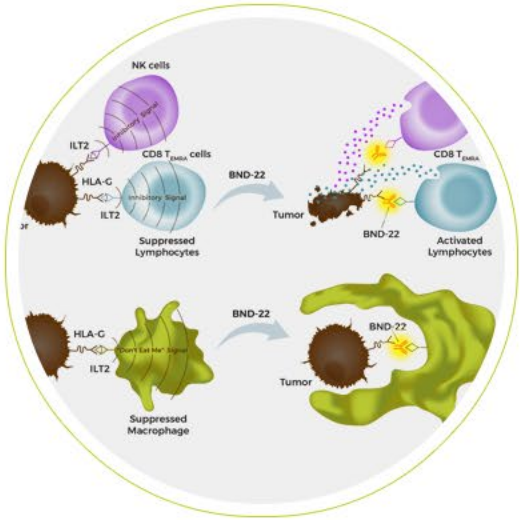
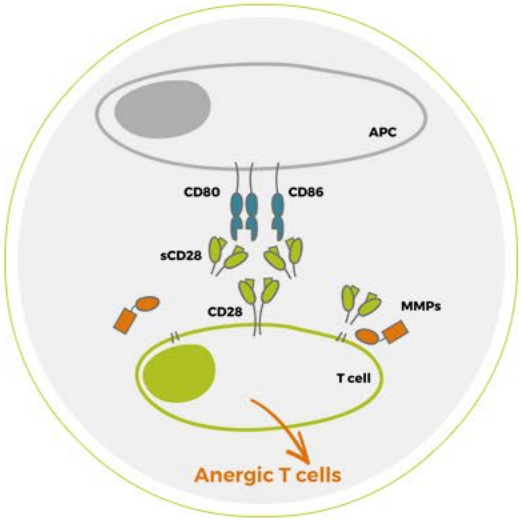
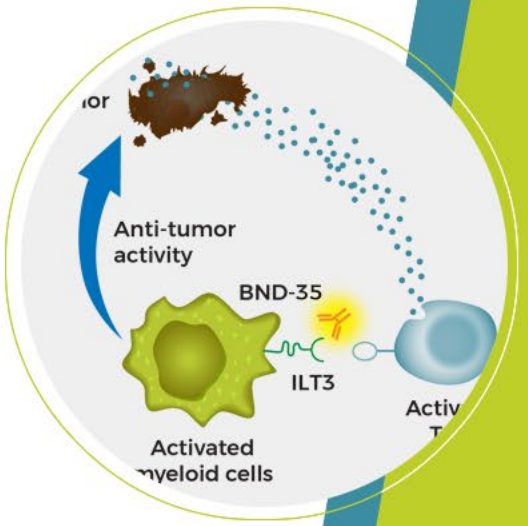
BIOND BIOLOGICS







Corporate Presentation

May 2021

Company Overview

About Us

Biond Biologics is a private clinical-stage biopharmaceutical company, developing novel immunotherapies for cancer and a platform enabling the intracellular delivery of biologics

Our Innovation

- At the forefront of research of immune-evasion mechanisms and its translation into novel cancer therapeutics
- Advanced in-house research capabilities and access to fresh tumor and blood samples from cancer patients
- A Transformative platform enabling delivery of biologics into cells, targeting intracellular “undruggable” proteins

The Team

- Proven track record for developing novel drug candidates from scientific concept to clinical trials
- Highly experienced in fund raising - securing private and public funding
- Successfully partnering with large biopharma companies:
  - July 2015- Merck/cCAM; CM-24 mAb, phase-1 asset (M&A, **$95M upfront**)
  - Jan 2021- Sanofi/Biond; BND-22 mAb, IND ready asset (Licensed, **$125M upfront**)

Financial highlights

FINANCING

$21M
in equity financing since launch

ISRAEL BIOTECH FUND
HAREL Insurance & Finance
SBI JI
Bristol-Myers Squibb

PARTNERSHIP WITH SANOFI

SANOFI

$125M
upfront payment

- In January 2021 Biond signed a licensing agreement with Sanofi for BND-22
- Terms: **$125M upfront payment and over $1B** in development, regulatory, and sales milestones, as well as tiered double digit royalty payments
- Biond is leading the BND-22 phase 1 study for safety and tolerability as a single agent and combination
- Sanofi will continue clinical development and commercialization responsibilities thereafter

Experienced leadership

Tehila Ben Moshe, PhD
CEO

cCAM Biotherapeutics · PROTALIX Biotherapeutics

Ori Shilo, MBA
CFO

RedHill Biopharma · ProSeed Capital Holdings CVA

Yair Sapir, PhD
COO

cCAM Biotherapeutics

Avidor Shulman, PhD
VP R&D

PROTALIX Biotherapeutics

Itay Friedman, MD
VP Clinical Development

Bristol-Myers Squibb

Advisory Boards

Board of Directors

- **Tehila Ben Moshe, PhD**
  CEO, Biond Biologics
- **Ori Shilo, MBA**
  CFO, Biond Biologics
- **Yuval Cabilly, PhD**
  Co-founder and managing Partner, Israel Biotech Fund
- **Ronit Bendori, PhD**
  General Partner, Evergreen
- **Tomer Goldberg**
  VP, Managing Director, Harel Insurance & Finance
- **Jerry Zeldis, MD, PhD**
  Former Chief Medical Officer, Celgene

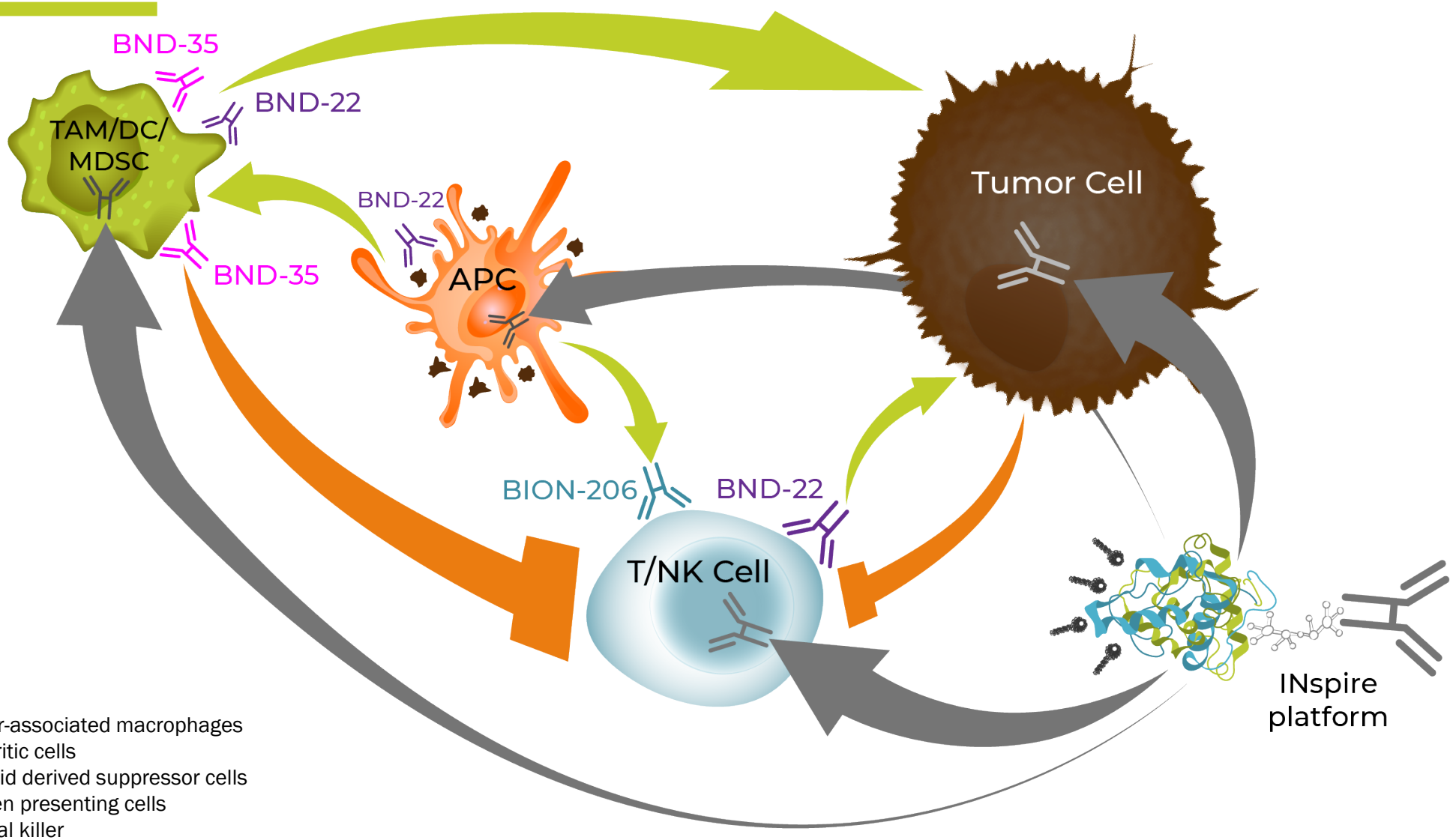
Scientific Advisory Board

- **Alan Korman, PhD**
  Former VP Immuno-Oncology Discovery at BMS
- **Jeffrey Weber, MD, PhD**
  Deputy Director, Perlmutter Cancer Center, NYU Langone Medical Center
- **Pavel Pisa, MD, PhD**
  Former Head of Translational Medicine at Roche
- **Gal Markel, MD, PhD**
  Deputy Director General, Rabin Medical Center

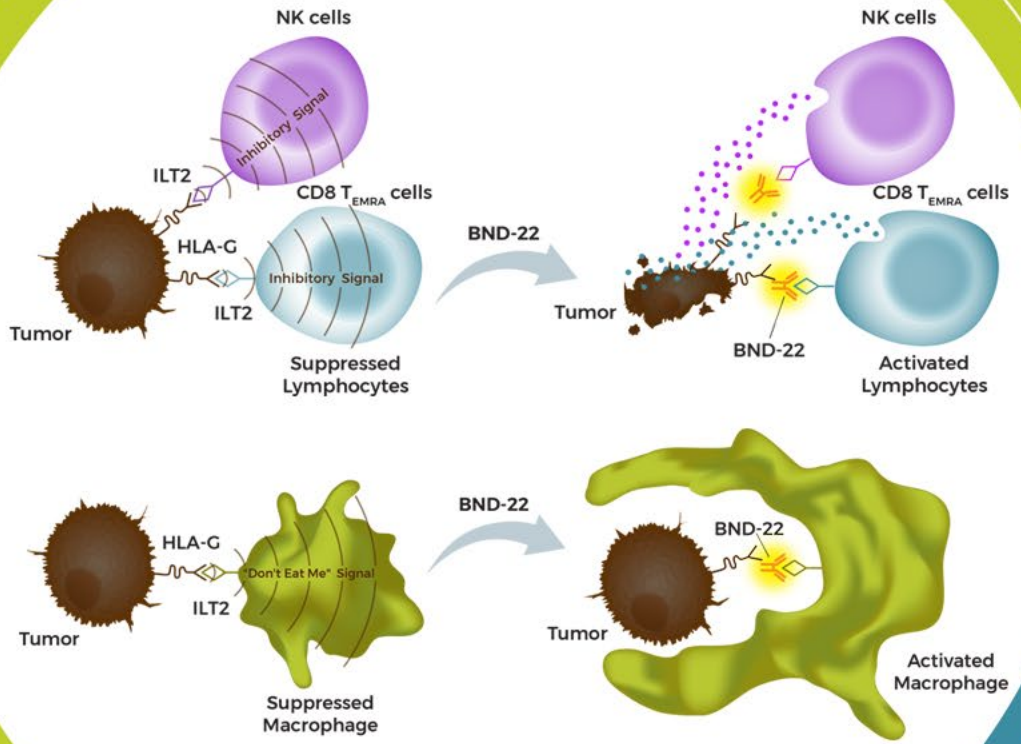
Pipeline of first-in-class drug candidates

Program	Discovery	Pre-Clinical Development	IND enabling Studies	Phase 1
Immuno-Oncology				
BND-22: ILT2 (LILRB1) anti-ILT2 blocking mAb			Phase 1 on-going	
BION-206: Soluble CD28 reduction Overcoming anti-PD-1 resistance by targeting CD28 shedding				
BND-35: ILT3 (LILRB4) anti-ILT3 blocking mAb				
INspire – Intracellular Delivery Platform				
BION-301: Intracellular Oncology Target Biologic agent targeting oncogenic cell signaling regulator				

