



Biolnvent

**UNLEASHING IMMUNITY
TO FIGHT CANCER**

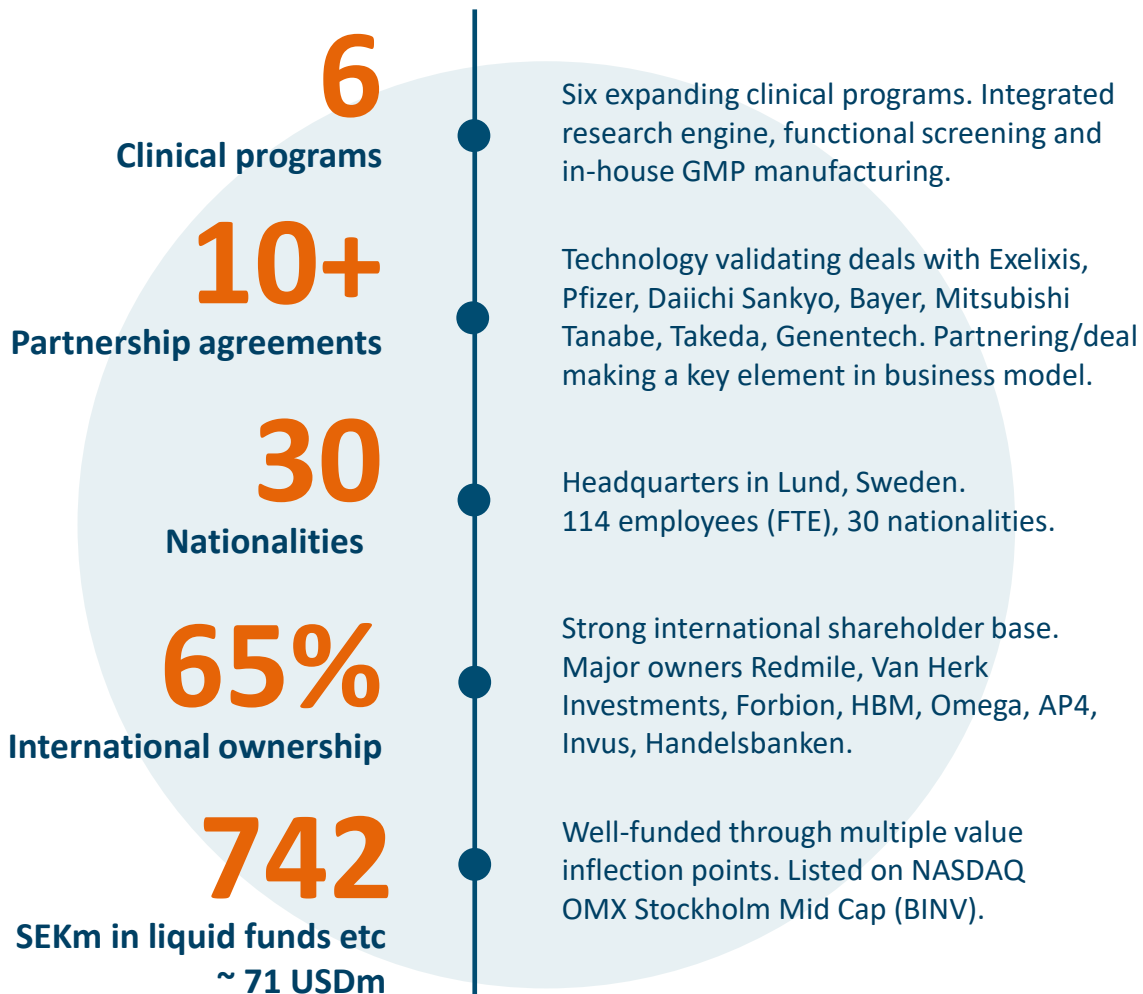
May 2025

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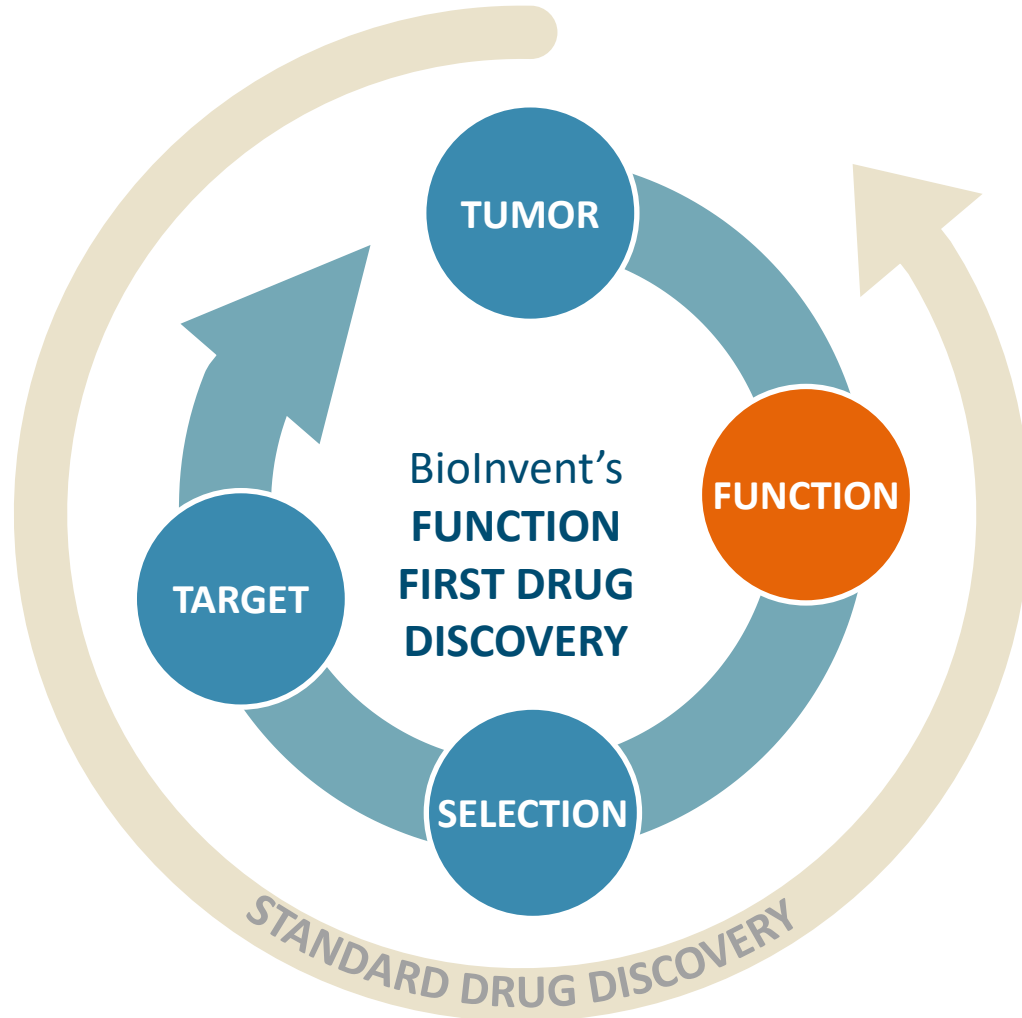
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Translating complex cancer biology into innovative antibody therapies

Mar 31, 2025

BUILDING A PIPELINE: OUR STATE-OF-THE ART ANTIBODY TECHNOLOGY



Proprietary **F.I.R.S.T.**[™] platform is the engine discovering novel cancer treatments

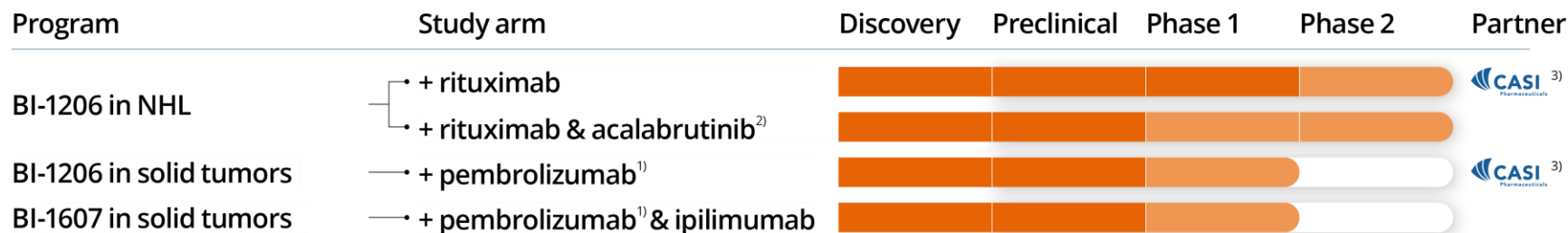
While others often focus on the targets and test function at the end, **we start from the function** (drug efficacy).

