (PD-1)
		INCA00186 (CD73) + **retifanlimab** (PD-1)
INCA00186 (CD73)	**Dose escalation/ expansion** ➢ Solid tumors ➢ Progressed on prior SOC, including PD-L1	**INCB106385** (A_{2A}/A_{2B}) + **INCA00186** (CD73)
		INCB106385 (A_{2A}/A_{2B}) + **INCA00186** (CD73) + **retifanlimab** (PD-1)

Q&A

ir@incyte.com

investor.incyte.com