Immuno-oncology pipeline and intracellular delivery platform



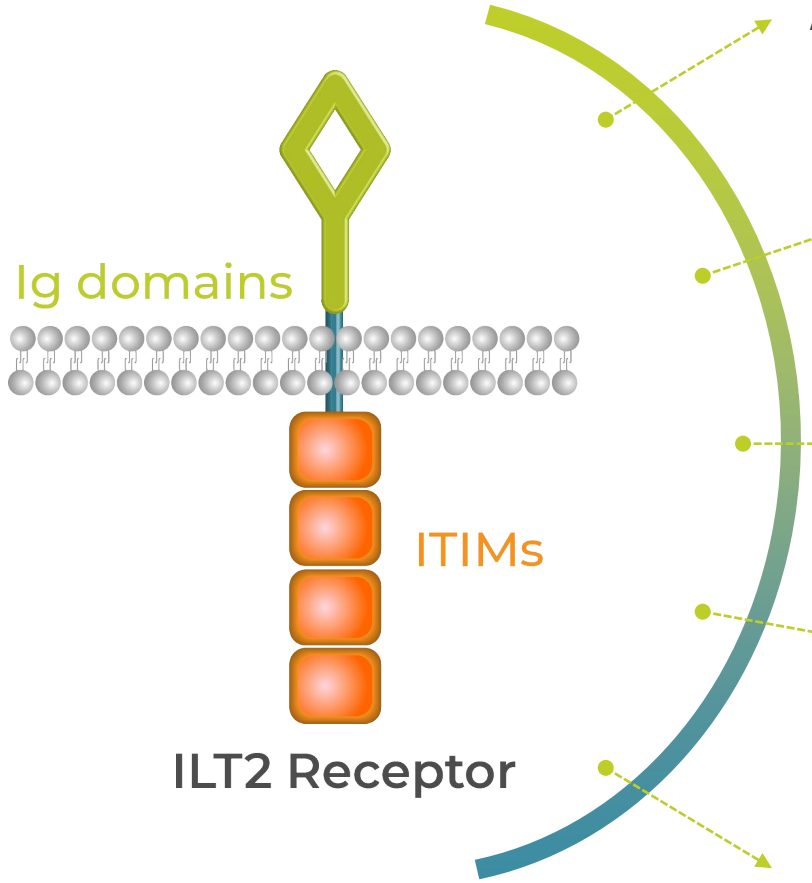
TAM: Tumor-associated macrophages
DC: Dendritic cells
MDSC: Myeloid derived suppressor cells
APC: Antigen presenting cells
NK: Natural killer



BND-22

ILT2 Blocking Antibody

ILT2: a multi-cell inhibitory immune checkpoint, on innate and adaptive immune cells



An inhibitory immunomodulatory receptor (aka LILRB1, CD85j)

Expressed on multiple immune cell types: Lymphoid cells (T cells, NK cells), Myeloid cells (macrophages).

Binds with the highest affinity to human leukocyte antigen (HLA)-G, a known immunosuppressive molecule expressed by multiple tumor types

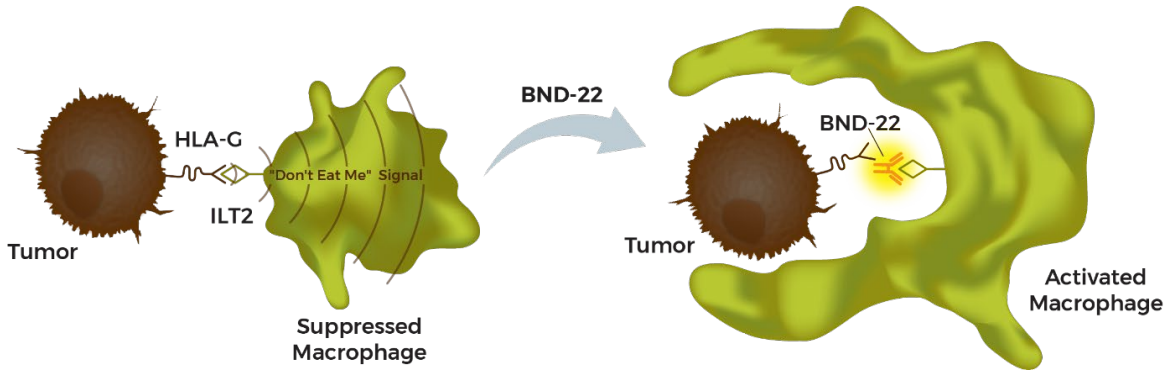
Generates inhibitory signals via ITIM-mediated recruitment of SHP-1, resulting in potent inhibition of immune effector functions when bound by MHC ligands

Extracellular Ig-like domains bind to classical and non-classical MHC-I molecules

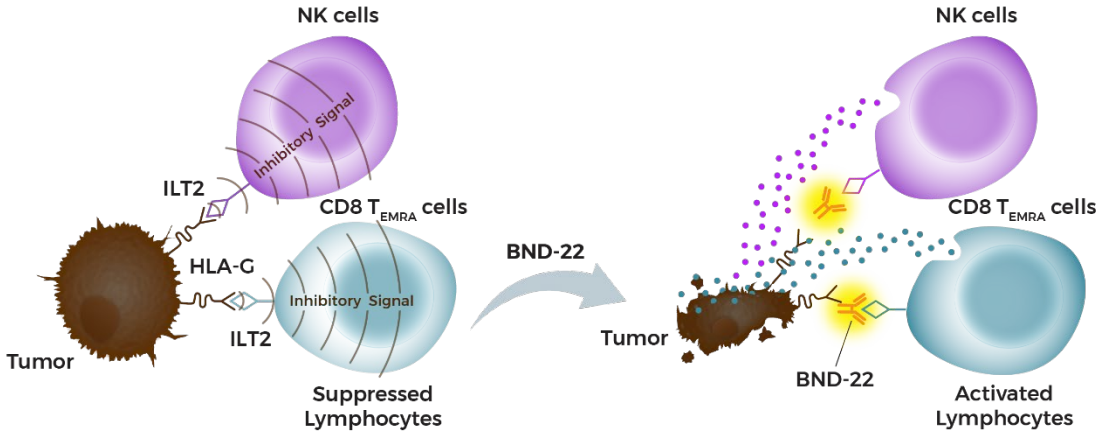
ILT2, Ig-like transcript 2; IgSF, Immunoglobulin superfamily; ITIM, Intracellular tyrosine-based inhibitory motifs; SHP1, Src homology region 2 domain-containing phosphatase 1; MHC, Major histocompatibility complex; HLA, Human leukocyte antigen

BND-22 is an antagonist antibody that blocks ILT2, on innate and adaptive immune cells

BND-22 enhances the ability of macrophages to phagocytose tumor cells



BND-22 enhances anti-tumor activity of T cells and NK cells

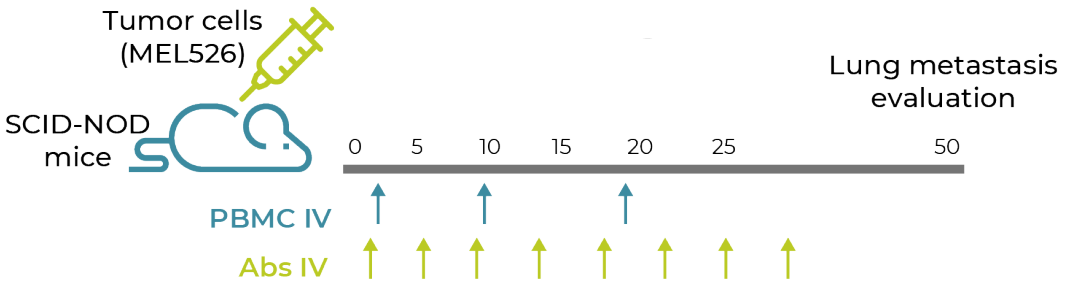


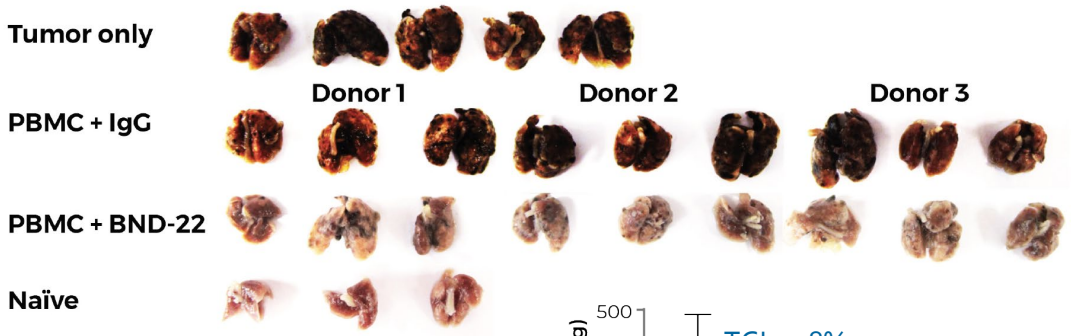
BND-22 is a humanized IgG4 antibody that enhances the anti-tumor activity of immune cells by blocking ILT2 from binding to HLA-G and MHC-I

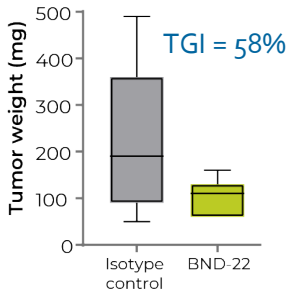
TEMRA, effector memory T cells re-expressing CD45RA

BND-22 enhances anti-tumor activity in-vivo

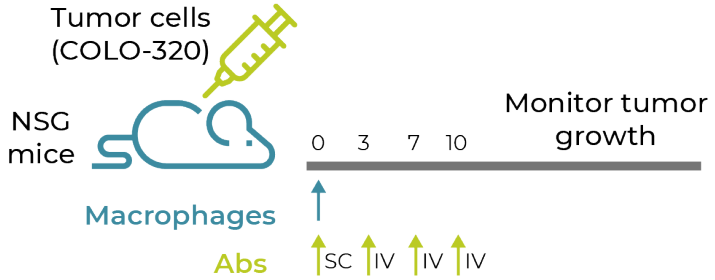
Melanoma lung lesion + PBMC

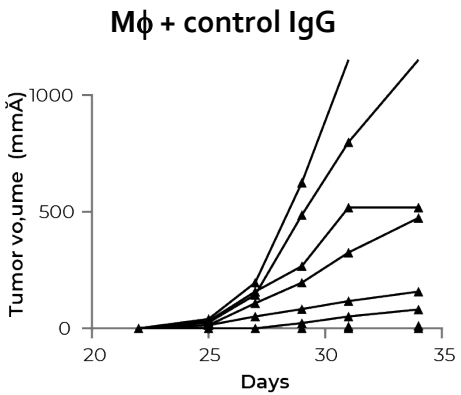


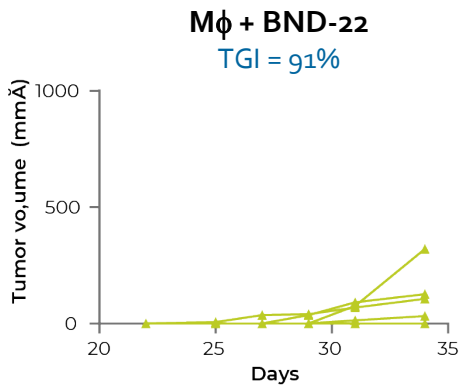




SC colon cancer+ macrophages

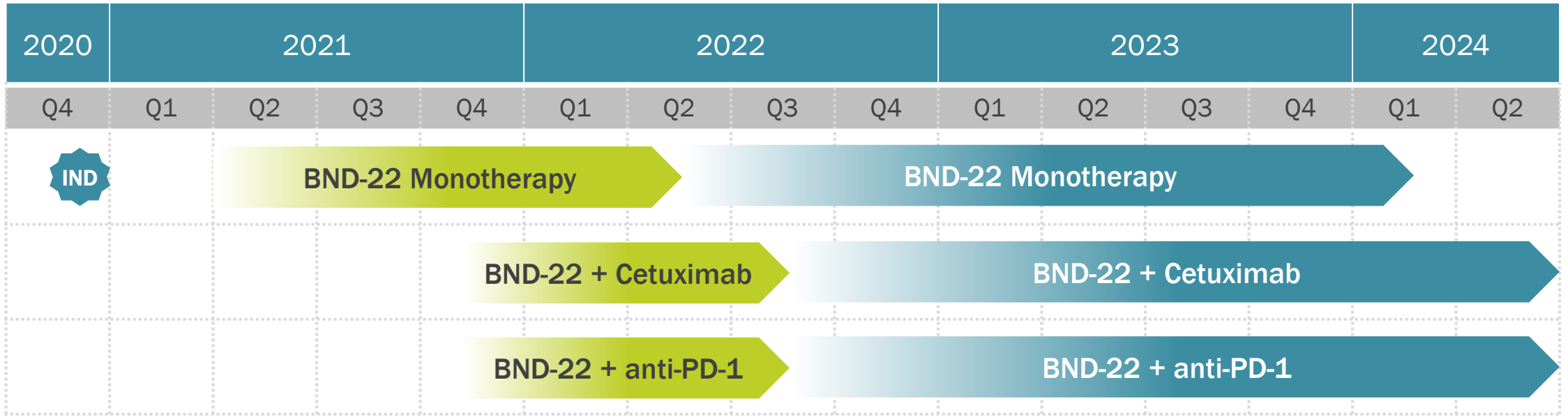






Tumor weight was calculated by subtracting naïve mice lung weight form the lung weight of the different mice. TGI – tumor growth inhibition.
*P<0.05, Student's T test compared to control IgG. N = 5-9 mice for each group.