STRONG PROPRIETARY CLINICAL PIPELINE WITH MULTIPLE VALUE DRIVERS

TNFR2



FcyRIIB



CTLA-4



1) Supply agreement with MSD
 2) Supply agreement with AZ
 3) Licensed to CASI for China, Hong Kong, Macau and Taiwan
 4) 50/50 co-development collaboration with Transgene





ANTI-TNFR2

BI-1808

BI-1910

BIOINVENT LEADS THE WAY IN TNFR2 BIOLOGY

- A New And Exciting Potential Treatment Opportunity

Out of hundreds of antibodies
two highly potent candidates with
different MoAs were selected:

BI-1808 - a ligand-blocking FcγR-engaging mAb

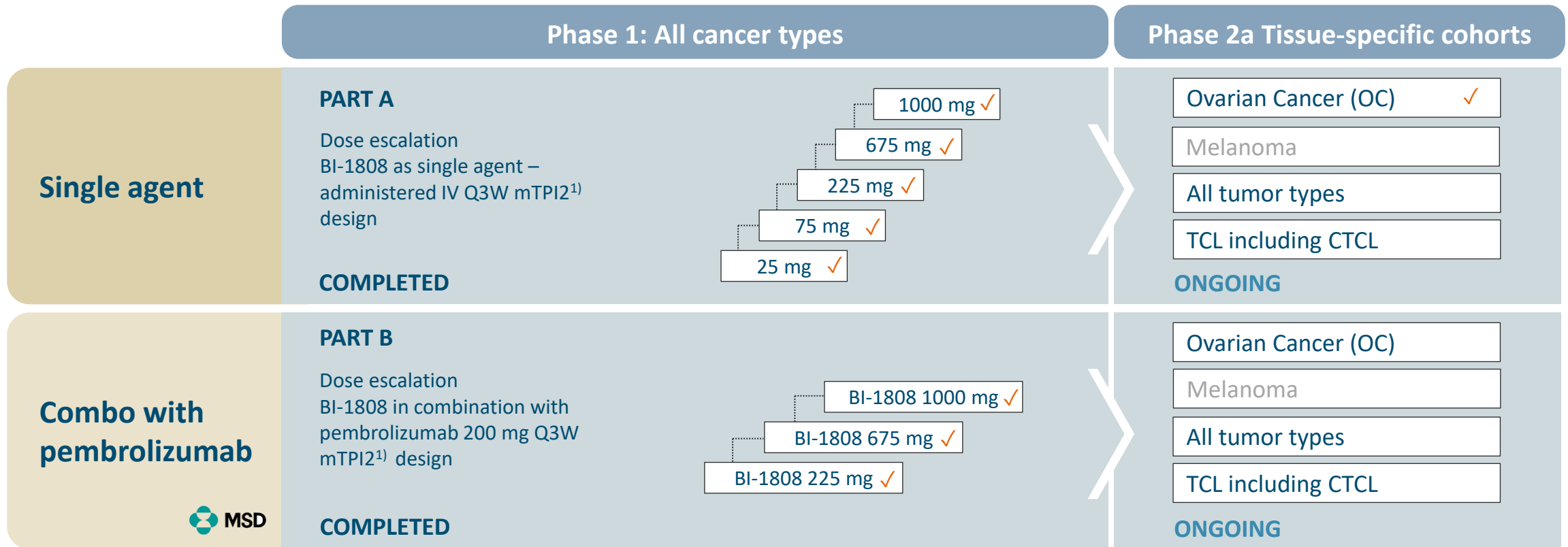
BI-1910 - an agonist mAb

Our focus is to pursue both MoAs to ensure patient benefit

Competitors are developing either agonists or antagonists

Drug Name	Company Name	Stage	Description
BI-1808	BioInvent	Phase 2	Human IgG1 Blocker/Depleter
BI-1910	BioInvent	Phase 1	Human antibody Agonist
LBL-019	Nanjing Leads Biolabs	Phase 1/2	Humanized IgG1 Blocker
SIM-0235	Simcere	Phase 1	Humanized IgG1 antibody Blocker/Depleter
HFB-200301	HiFiBiO	Phase 1	Humanized murine (IgG1) Agonist
NBL-020	NovaRock Biotherapeutics/ CSPC	Phase 1	Humanized IgG? Blocker
BIR-2101	BITT / BeiGene	IND-approved	Humanized IgG2 (variant) Antagonist
APX-601	Apexigen/Pyxis Oncology	IND ready	Humanized rabbit IgG1 Blocker/Antagonist
AN3025	Adlai Nortye/Biotime	IND-enabling	Humanized IgG1 (variant) Antagonist

BI-1808: KEYNOTE-D20 PHASE 1/2A CLINICAL STUDY DESIGN



WHAT'S NEXT?

- Additional single agent Phase 2a data mid-2025E
- First Phase 2a pembrolizumab combination data H2 2025E

BI-1808: STRONG SINGLE AGENT ACTIVITY IN PHASE 1/2A

CTCL COHORT

EHA June 2024 & September 2024

- **3 partial response (PR)** currently ongoing and deepening
- **1 patient with stable disease (SD)**
- 4 evaluable CTCL patients

SOLID TUMORS

ASCO May/June 2024

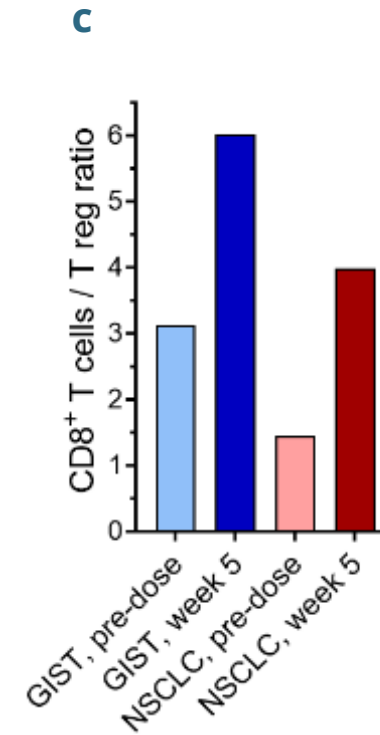
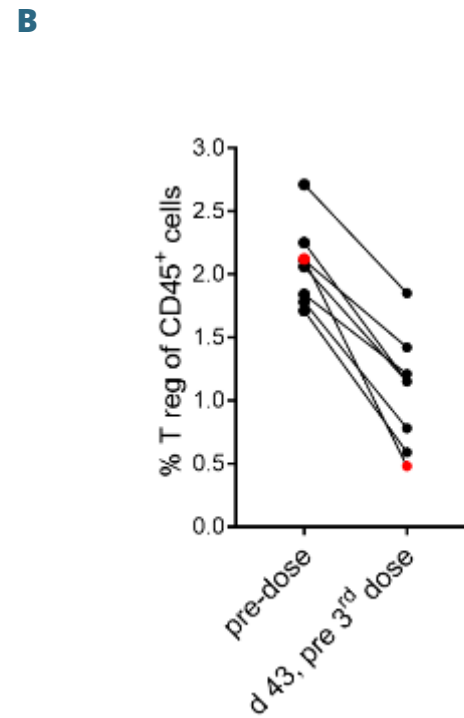
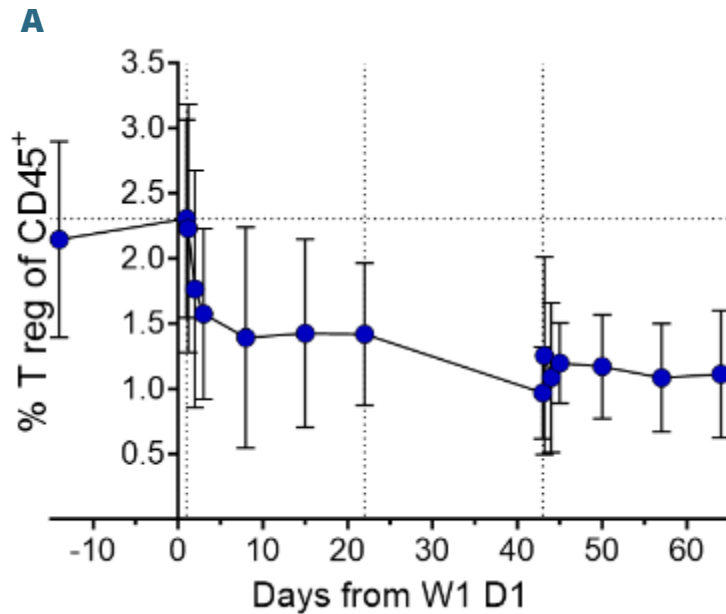
- **1 complete response (CR)** in ovarian cancer
- **1 PR** in GIST that continues to improve after more than 88 weeks (Jan 2025)
- Furthermore, **9 patients** showed **SD** (26 evaluable patients)

Furthermore, promising signs of efficacy and favorable safety profile observed in **Phase 1 dose escalation** with **BI-1808 in combination with pembrolizumab*** also presented at ASCO 2024. Phase 2a dose expansion combo study ongoing.

BI-1808 Orphan Drug Designation TCL (March 2025)
CTCL Fast Track Designation (April 2025)

BI-1808 SINGLE AGENT EFFICACY

Induces significant regulatory T-cell depletion and clear signs of CD8⁺ T-cell activation in responding patients



Tumor biopsies collected pre-, and 5 weeks post-treatment were stained for Foxp3+ CD4+ Treg cells and CD8+ T cells using immunofluorescence.

Percentages of stained area were quantified and a pre- and post-treatment CD8+/T reg ratio were calculated.

BI-1808 increases intratumoral CD8+/T reg ratio

Data from the 1000 mg monotherapy cohort.