BND-22 development plan: potential initial efficacy signals by mid-2023



Dose Escalation
8 sites; US and Israel

Dose Expansion
15-20 sites; US, EU and Israel

IND, Investigational New Drug; FPI, First Patient In

BND-22 Target Product Profile

Product Description

- Ig-Like Transcript 2 (ILT2) blocking antibody

Scientific Rationale

- Binding of MHC-I molecules to the ILT2 receptor expressed by macrophages, T-cells and NK cells inhibits anti-tumor effector functions of these cells
- Upregulation of ILT2 ligands, (E.g., HLA-G) occurs in multiple tumor types and is associated with poor prognosis

MOA/Clinical Pharmacology

- BND-22 is an antibody that binds to the ILT2 receptor and blocks its interaction with MHC-I molecules
- Releases ILT2 pathway-mediated inhibition of the innate and adaptive anti-tumor immune response
- Blocking ILT2 activity enhanced macrophage phagocytosis and NK and T cells cytotoxicity activity against cancer cells
- Extensive biomarker/ PD marker strategy in place

Strategic Context / Differentiation

- Novel multi-cell checkpoint inhibitor enhancing the anti-tumor activity of both the innate and adaptive immune systems with the potential to overcome PD-1 resistance
- Preclinical data support combination with cetuximab, and PD-1 blockers

Indication(s) and patient population

- HLA-G-expressing solid tumors
- Patients with unrespectable or metastatic disease, with disease progression following prior systemic therapies

Stage

- Biond Biologics and Sanofi enter into global licensing agreement Q3 2020
- Phase I initiated Q1 2021

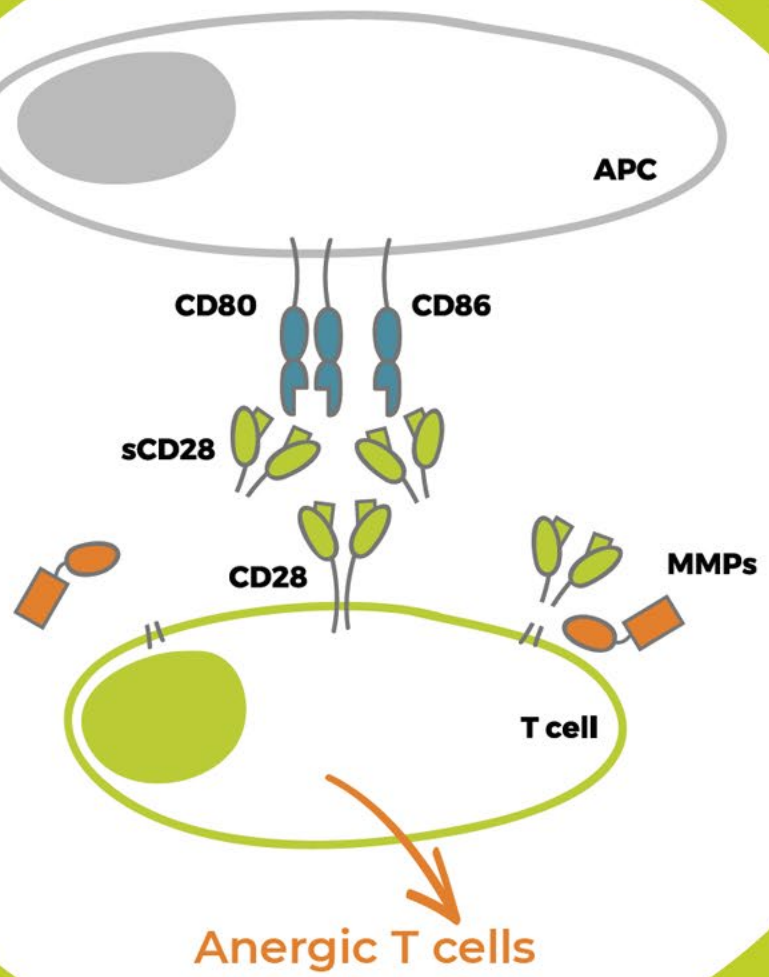
BND-22: Summary (OPTIONAL)

Using In-house research capabilities BND-22 was developed from scientific concept to clinical trials

First-in-human, phase 1 study, Initiated in Q1 2021 (single agent and combination with approved therapeutics)

A humanized IgG4 antibody that enhances the anti-tumor activity of immune cells by blocking ILT2 from binding to HLA-G and MHC-I

BND-22 was licensed to Sanofi with upfront payment of $125M, over $1B in milestones and royalty payments



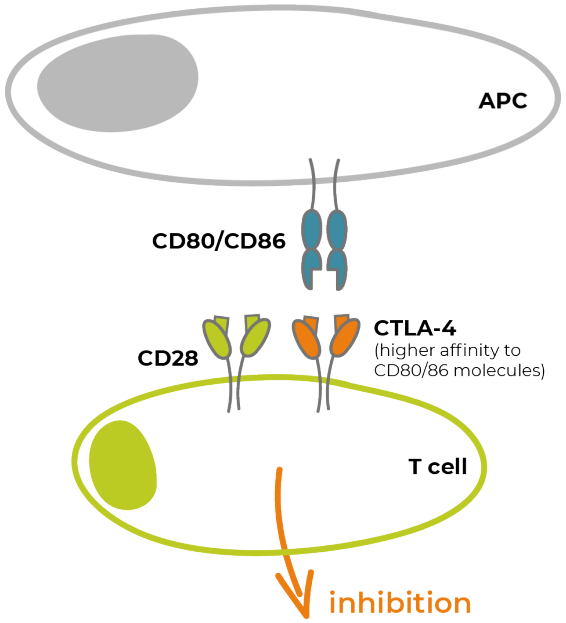
BION-206

Targeting CD28 Shedding

BIOND BIOLOGICS

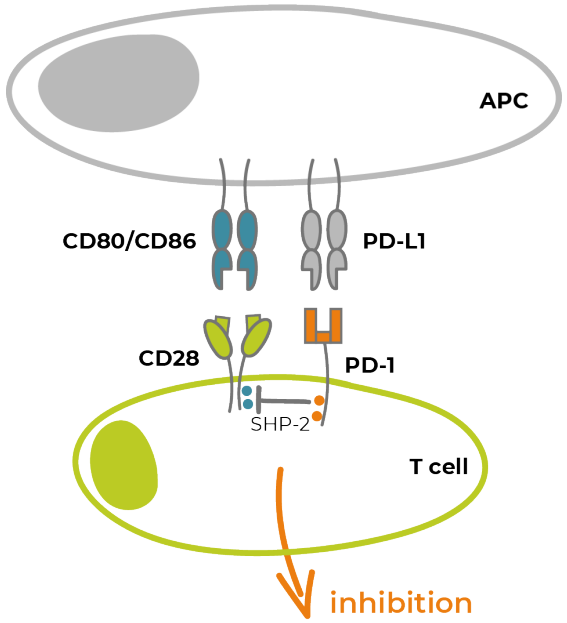
CD28 pathway's central role is validated by current approved immunotherapies

CTLA-4 regulatory pathway: Competition on CD80/86 binding



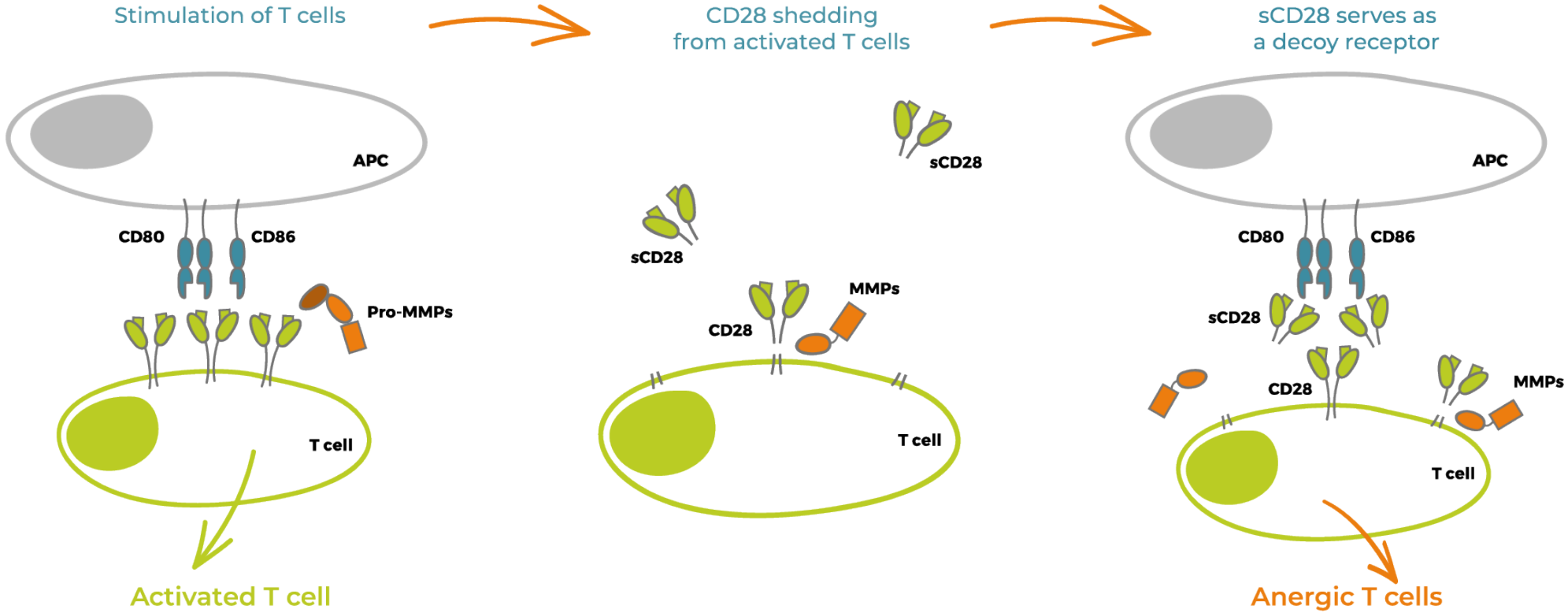
Anti-CTLA4 blocking antibody
Approved in melanoma and RCC

PD-1 regulatory pathway: suppression by dephosphorylation of CD28



Anti-PD1 blocking antibody
Approved in multiple tumor types e.g., melanoma, lung, RCC, H&N, HCC, bladder

Model for the immuno-suppressive effect of CD28 shedding



During the stimulation of T cells, Matrix Metalloproteinases (MMPs) are upregulated and cleave CD28 at its stalk region, releasing a dimeric soluble CD28.

sCD28 acts as a decoy receptor by binding to CD28 cognate ligands, CD80 and CD86 on antigen presenting cells (APC). Activated T cells with lower membranal CD28 density and insufficient B7 mediated signaling become anergic and cannot generate proper immune response against malignant cells.

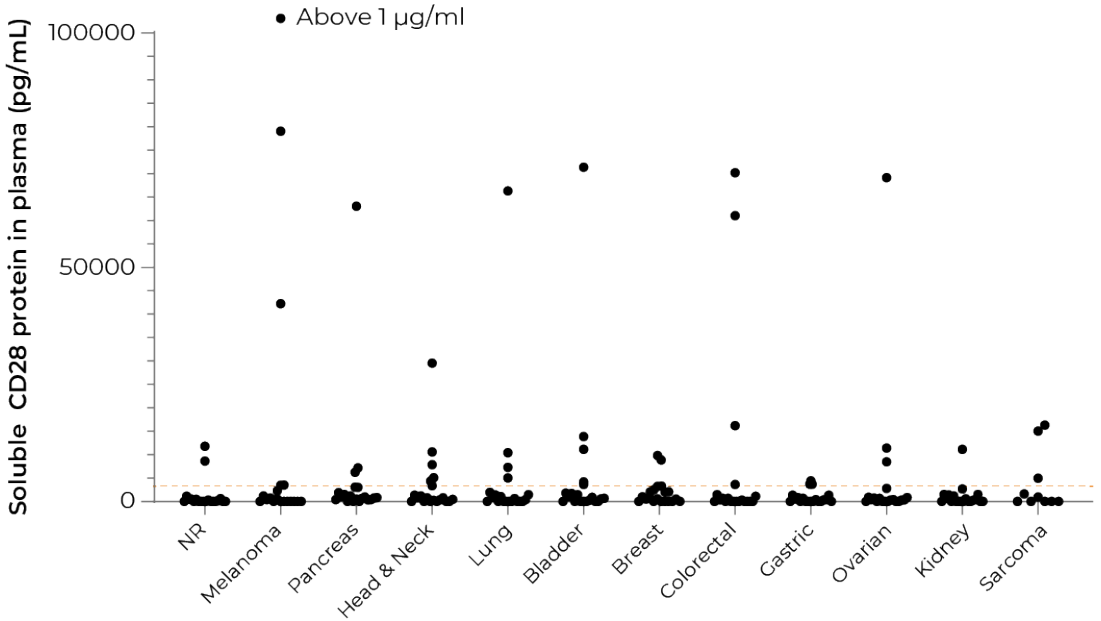
CD28 shedding is a novel immune regulatory pathway in cancer patients

The BION-206 program is based on novel Biond discoveries:

Aberrant levels of **soluble CD28** were found in cancer patients' plasma (WO 2019/175885)

The CD28 receptor was found to be cleaved from activated T cells by cancer related MMP's (PCT/IL2020/051243)

Soluble CD28 promotes an immuno-suppressive environment

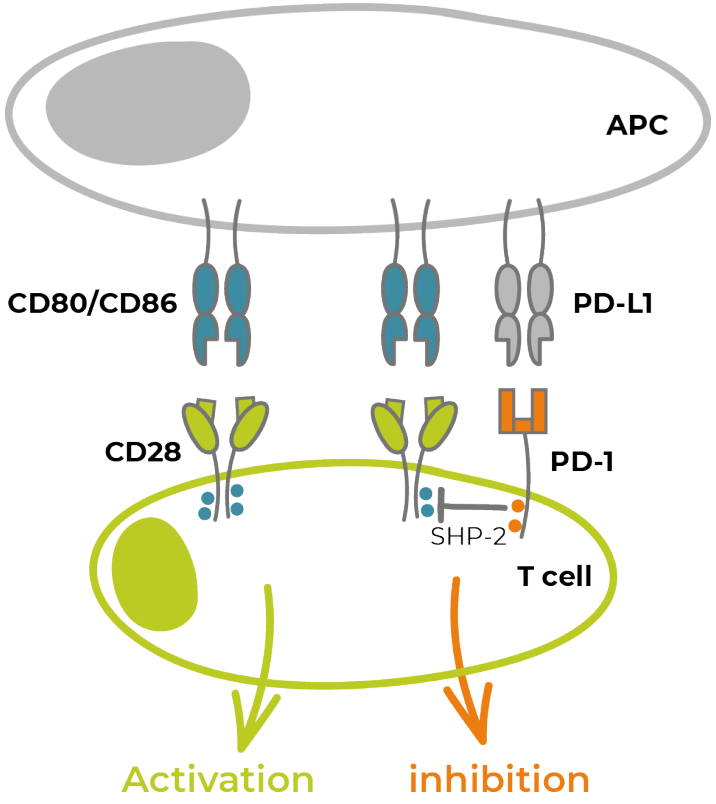


- 11 tumor types were surveyed
- 15% of samples of studied tumors plasma contain a higher level of soluble CD28 compared to plasma from healthy subjects

MMP, matrix metalloproteinases

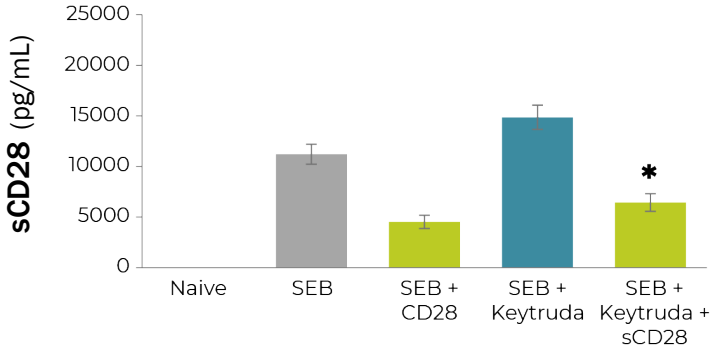
Soluble CD28 attenuates anti-PD-1 effect in cancer

PD-1 therapy is uniquely sensitive to CD28-B7 axis activation (T-cell – APCs)



Kamphorst AO, Science, 2017; Hui E, Science, 2017

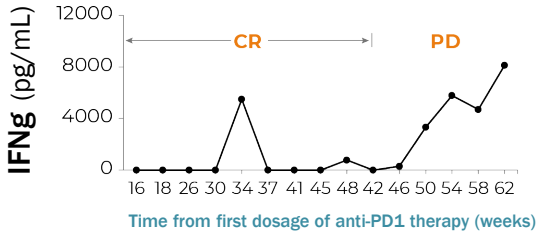
Soluble CD28 attenuates anti-PD-1 effect in cancer PBMC



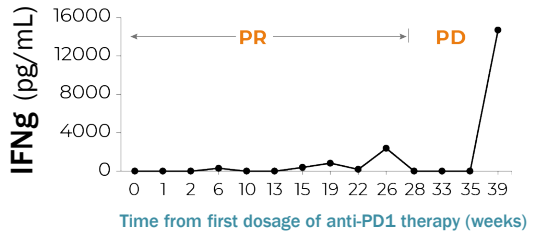
H&N Cancer donor #9

* P<0.05, unpaired student T.test Compared to MK3475 treatment

Soluble CD28 dynamics relates with response to PD-1 pathway therapy



Urothelial carcinoma donor treated with Nivolumab



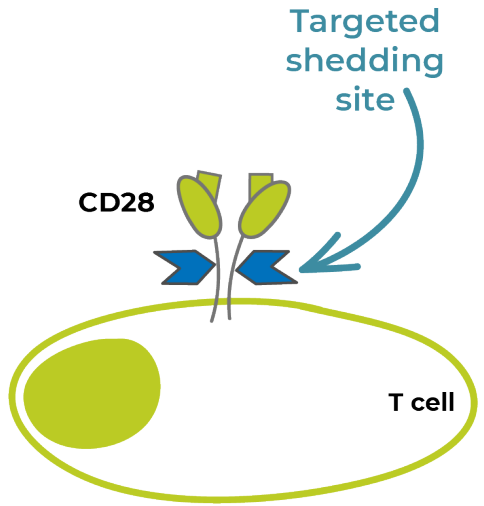
Melanoma donor treated with Nivolumab

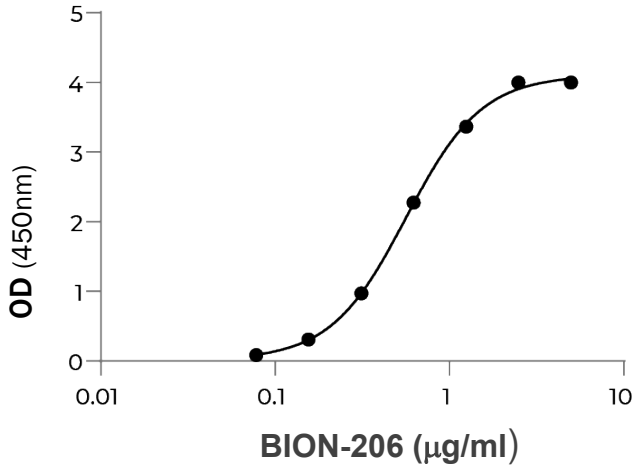
CR- Complete response: PR - Partial response,: PD - progressive disease

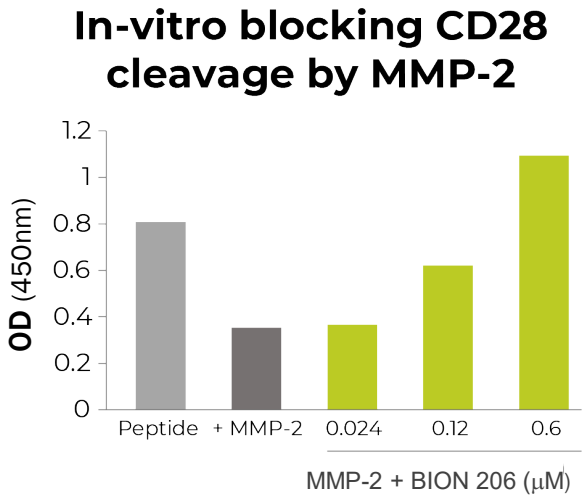
Lead BION-206 agent is in pre-clinical development

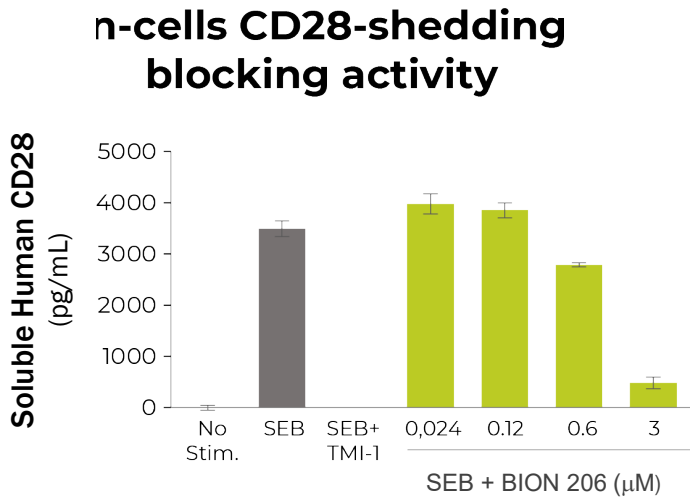
A lead clone has been isolated and characterized for:

- Specific binding to CD28 proteolytic site
- Clean safety profile – no agonistic or antagonistic activity
- Prevents receptor shedding in various immune assays