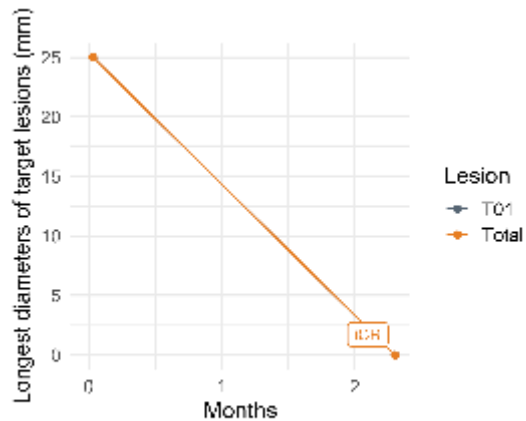
The data show substantial **T-reg depletion** compared to baseline. Panel B shows the individual patient drop in T-reg. Red dots indicate the drop in the GIST patient. (Dashed horizontal line = baseline. Dashed vertical lines = BI-1808 dosing occasions)

BI-1808 SINGLE AGENT CASE STUDY: COMPLETE RESPONSE IN OVARIAN CANCER

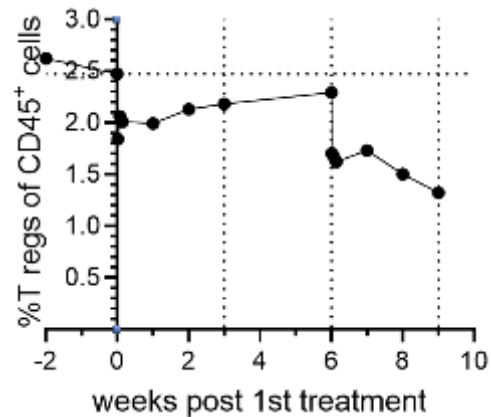
Baseline



2 months



Tumor assessment vs time on study



T reg levels vs time on study

Dashed lines indicate administration of BI-1808

63-year-old patient with ovarian cancer, Stage IIIA at diagnosis, entered the study with PD.

Four previous lines of treatment:

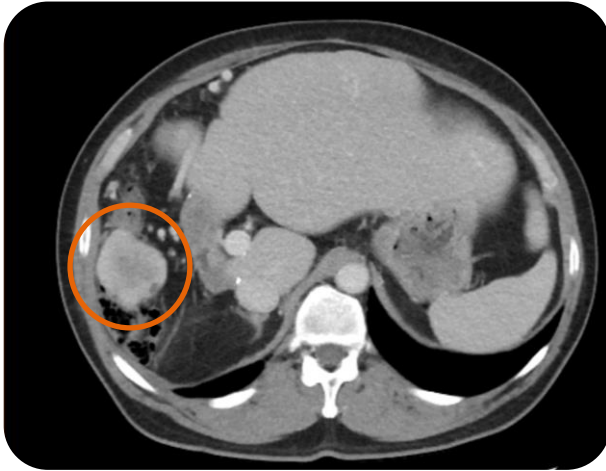
- Paclitaxel/carboplatin
- Carboplatin/doxorubicin
- Olaparib
- Bevacizumab/topotecan

Patient had **one target lesion** of 25 mm and **two larger non-target** cystic lesions.

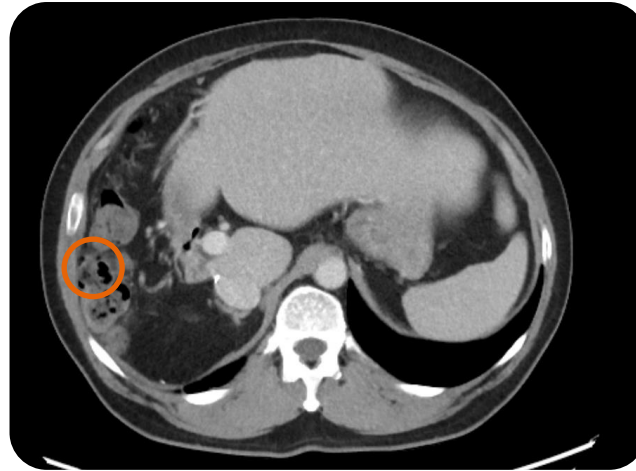
At **first post-treatment scan**, 9 weeks after the start of treatment, **no quantifiable tumor mass could be measured**.

BI-1808 SINGLE AGENT CASE STUDY: ROBUST PR IN A PATIENT WITH GIST

Baseline



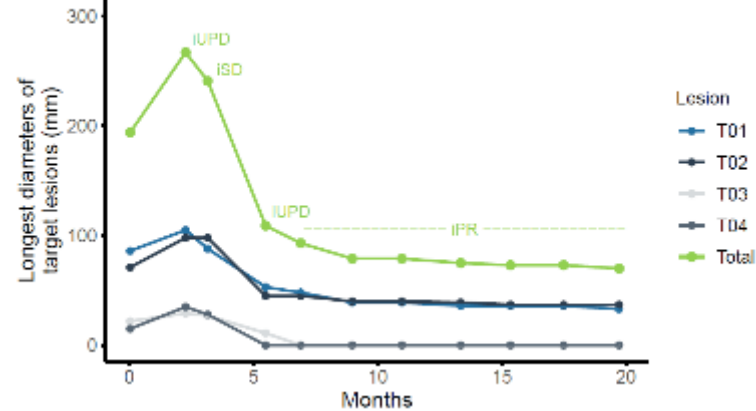
Follow-up 13 months



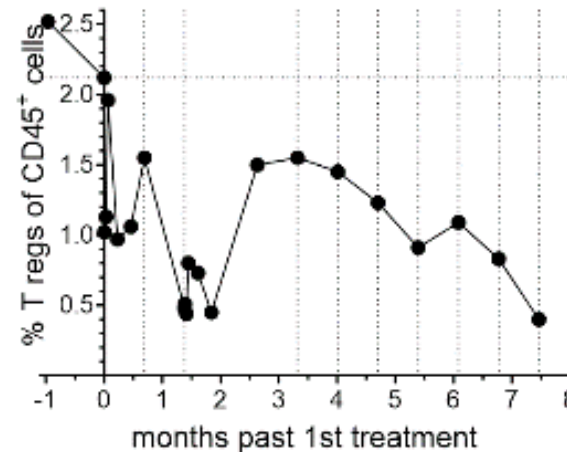
55-year-old male patient with GIST, who presented with clinical PD for more than 6 months with multiple metastatic lesions. **12 previous lines of therapy.**

The partial response continues to improve after more than 80 weeks (Dec 2024).

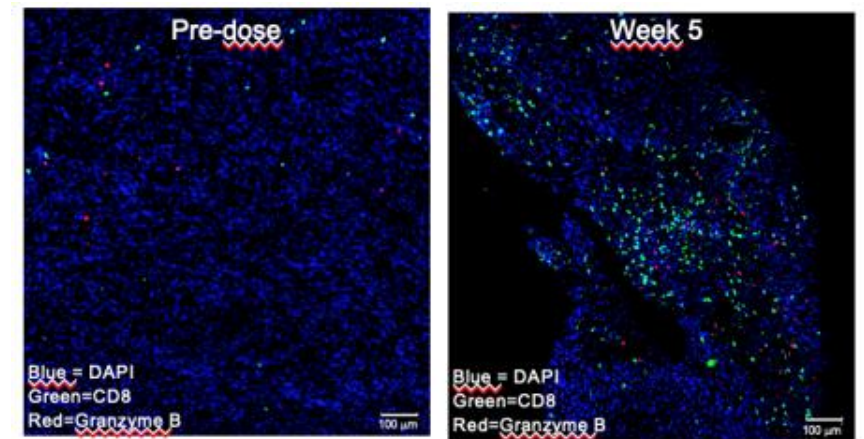
Target lesion progression
0101-0004



Tumor assessment vs time on study (days)



T reg levels vs time on study. Dashed lines indicate administration of BI-1808

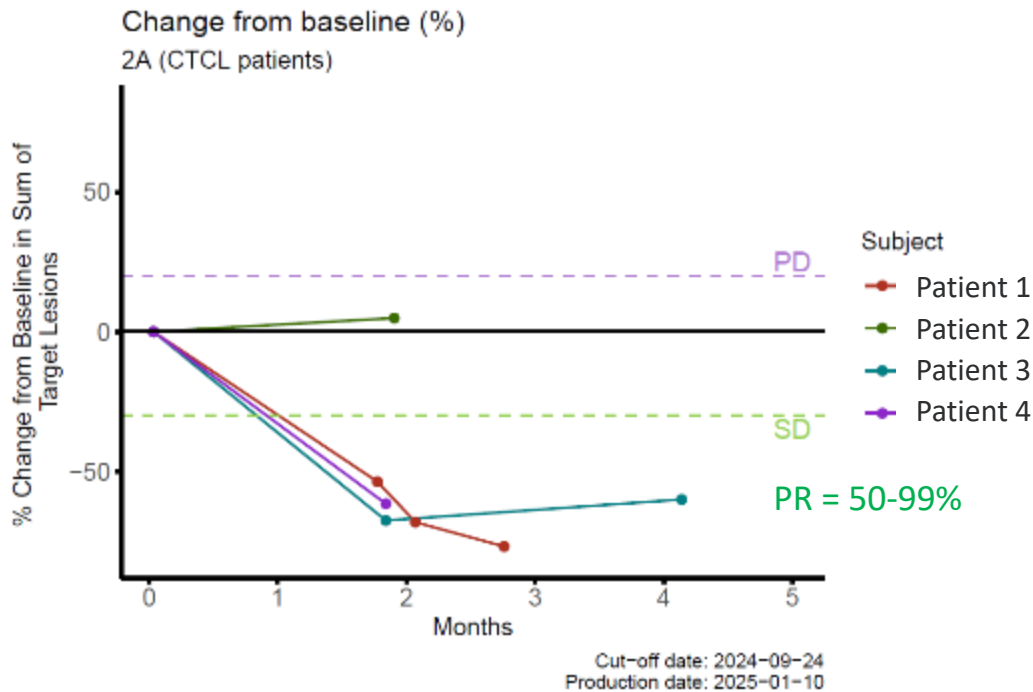


BI-1808 shows evidence of CD8+ tumor infiltration which is associated with tumor regression

BI-1808: OUTSTANDING EARLY RESPONSES IN HEAVILY PRE-TREATED CTCL PATIENTS

- 4 patients are evaluable post treatment, out of 6 patients treated with BI-1808 single agent
- 3 exhibited partial response (50-99% decrease from baseline), with 1 patient showing stable disease

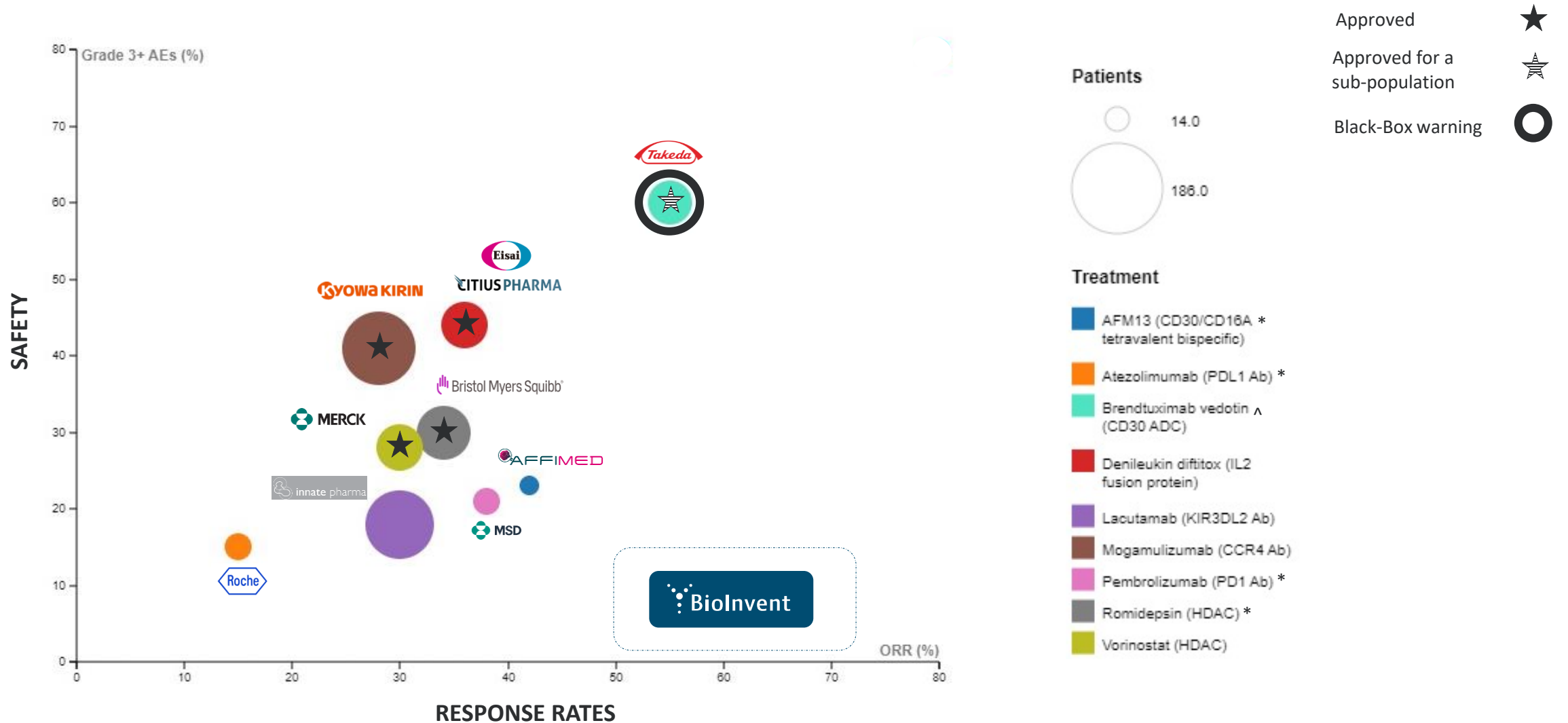
Skin Lesions (mSWAT assessment)



Prior Treatment in responding CTCL patients

Patient No.	Diagnose	Regimen	Prior treatment	Best prior response	BI-1808 response
3	MYCOSIS FUNGOIDES	Regimen 1	BEXAROTENE	Not Evaluable (NE)	PR
		Regimen 2	METHOTREXATE VALCHLOR GEL	Partial Response (PR)	
		Regimen 3	DURVALUMAB	Partial Response (PR)	
4	MYCOSIS FUNGOIDES	Regimen 1	METHOTREXATE	Stable Disease (SD)	PR
		Regimen 2	TTI-621	Complete Response (CR)	
		Regimen 3	BNZ-131-1-40	Stable Disease (SD)	
		Regimen 4	LENALIDOMIDE /DURVALUMAB	Partial Response (PR)	
		Regimen 5	METHOTREXAT / IMIQUIMOD CREAM	Not Evaluable (NE)	
		Regimen 6	MOGAMULIZUMAB	Stable Disease (SD)	
1	SEZARY SYNDROME (IV)	Regimen 1	MOGAMULIZUMAB	Stable Disease (SD)	PR
		Regimen 2	PEGASYS 180 MCG/ML SUBCUTANEOUS SOLUTION (PEGINTERFERON ALFA-2A)	Stable Disease (SD)	
		Regimen 3	ROMIDEPSIN	Unknown	

BASED ON EARLY DATA, BI-1808 LOOKS POISED TO BE **BEST-IN-CLASS** IN R/R CTCL LANDSCAPE



BI-1808 POSITIONING IN THE MARKET LANDSCAPE

CTCL

BI-1808 can be **developed as frontline** for the treatment for **Mycosis Fungoides** and **Sézary Syndrome (CTCL)**:

- Exceptional Safety and Tolerability profile for the treatment of a chronic devastating disease
- All available therapies are deficient from the safety and efficacy standpoint
- ORR \geq 40% will comfortably place BI-1808 as the treatment of choice in the **front line**
- Potential market opportunity as first line monotherapy
- High market potential in a short timeframe.

Solid Tumors

The **largest commercial** potential of BI-1808 is for the treatment of **solid tumors**:

- Demonstrated single agent activity and induction of antitumor immunity in several patients across different types of malignancies (OC, NSCLC, GIST, TCL)
- Demonstrated synergistic activity with anti-PD1 in preclinical models
- Exceptional safety profile makes it ideal for a combination component with anti-PD1/L1 in several tumor types

BI-1910: PROMISING SINGLE AGENT PHASE 1 DATA (JAN 2025)

A differentiated, agonist approach to treating solid tumors

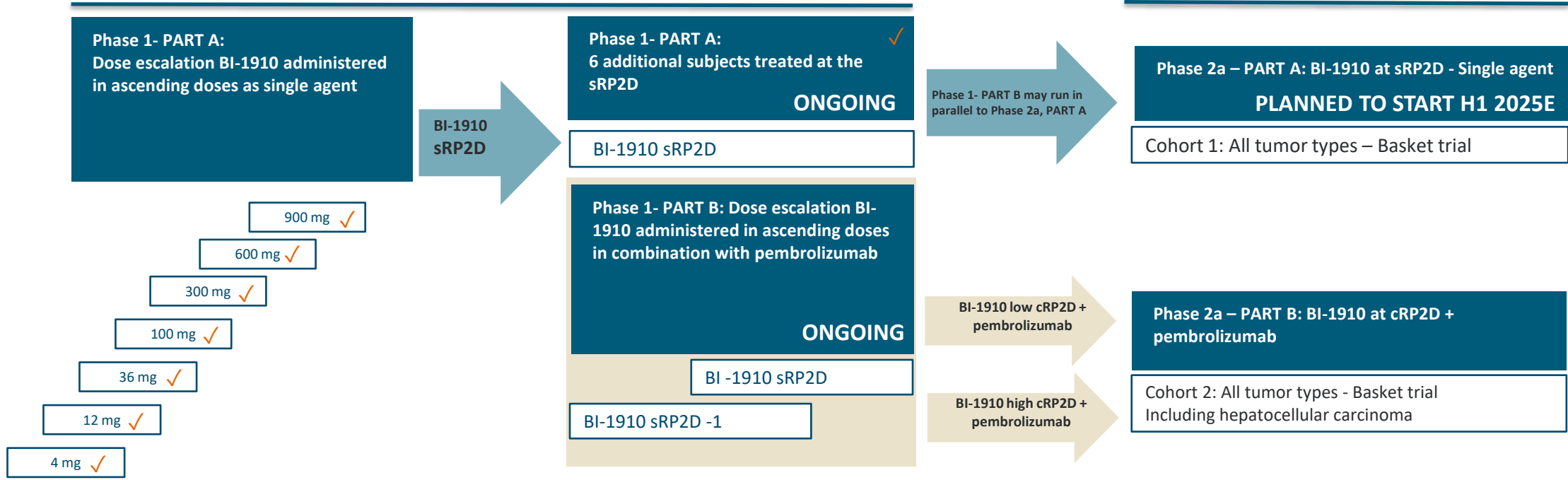
ESMO 2024 and Jan 2025 **SINGLE AGENT** data:

- **Stable disease** (6/12 evaluable patients) **best clinical responses**
- No notable adverse events even at the highest doses tested
- BI-1910 single agent **Phase 1** Part A **dose escalation completed** and reached a biologically active dose level
- Favorable pharmacokinetic data and a **robust target engagement**, showing evidence of induction of T-cell proliferation

BI-1910 STUDY DESIGN

All Solid Tumors Phase 1

Tissue-specific cohorts Phase 2a



WHAT'S NEXT?