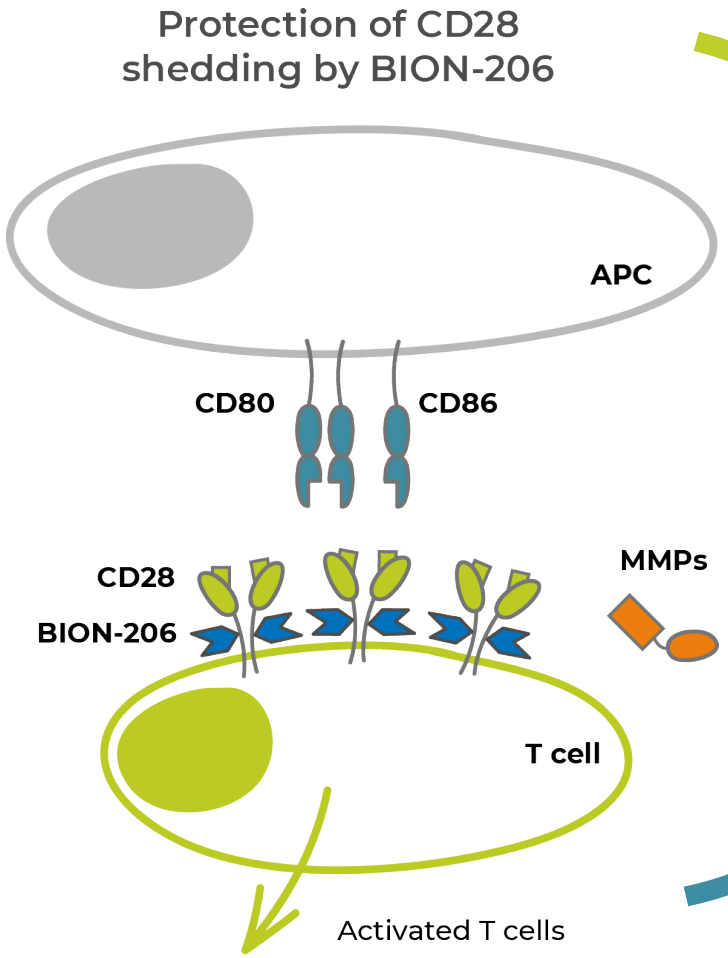








BION-206 is a first-in-class immuno-oncology agent targeting the CD28/B7 axis



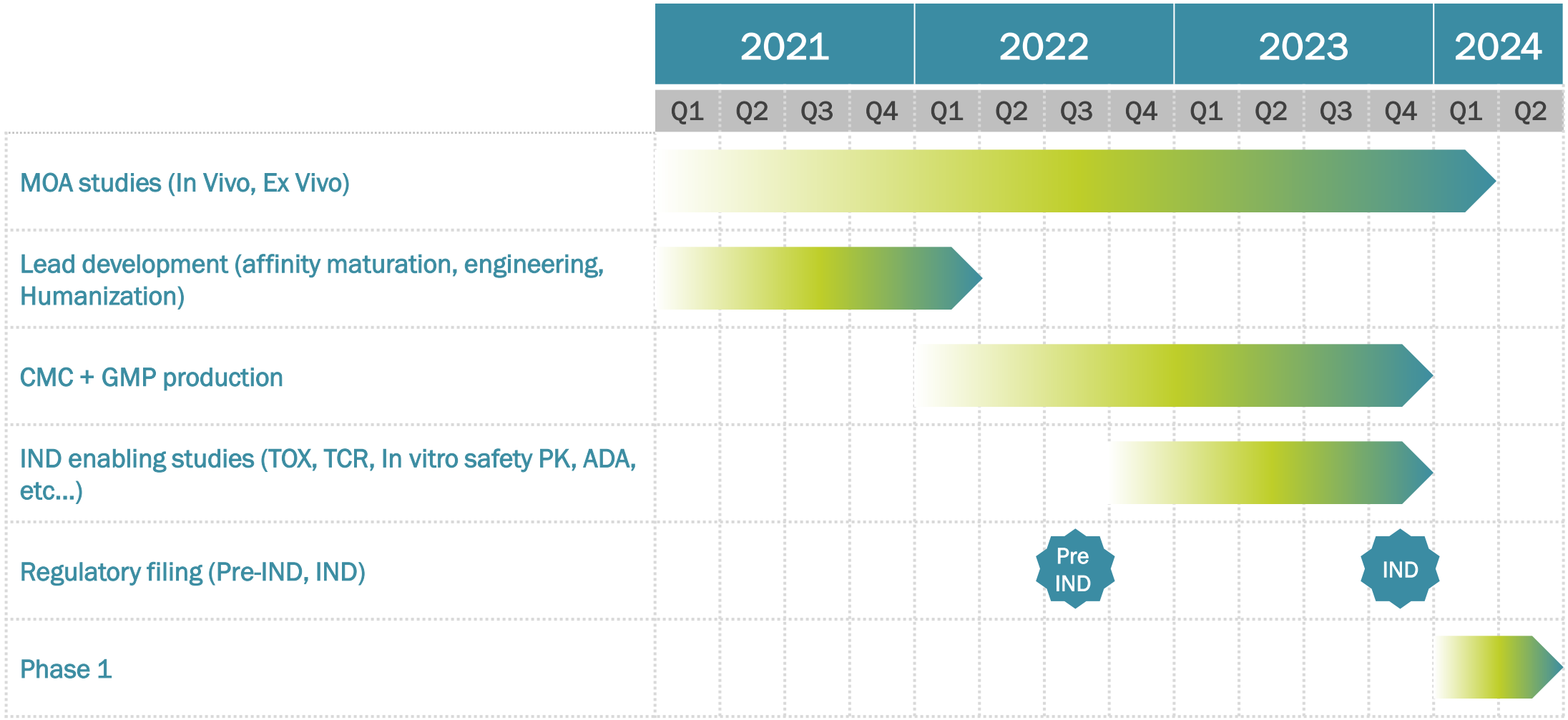
Lowers soluble CD28 levels thus preventing its immunosuppressive effect

Restores CD28 signaling in T cells

Enables efficient stimulation of T cells in lymph nodes and the TME

Enhances the effect of PD1 blockade

BION-206 Program Gannt



BION-206 Target Product Profile

Product Description

Antibody fragment targeting the CD28 receptor

Scientific Rationale

- CD28 receptor is shed from activated T cells. The soluble forms serve as a decoy receptor and were found in the serum of cancer patients
- Soluble CD28 was found to inhibit T cells activity, and attenuate the activation signal of anti-PD-1 blockade
- The identified CD28-cleaving MMPs are known to be highly expressed in tumor tissues

MOA/Clinical Pharmacology

- BION-206 binds to the shedding region of CD28 and sterically hinders access for MMPs
- BION-206 is designed to augment T cells activation, particularly memory T cells

Strategic Context / Differentiation

- A novel regulatory mechanism in the CD28/B7 axis (1st in class)
- Has the potential to overcome PD-1 resistance

Indication(s) and patient population

- Solid tumors with immune infiltration in patients with unresectable or metastatic disease, including anti-PD1 refractory patients

Stage

- Pre-clinic

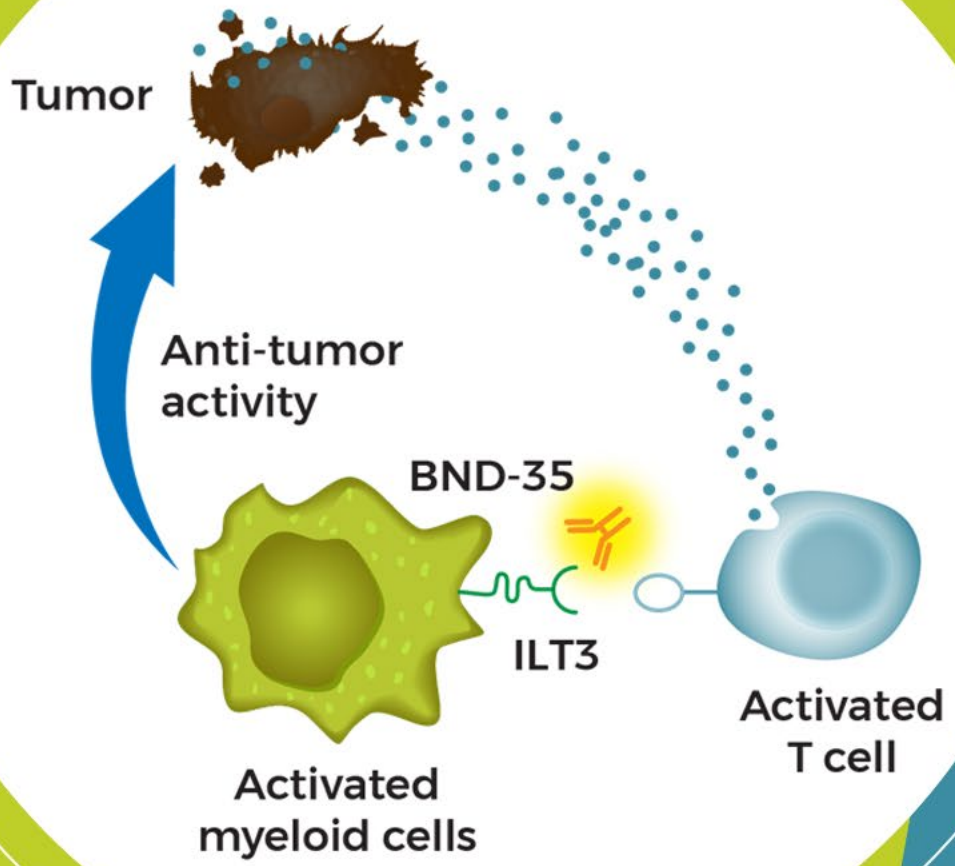
BION-206: Summary OPTIONAL

A novel regulatory mechanism discovered by Biond in the CD28/B7 axis (1st in class)

Lead BION-206 agent was selected and is under pre-clinical development

BION-206 binds to the shedding region of CD28 and sterically hinders cleavage resulting in augment T cells activation

Targets solid tumors with immune infiltration in patients with unresectable or metastatic disease, including anti-PD1 refractory patients

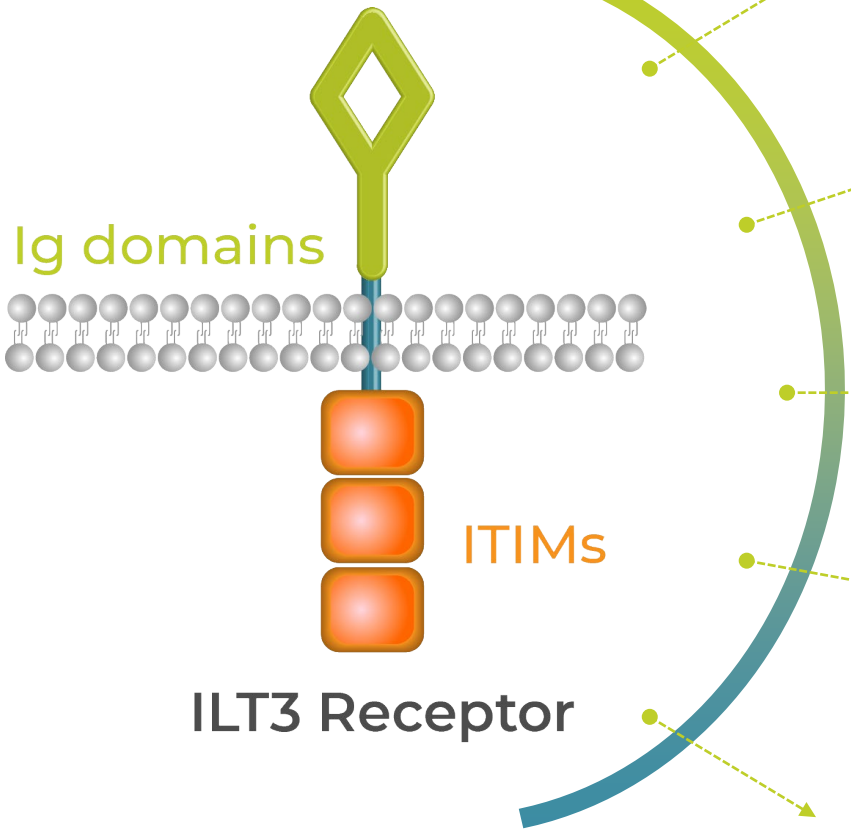


BND-35

ILT3 Blocking Antibody

BIOND BIOLOGICS

ILT3: a key protein driving suppressive myeloid cells activity in cancer



Immunoglobulin-like transcript 3 (ILT3) is an inhibitory immune-receptor containing three ITIM sequences

Can be found on suppressive myeloid cells in the TME: TAM, MDSC and DCtol

Exists in membranal and soluble forms which are both active

Inhibits the effector activity of T cells and enhances the suppressive activity of myeloid cells