- Initial Phase 2a single agent data H2 2025E
- Phase 1 pembrolizumab combination data H2 2025E

ANTI-Fc γ RIIB

BI-1206 + rituximab + acalabrutinib

BI-1206 + pembrolizumab

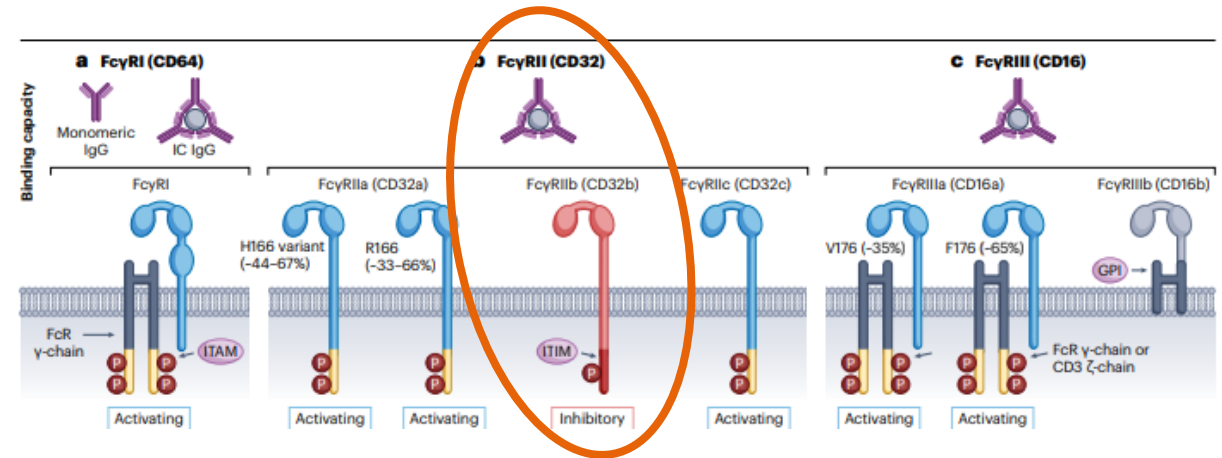
BI-1607

LEVERAGING OUR Fc γ RIIB TARGET EXPERTISE WITH A MULTI-PRONGED APPROACH

We have developed two antibodies with different mechanisms of action to tackle different needs

BI-1206 is an Fc-competent IgG1 antibody that enhances anti-CD20 and anti-PD-1 therapies. In **two separate programs**.

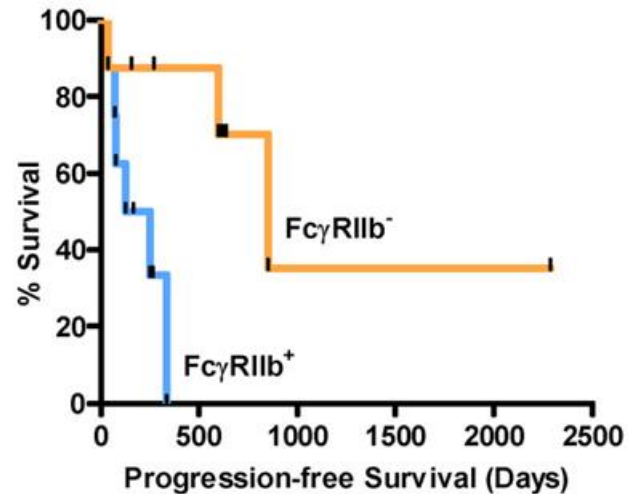
BI-1607 has a different MoA compared to BI-1206 having been engineered for reduced Fc-binding to Fc γ R.



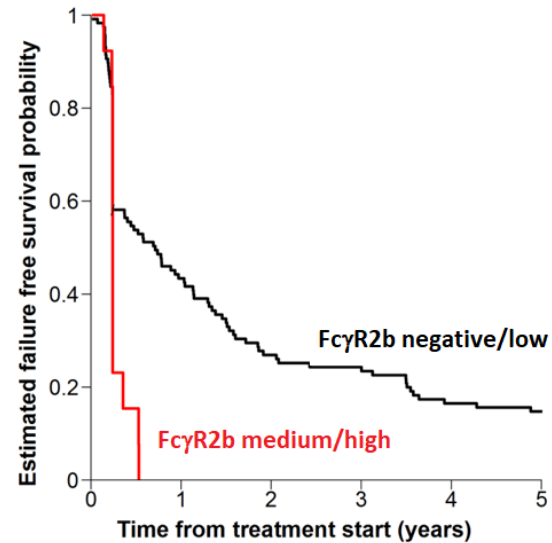
Galvez-Cancino, F., Simpson, A.P., Costoya, C. et al. Fc γ receptors and immunomodulatory antibodies in cancer. *Nat Rev Cancer* 24, 51–71 (2024). <https://doi.org/10.1038/s41568-023-00637-8>

FcγRIIB EXPRESSION CORRELATES INVERSELY WITH SURVIVAL

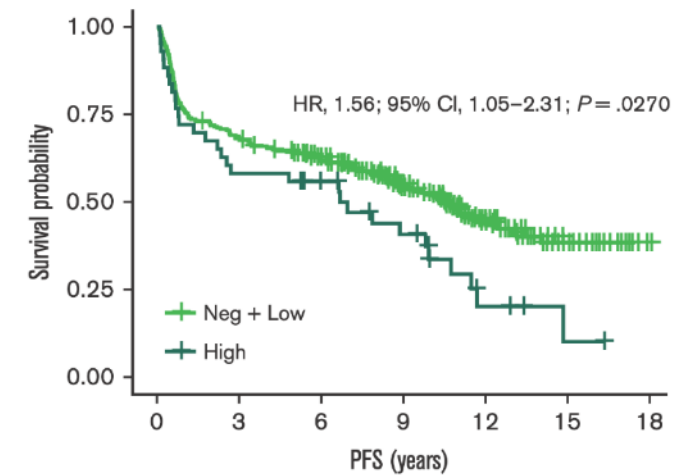
Mantle Cell Lymphoma (MCL)



Follicular Lymphoma (FL)



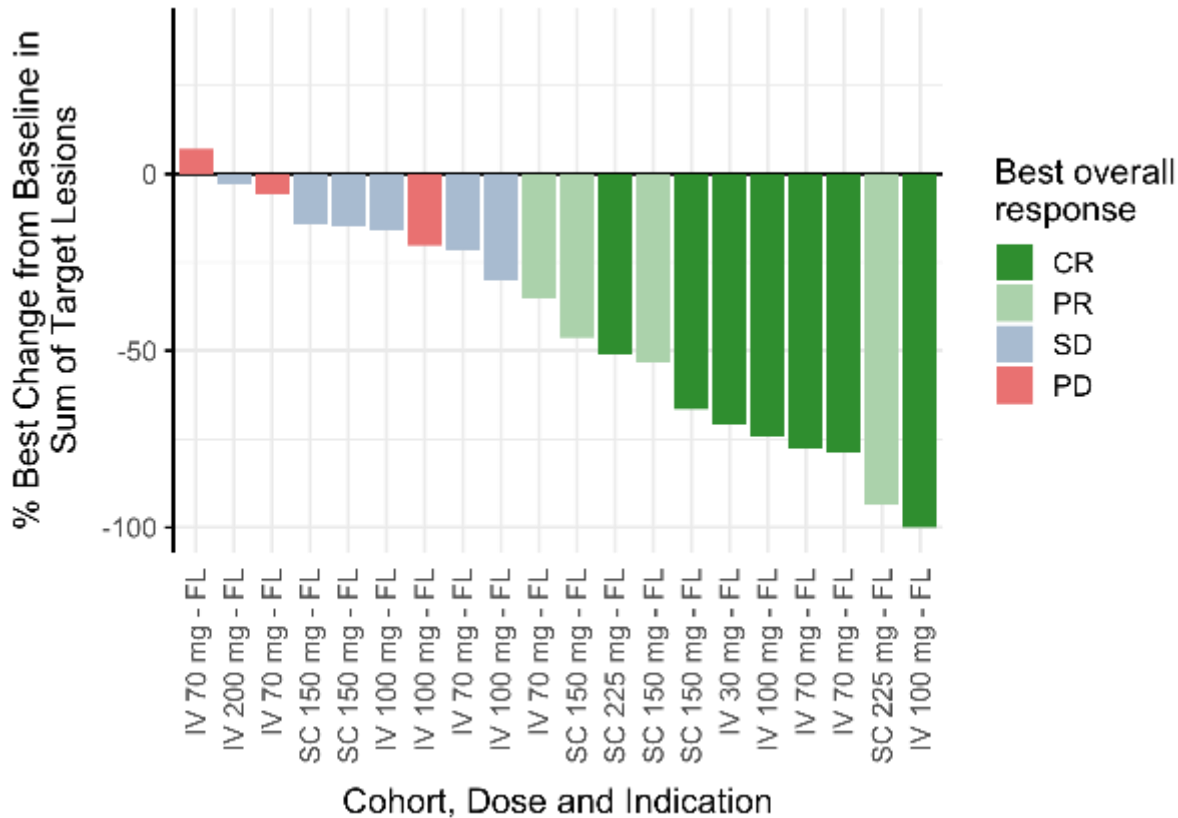
Diffuse Large B-Cell Lymphoma



High FcγRIIB expression is associated with shorter survival in patients receiving rituximab therapy