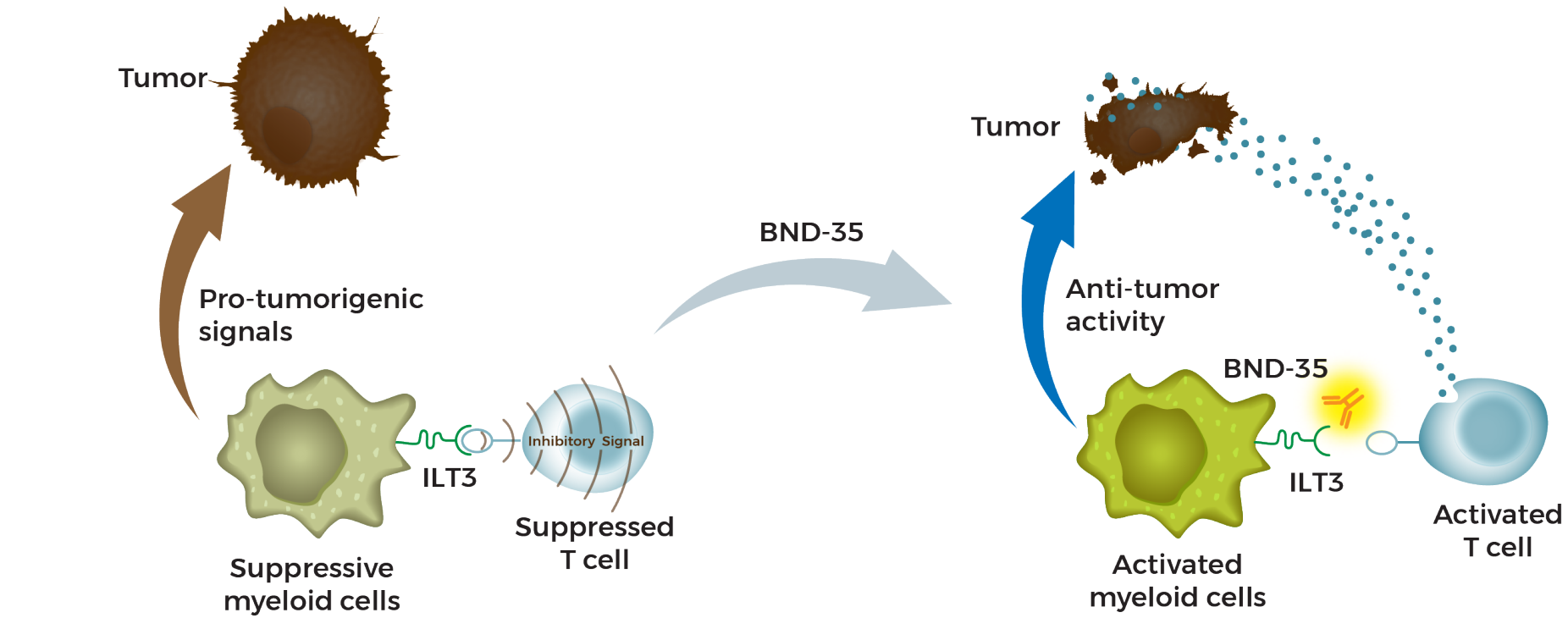
Reported T cells ligands include APOE, ALCAM, PI16

ILT3, Ig-like transcript 3; ITIM, Intracellular tyrosine-based inhibitory motifs; TAM, Tumor-associated macrophages, MDSC, Myeloid-derived suppressor cells; Dctol, Tolerogenic dendritic cells;

BND-35 is an antagonist antibody that blocks ILT3

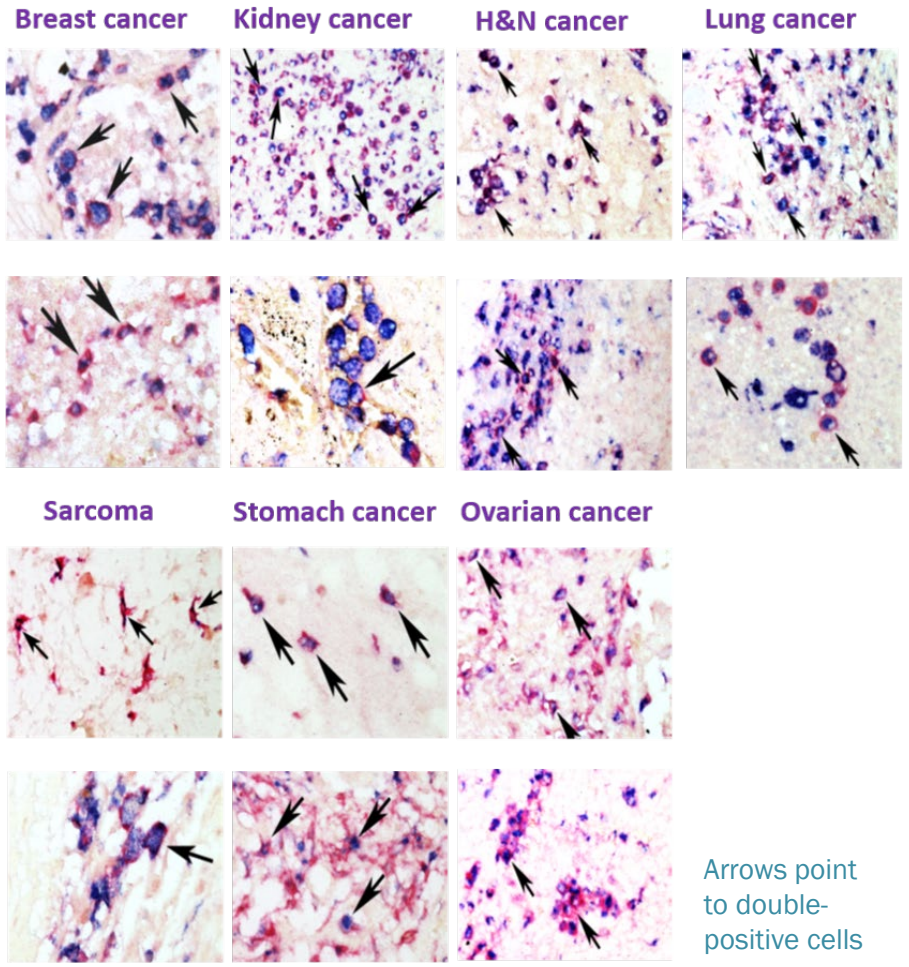
BND-35 promotes an inflammatory TME

- Decreases activity of suppressive myeloid cells
- Increases effector T cell activity



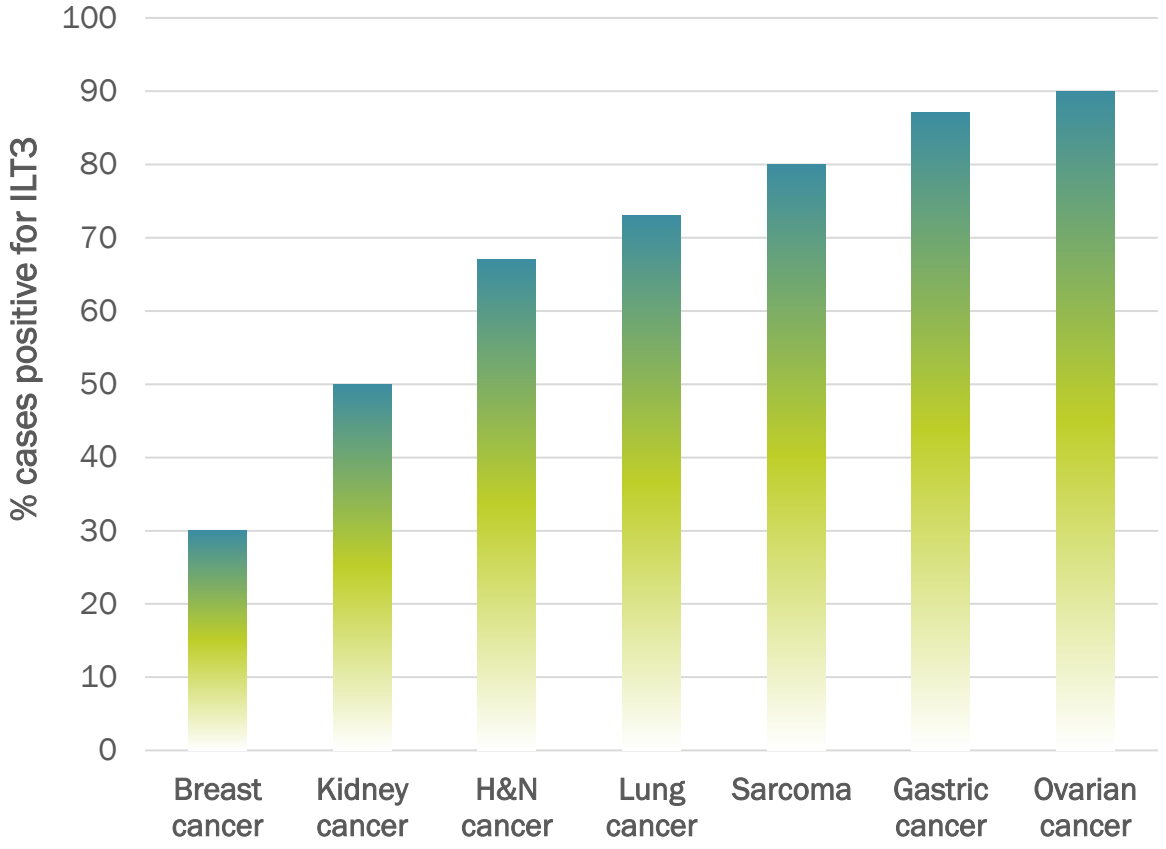
ILT3 is highly prevalent in myeloid cells in the tumor microenvironment of different cancer types

IHC staining of ILT3 (red staining) and CD68 (blue staining)



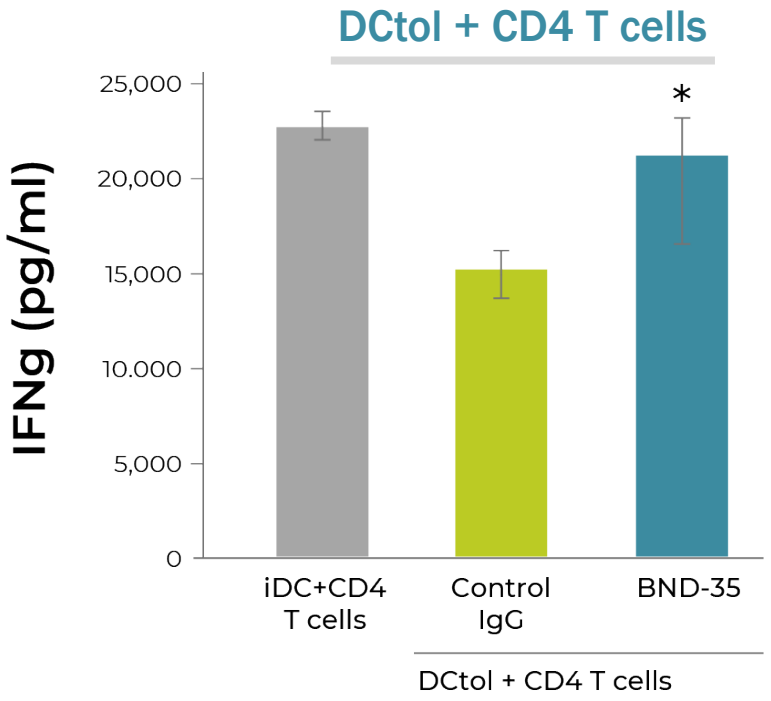
Arrows point to double-positive cells

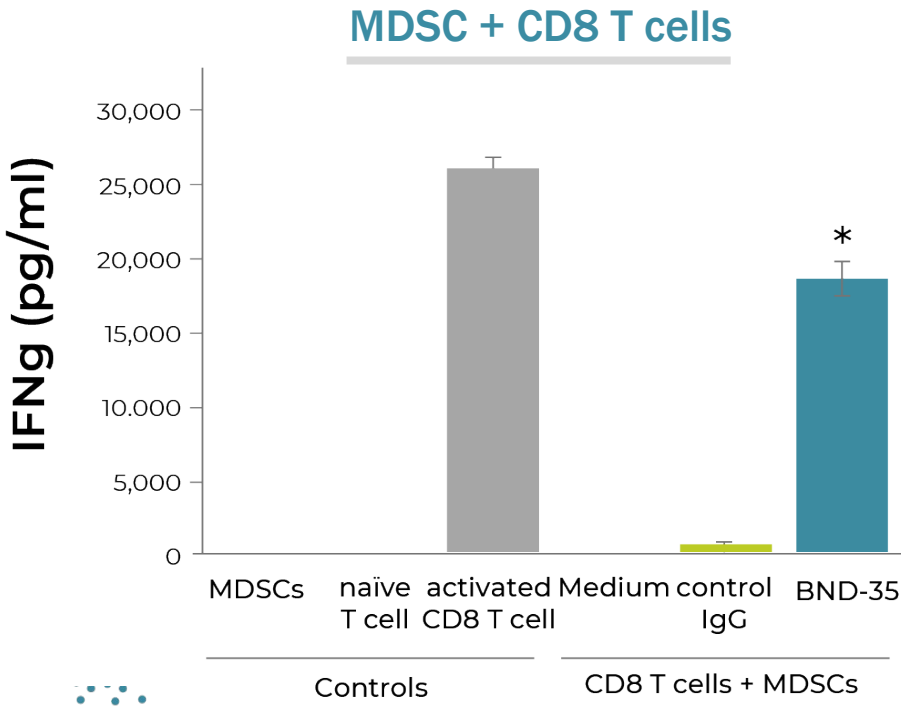
ILT3 levels in various cancers (IHC)

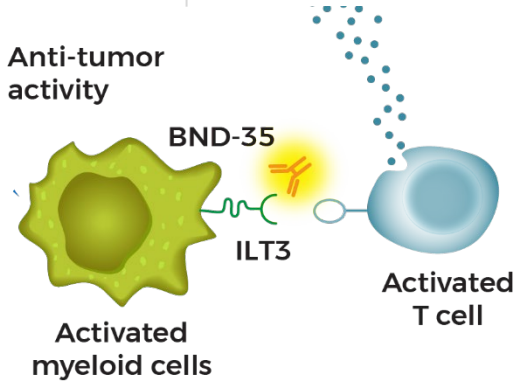


Cases were considered Target -positive if >200 ILT3+ cells were detected

BND-35 restores T cell activity inhibited by various suppressive myeloid cells







DCtol, tolerogenic dendritic cells;
MDSC, myeloid-derived suppressor cells

* P<0.05; un-paired Student's T-test compared to control IgG

BND-35 Program Gannt

BND-35 Target Product Profile

Product Description

- Ig-Like Transcript 3 (ILT3) receptor antagonist antibody

Scientific Rationale

- Suppressive myeloid cells in the tumor microenvironment (TME) limit the potency of therapeutic interventions
- ILT3 is expressed by suppressive myeloid cells in cancer patients and has a key role in the activity of these cells
- ILT3 inhibits the effector activity of T cells and enhances the suppressive activity of myeloid cells

MOA/Clinical Pharmacology

- BND-35 is an antibody that binds to the ILT3 receptor and disrupts its interaction with its T cell ligand,
- Releases ILT3 mediated immuno-supression in the TME to enable efficient anti-tumor immune activity

Strategic Context / Differentiation

- Checkpoint inhibitor targeting immuno-supresisve cells in the TME
- ILT3 is a new, emerging target in cancer immunotherapy

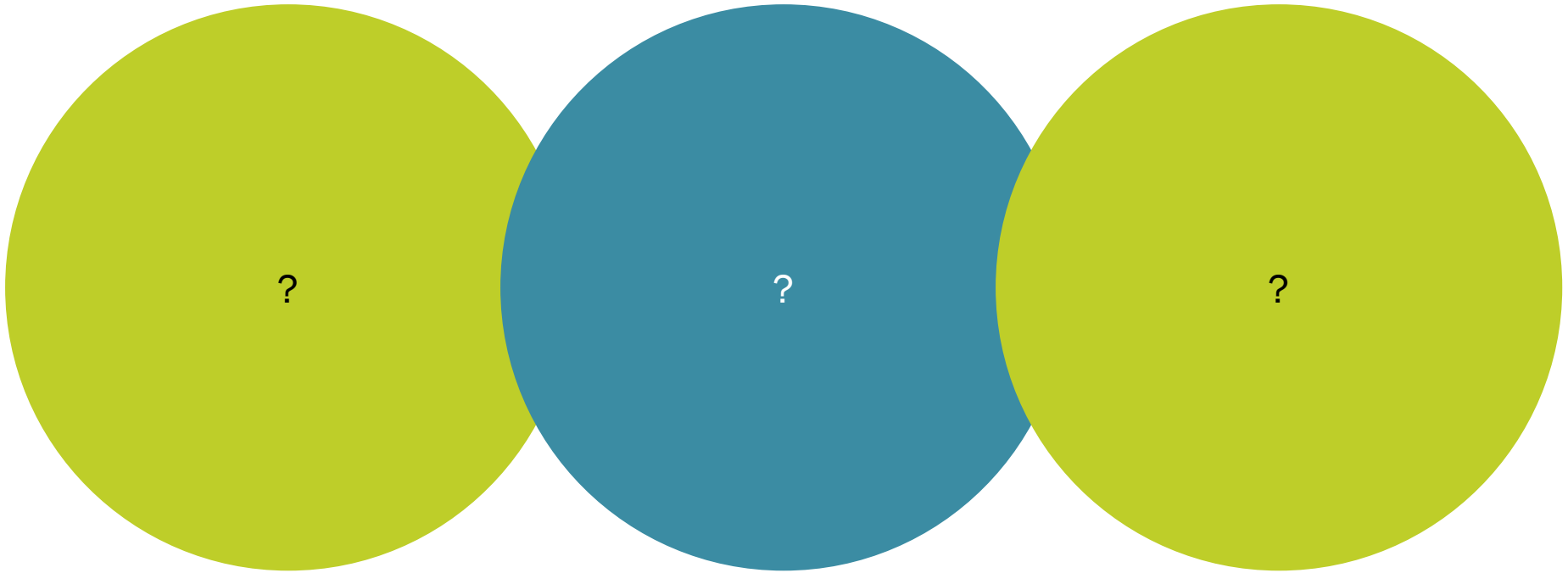
Indication(s) and patient population

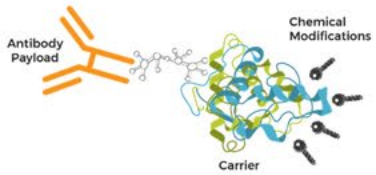
- Solid tumors known to have a highly suppressive tumor microenvironment
- Patients with unresectable or metastatic disease, with disease progression following prior systemic therapies including PD(L)-1 blockers

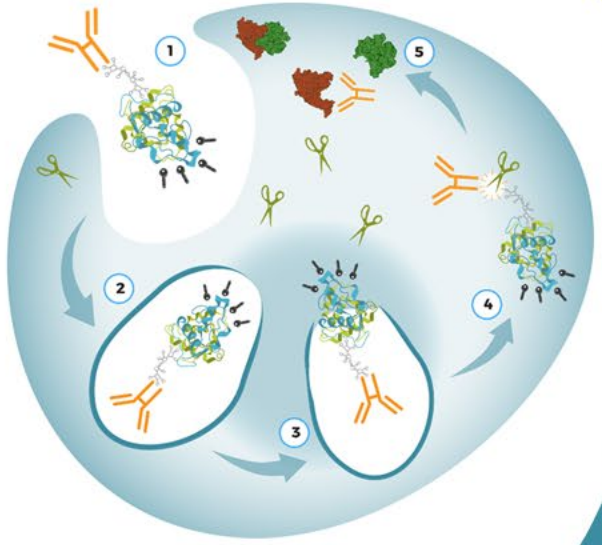
Stage

- Pre-clinic

BND-35: Summary







INspire

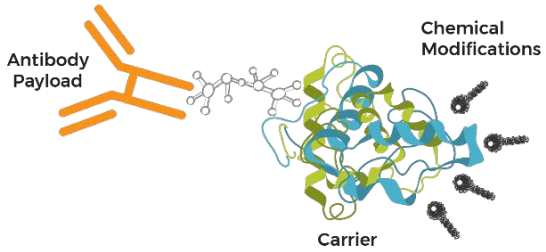
Biologics Intracellular Delivery Platform

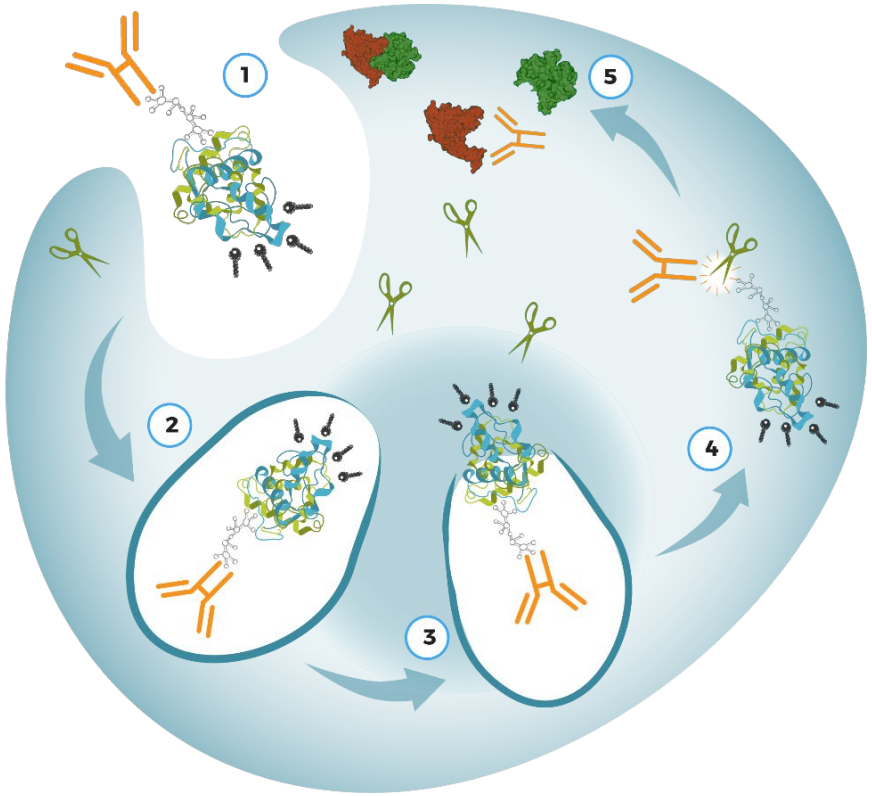
BIOND BIOLOGICS

Platform enabling intracellular delivery of biologics

Biond's INspire intracellular delivery platform is based on scalable chemical modifications applied to a carrier that enable:

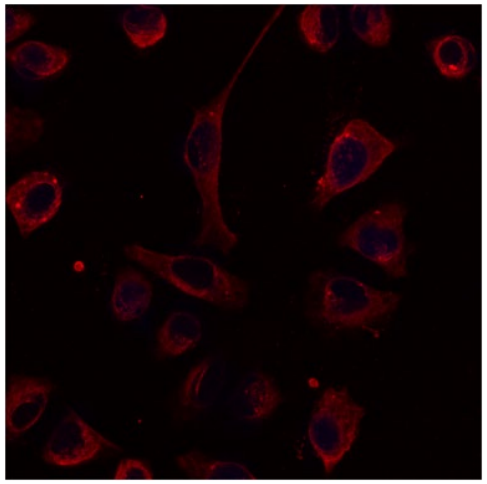
- Cell membrane-crossing by exploiting natural endocytosis
- Efficient endosomal escape
- Cytoplasm dispersibility



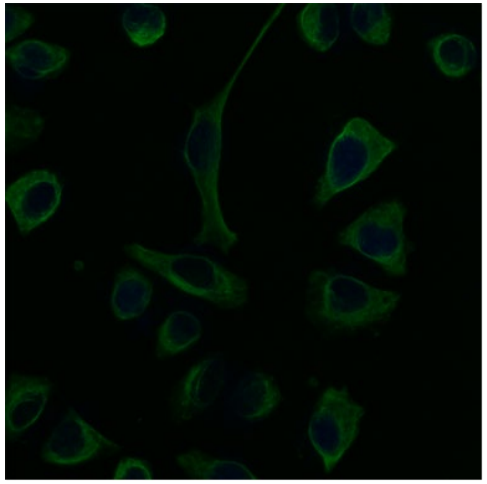


INspire: Endosomal escape, cytoplasmic dispersibility and target binding of internalized antibody

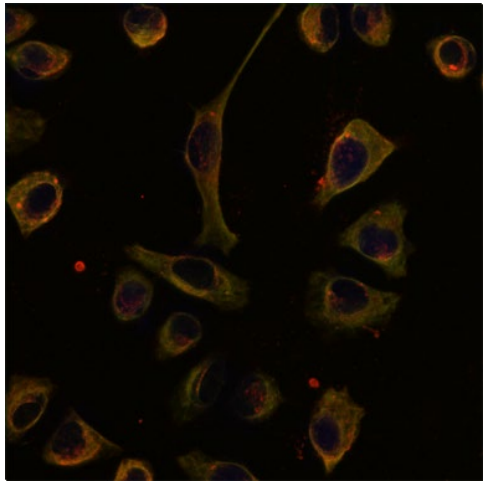
Anti-Vimentin Antibody (cytoskeletal protein) successfully delivered, released, and bound to its target inside cancer cells