BI-1206: PHASE 1 CLINICAL DATA IN FL PATIENTS DEMONSTRATES STRONG EFFICACY AND SAFETY SIGNALS

BI-1206 + rituximab responses in 20 relapsed/refractory FL pts



Outcomes

(October 2024, SC + IV)



No safety or tolerability concerns

All TEAEs were manageable

Resolved without clinical complication

SC particularly well-tolerated



ORR of 55%, **CRR** of 35%, **DCR** 85%

7 complete responses (CR)

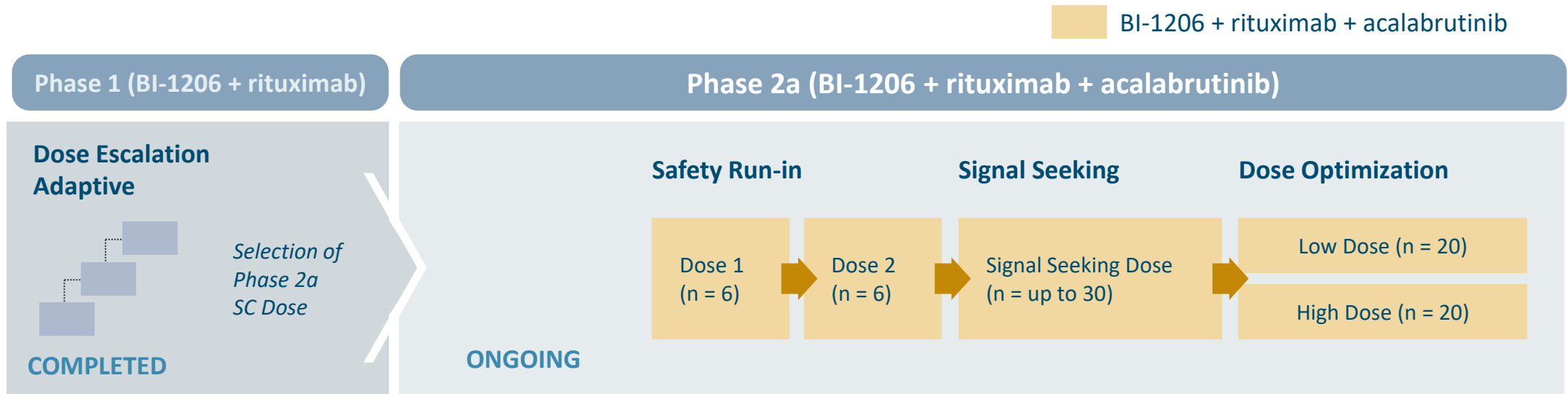
4 partial responses (PR)

6 patients with stable disease (SD)

CRs have been **long-lasting**, three of them **lasting years after** end of treatment

BI-1206 IN NHL: COMBINATION WITH RITUXIMAB AND ACALABRUTINIB

- **Phase 1 dose-escalation** study with BI-1206 subcutaneous (SC) + rituximab **completed**
- Approximately **30 patients** expected to be enrolled in Phase 2 signal seeking part (Spain, Germany, the US, and Brazil)



Additional Phase 2a triplet data mid-2025E

BI-1206 IN NHL: COMBINATION WITH RITUXIMAB AND ACALABRUTINIB

Promising initial efficacy Phase 2a data from BI-1206 SC triple combination

- First two patients (as of January 2025):
 - **1 complete response (CR)**
 - **1 partial response (PR)**
 - The treatment has been well-tolerated with no safety or tolerability concerns
- Phase 1/2a clinical study in patients with NHL who have **progressed or are refractory to rituximab**
- The **conveniency and safety profile** of this **triplet** should be **very competitive** in the treatment landscape of NHL

BI-1206 POSITIONING IN THE MARKET LANDSCAPE

Follicular lymphoma (FL)

Potential as 2nd line for the treatment of FL:

- **Highly convenient and safe**, combined with the two most successful drugs in this space, in a **chemotherapy-free** regimen:
 - Rituximab: will remain the backbone of treatment in NHL for years to come
 - Acalabrutinib: best-in-class drug for the treatment of MCL
 - SC formulation brings significant convenience. In the long-term both BI-1206 and rituximab can be administered SC (acalabrutinib is administered orally)
- ORR \geq 75% would place the triplet as a very competitive option in the **second line**
- No cytokine release syndrome, no neurotoxicity and no safety concerns makes this triplet **ideal for the treatment of patients in community hospitals**

Solid tumors

The **largest** commercial potential of BI-1206 is for the treatment of **solid tumors**:

- **Enhances the activity** of pembrolizumab
- Demonstrated **synergistic activity** with anti-PD1 in preclinical models
- Strong signals observed **in heavily pretreated patients** with metastatic melanoma (cutaneous and uveal melanoma), and very likely extendable to other tumor types
- **Exceptional safety profile** makes it ideal for a combination component with anti-PD1/L1 in several tumor types

BI-1206 IN SOLID TUMORS: COMBINATION WITH **PEMBROLIZUMAB**

Promising efficacy signals in Phase 1

(December 2024)

- **1 complete response (CR)** (lasting for approx. two years)
- **1 partial response (PR)** in uveal melanoma
- **8 patients with stable disease (SD)** including one long-lasting (≥ 2.5 years)
- **28 evaluable patients**
- Co-administration of BI-1206 with pembrolizumab was **well-tolerated** in a heavily pretreated population

Abstract #2593

Phase 1/2a Clinical Trial of BI-1206, an Anti-CD32b (FcyRIIB) Antibody, in Combination with Pembrolizumab in Subjects with Advanced Solid Tumors Previously Treated with Anti-PD-1/L1

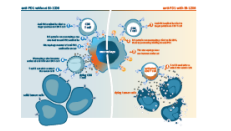
A. Caronni, J. Vachani, S. Akhavan, F. Asari, G. Falck, V. P. M. Burgener, L. M. M. ...

Conclusions

Co-administration of BI-1206 with pembrolizumab was well tolerated in a heavily pretreated population, with promising responses to treatment observed in melanoma, including uveal melanoma, who previously failed anti-PD1 therapy.

Background

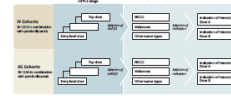
PD-1 blockade has demonstrated positive anti-tumor activity across multiple tumor types. While the anti-tumoral response can be substantial and even curative, response rates remain low in many cancer types. Long-lasting responses are only observed in a minority of patients, and additional immunotherapeutic strategies are needed.



Methods

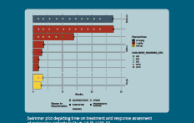
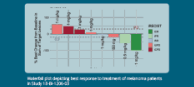
This is a Phase 1 trial in patients with advanced solid tumors who received prior treatment to evaluate safety, tolerability and PD-1 or BI-1206 as monotherapy and in combination with pembrolizumab 200 mg Q3W using a PR3 design.

Phase 2 will assess the efficacy of BI-1206 and pembrolizumab in immunogenic tumors at PD-1, followed by a dose optimization phase for safety/efficacy in indications with positive signals.



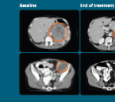
CD32b blockade by BI-1206 in combination with pembrolizumab lead to responses in melanoma patients who previously failed on anti-PD1 therapy

IV administration of BI-1206 lead to sustained blockade of CD32b for 5-7 days. This may be important to maximize anti-PD-1 efficacy, sparing FcγR-dependent CD8+ T cell phagocytosis and minimizing PD-1/L1 immune-suppressive signaling. Subcutaneous administration shows great promise to provide a further extended duration of receptor occupancy with increased tolerability.



Case study 1: PR

68 YO female, uveal melanoma. No response to prior immunotherapy or chemotherapy. Multiple lines of FCR and ChemP. Progression when entering Study. Dose-to-toe and partial response at 100 mg on BI-1206 in combination with pembrolizumab 200 mg Q3W during active tumor response. Control with tumor burden reduced by 50% at end of trial.



Timepoint	CD8+ T cells	PD-1 expression
Baseline	Low	High
10 weeks	High	Low
20 weeks	High	Low
30 weeks	High	Low

Case study 2: SD

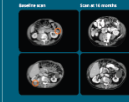
78 YO female, with stage IV melanoma. 8 lines of prior treatment. Toxicity of these prior lines prevented PD therapy and PD-1, CTLA-4, and a 100 mg BI-1206 in combination with pembrolizumab 200 mg Q3W during active tumor response. Control with tumor burden reduced by 50% at end of trial.



Timepoint	CD8+ T cells	PD-1 expression
Baseline	Low	High
10 weeks	Low	High
20 weeks	Low	High
30 weeks	Low	High

Case study 3: CR

77 YO male melanoma patient, Stage IV. Deep Tumor Response at 100 mg BI-1206 in combination with pembrolizumab 200 mg Q3W during active tumor response. Control with tumor burden reduced by 50% at end of trial.



Timepoint	CD8+ T cells	PD-1 expression
Baseline	Low	High
10 weeks	High	Low
20 weeks	High	Low
30 weeks	High	Low

Results

Dose escalation with BI-1206 intravenously (IV) has been completed with the final BI-1206 dose of 0.5 mg/kg through 2.5 mg/kg. The most frequent side effect observed was rash (30.0% overall incidence). Adverse events were generally mild to moderate. Adverse events were generally mild to moderate. Adverse events were generally mild to moderate.

Subcutaneous (SC) administration of BI-1206 was well tolerated with no significant local reactions. In addition to mitigating the SC administration also led to extended duration of blockade, as demonstrated through prolonged receptor occupancy by CD32b. SC dose escalation is still ongoing.

Subjects were heavily pretreated, with a median of 4 lines of therapy, and most patients had received previous immunotherapy. 28 patients had received prior anti-PD-1 therapy, 19 of which had progressed within 12 months.

After receiving BI-1206-pembrolizumab, 7 patients showed a CR, including one lasting 24 months in a heavily treated metastatic melanoma patient. Furthermore, long-lasting PR (24 months) was observed in a uveal melanoma patient, and confirmed CR was observed in a metastatic melanoma patient who previously received three prior anti-PD-1 containing treatments (one including anti-CTLA4).

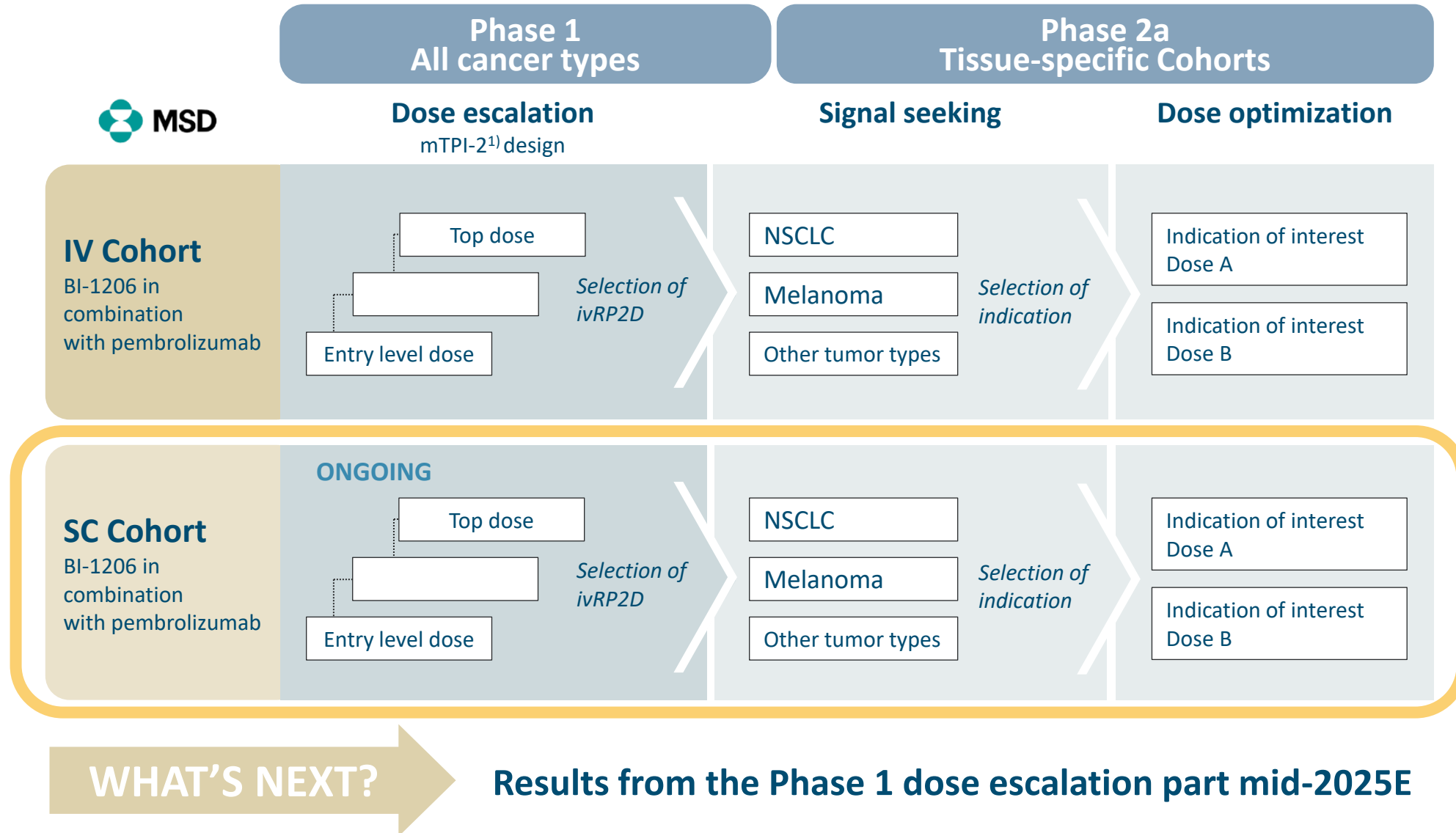
Case	Response	Duration	Notes
1	CR	24 months	Uveal melanoma
2	PR	24 months	Metastatic melanoma
3	CR	24 months	Metastatic melanoma
4	SD	2.5+ years	Metastatic melanoma
5	SD	2.5+ years	Metastatic melanoma
6	SD	2.5+ years	Metastatic melanoma
7	SD	2.5+ years	Metastatic melanoma
8	SD	2.5+ years	Metastatic melanoma
9	SD	2.5+ years	Metastatic melanoma
10	SD	2.5+ years	Metastatic melanoma
11	SD	2.5+ years	Metastatic melanoma
12	SD	2.5+ years	Metastatic melanoma
13	SD	2.5+ years	Metastatic melanoma
14	SD	2.5+ years	Metastatic melanoma
15	SD	2.5+ years	Metastatic melanoma
16	SD	2.5+ years	Metastatic melanoma
17	SD	2.5+ years	Metastatic melanoma
18	SD	2.5+ years	Metastatic melanoma
19	SD	2.5+ years	Metastatic melanoma
20	SD	2.5+ years	Metastatic melanoma
21	SD	2.5+ years	Metastatic melanoma
22	SD	2.5+ years	Metastatic melanoma
23	SD	2.5+ years	Metastatic melanoma
24	SD	2.5+ years	Metastatic melanoma
25	SD	2.5+ years	Metastatic melanoma
26	SD	2.5+ years	Metastatic melanoma
27	SD	2.5+ years	Metastatic melanoma
28	SD	2.5+ years	Metastatic melanoma

Future plans
If data meet has been selected for signal testing in Phase 2/3 trials, with optimization dose for use of SC in Phase 2 will be determined after completion of dose escalation. The Phase 2/3 trials will be designed to evaluate the efficacy of BI-1206 in combination with pembrolizumab in subjects with advanced solid tumors (e.g., NSCLC, melanoma, and other tumors) who previously received prior anti-PD-1 immunotherapy. If positive efficacy signal is confirmed, an additional well-separated dose level will be included for dose optimization for safety, tolerability and efficacy. Dose optimization may be performed against more than one dose level formulation.



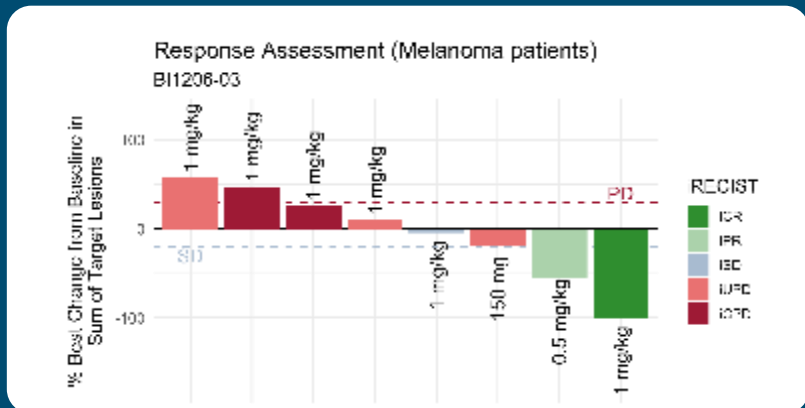
Further Phase 1 data BI-1206 & pembrolizumab* mid-2025E

PLANS FORWARD – STUDY DESIGN BI-1206 IN SOLID TUMORS



¹⁾ modified Toxicity Probability Interval 2

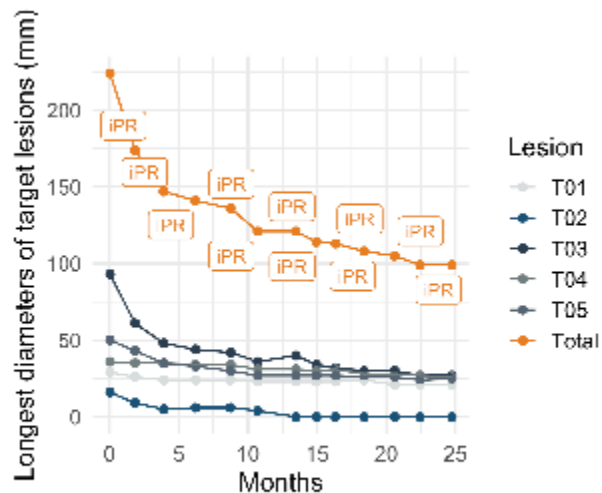
Co-administration of BI-1206 with pembrolizumab was well-tolerated in a heavily pretreated population, with promising responses observed in melanoma, and uveal melanoma, who previously failed anti-PD1 therapy.