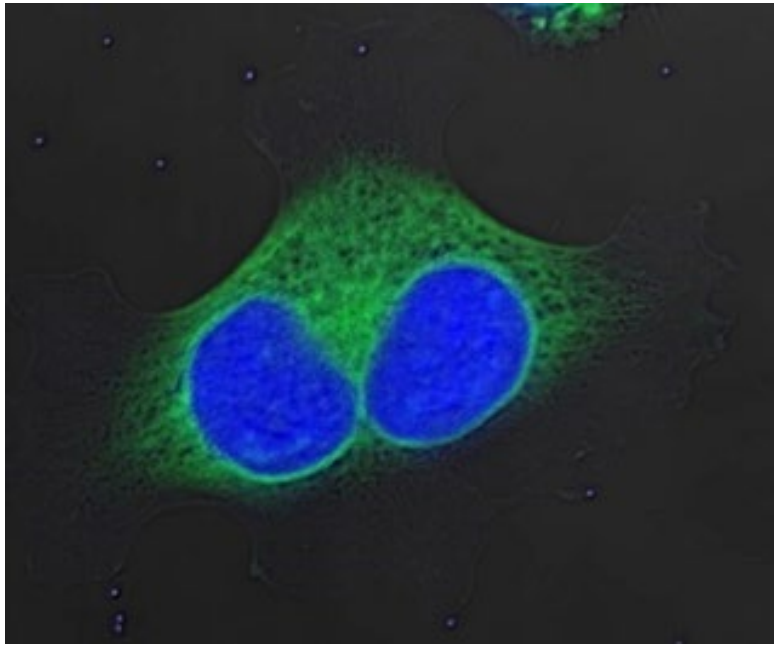
Anti-Ab (Red)
Nuclear Stain (Blue)



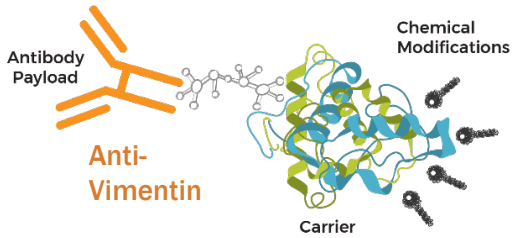
Anti-Vimentin (Green)
Nuclear Stain (Blue)



Anti-Ab (Red)
Anti-Vimentin (Green)
Nuclear Stain (Blue)

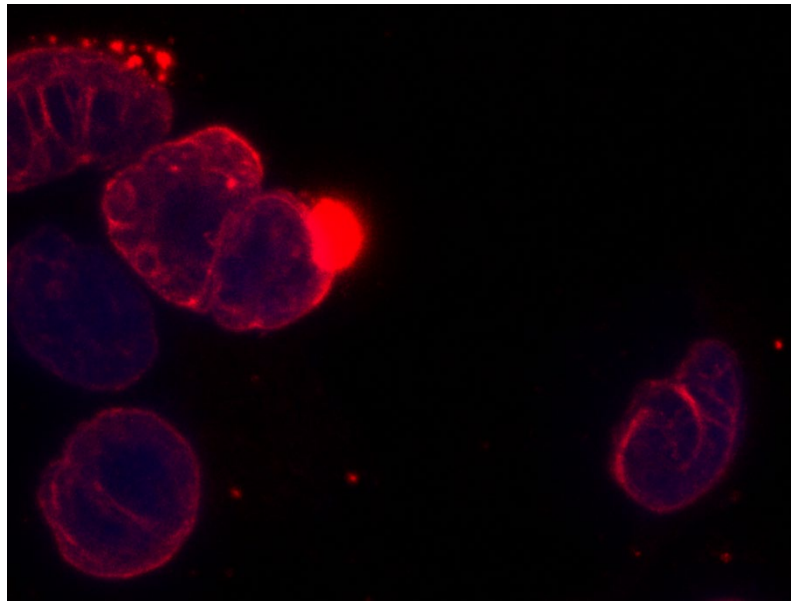


Anti-Ab. 647 (green) :
Nuclear Stain (blue)

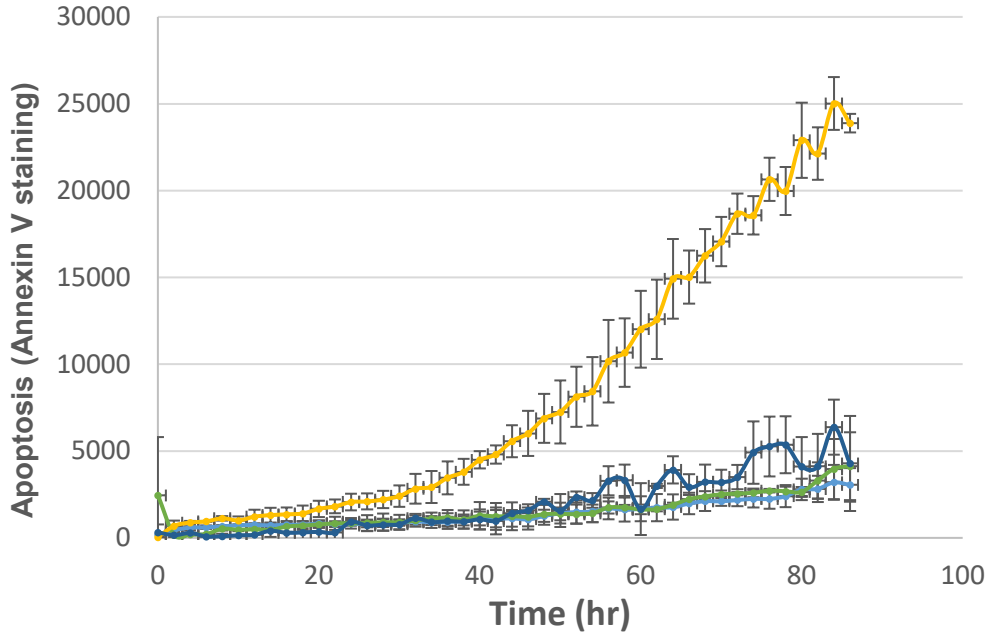


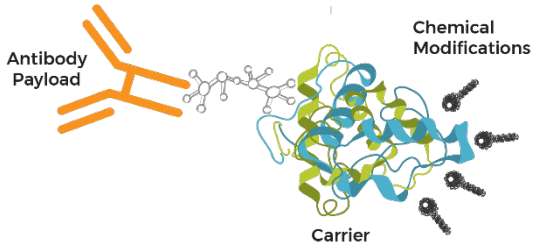
INspire: Intracellular delivery of anti mutated K-RAS protein (in-vitro PoC)

Anti-K-RAS^{G12V} protein internalized into lung adenocarcinoma cells and localizes to K-RAS sites (inner-side of cell membrane)



Effect of intracellularly delivered anti-K-RAS protein agent on apoptosis of KRAS^{G12D} pancreatic ductal carcinoma cell line

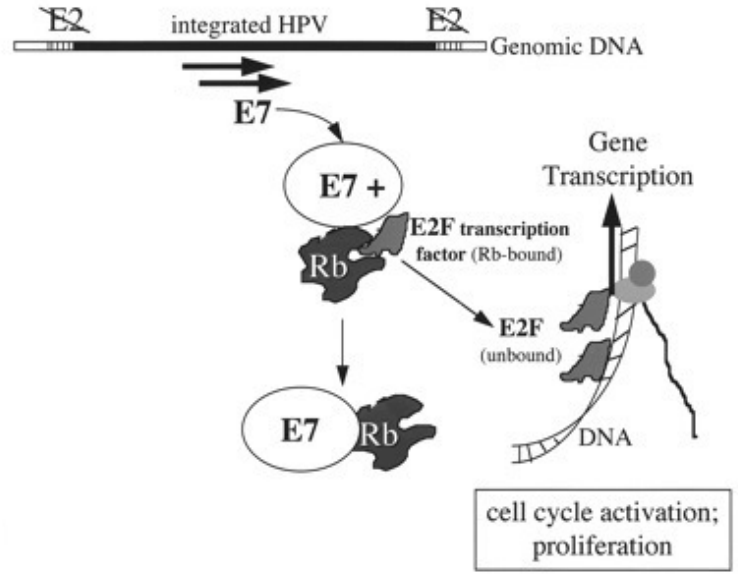


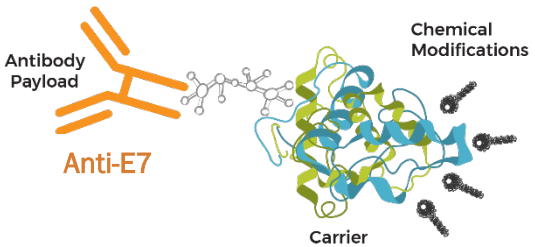


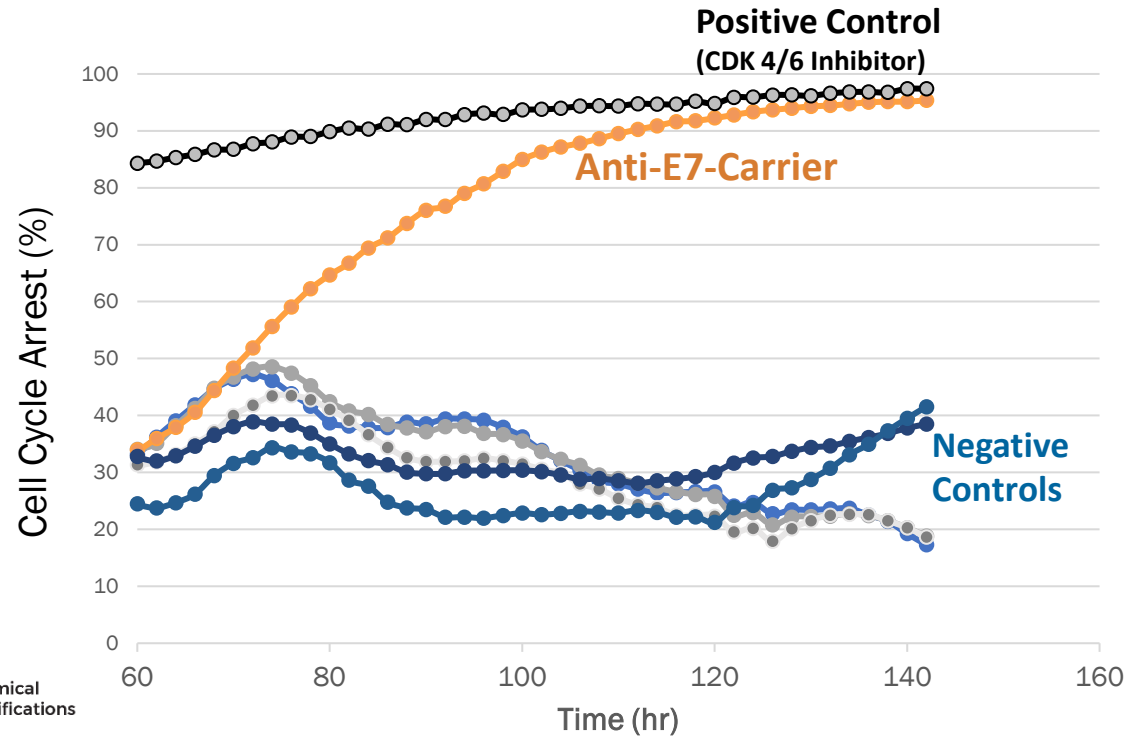
Annexin V staining - A common method for detecting apoptotic ("dying") cells

INspire: Intracellular delivery of anti-HPV-E7 (In-vitro PoC #2)

HPV-E7 is an oncoprotein that activates cell cycle (and cell proliferation). Intracellular delivery of an anti-HPV-E7 protein agent led to cell cycle arrest and killing of HPV18-E7+ cervical cancer cells







INspire Target Product Profile

Technology Description

- Therapeutic binding agents able to block or activate intracellular targets and pathways
- The agents are chemically linked to a proprietary chemically modified carrier enabling the transport of the agent inside cells

Scientific Rationale

- Biologic agents, e.g. antibodies, cannot enter cells
- Many cancer and other diseases are caused by abnormal intracellular proteins, protein-protein interactions or pathways which are deemed undruggable due to the requirement of interference by a biologic agent
- The **IN**spire agents can effectively address these undruggable targets and yield novel therapies

MOA/Clinical Pharmacology

- The ability to target intracellular targets with biologic agents enables to address targets that cannot be addressed with small molecules and exploits their selectivity and high affinity to avoid off-target effects

Strategic Context / Differentiation

- Novel technology inspired therapeutic agents with unique MOAs

Indication(s) and patient population

- The **IN**spire agents can be used to address multiple diseases and conditions
- The first **IN**spire product will address HPV-E7 cancers where there is still unmet need and very clear patient selection criteria

Stage

- Successful *in vitro* proofs of concept (HPV^+ and KRAS cancers)
- PK and biodistribution successful PoC
- *In vivo* proof of concept studies are ongoing

BION-300: Summary and next steps

Carrier platform enabling intracellular delivery of biologics targeting "undruggable" proteins

In vitro, proof-of-concept studies have demonstrated:

- antibody internalization
- endosomal escape
- cytoplasm dispersibility
- functional target binding

Preliminary in vivo studies have demonstrated efficient pharmacokinetics and biodistribution

Thank You

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BIOND BIOLOGICS