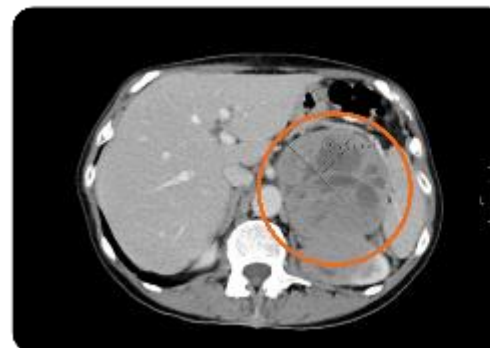
Case study: PR

69 YO female with **uveal melanoma**.

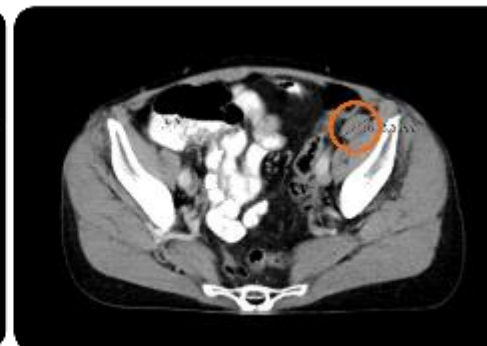
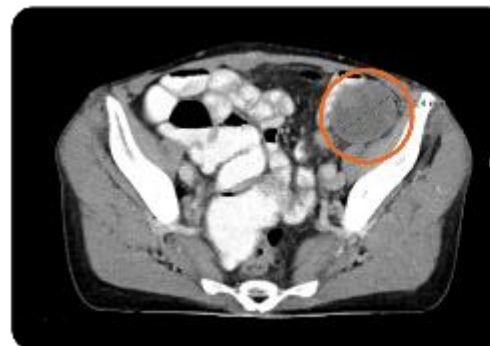
No response to prior immunotherapy or chemotherapy. Multiple lines of ICIs and Chemo. Progressing when entering study. Showed early partial response at first scan on BI-1206 + pembrolizumab, continued PR deepening during whole study duration (2years) with tumor burden reduced by 56% at end of trial.



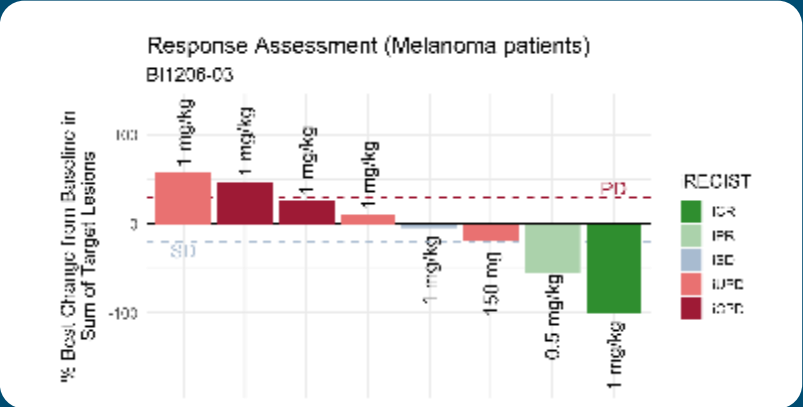
Baseline



End of treatment 2 years

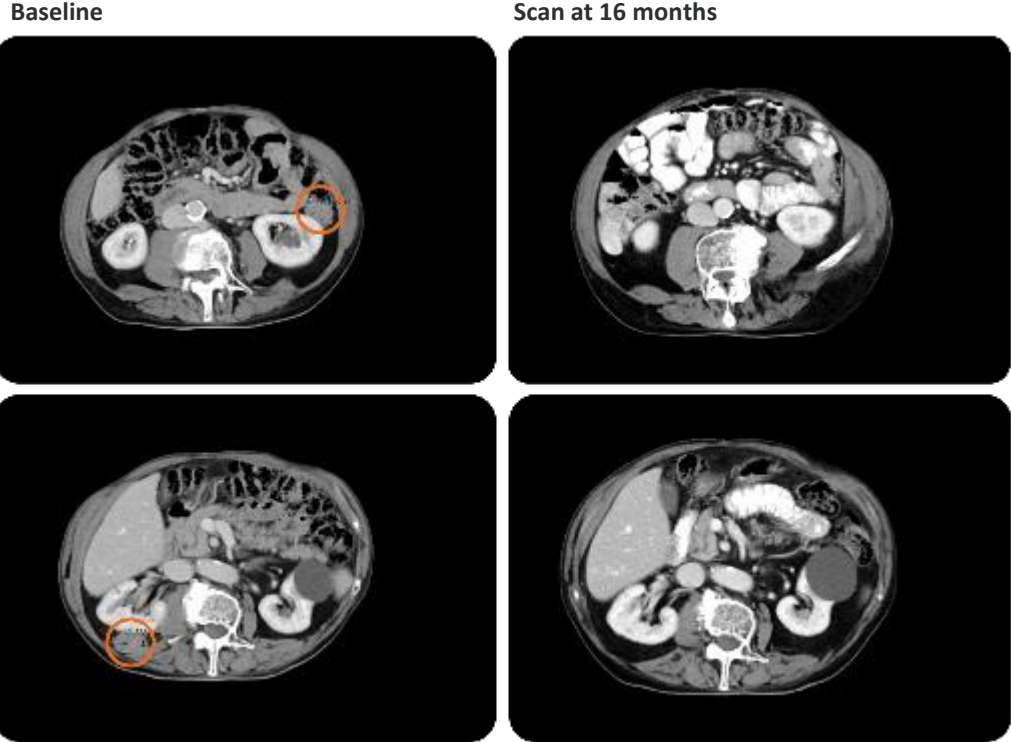
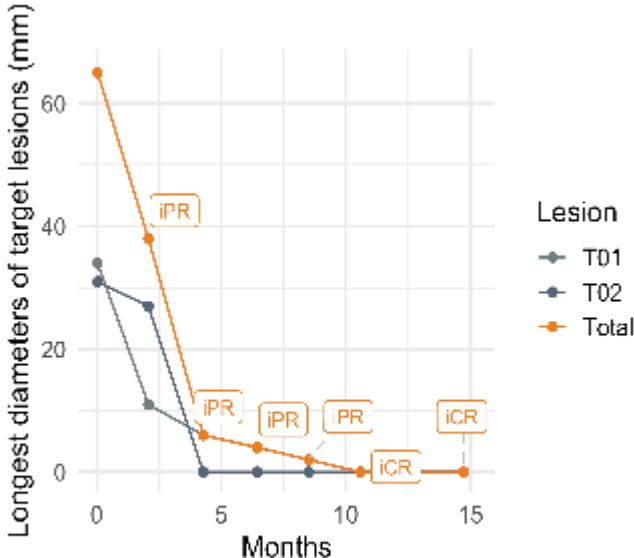


Co-administration of BI-1206 with pembrolizumab was well-tolerated in a heavily pretreated population, with promising responses to treatment observed in melanoma, including uveal melanoma, who previously failed anti-PD1 therapy.



Case study: CR

77 YO male melanoma patient, stage IV. Deep Partial Response at first scan at 2 months, evolving to CR at 10 months, still ongoing at 16 months. Three lines of previous ICI therapy, with PR as best prior response to ipilimumab + nivolumab.



BI-1607 HAS THE POTENTIAL TO INCREASE EFFICACY OF OTHER ANTIBODY DRUGS

BI-1607 has an antagonistic function

Blocking the inhibitory function of immune effector cells

- Tumor-associated macrophages express high levels of FcyRIIB and a major target of BI-1607 in the tumor microenvironment
- Given its high specificity and affinity for FcyRIIB, BI-1607 blocks other antibodies' binding to FcyRIIB
- Engineered for reduced Fc-binding, resulting in a differentiated mechanism of action vs BI-1206

Well-tolerated and stable disease in 6/11 patients

Phase 1 data of BI-1607 + trastuzumab presented at the San Antonio Breast Cancer Symposium Dec 2023.

Phase 1/2a Open-label Clinical Trial of BI-1607, an Fc Engineered Monoclonal Antibody to CD32b (FcyRIIB), in Combination with Trastuzumab in Subjects with HER2-positive Advanced Solid Tumors – CONTRAST

Julian Cortes¹, Anand Singh¹, Sina Samadpour¹, Sarah Rajan¹, Simon B Lord¹, Thomas O'Connor¹, Sharika Kumari¹, Shiva J Chakki¹, Maria Sotgiu¹, Ingrid Karkov¹, Linda Mitterbauer¹, Anna Kopyeva¹, Ingrid Righi¹, John Walker¹, Ellen Frensdorfer¹, Andrea Molinari¹

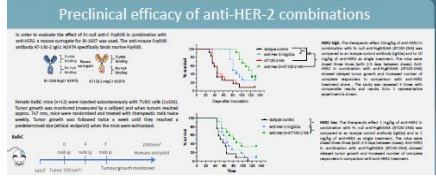
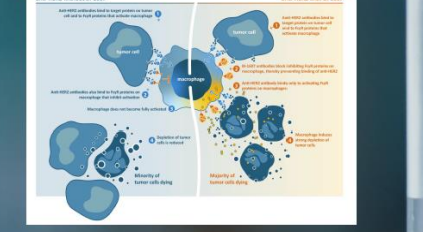
¹University of Leeds, ²Beckwith Pharmaceutical Research Center (BRCC), ³Paycom Software, ⁴University of Groningen, ⁵University of Cologne, ⁶University of Oxford, ⁷University of Cambridge, ⁸University of Liverpool, ⁹University of Manchester, ¹⁰University of Nottingham, ¹¹University of Southampton, ¹²University of Warwick, ¹³University of York, ¹⁴University of Exeter, ¹⁵University of Bath, ¹⁶University of Bristol, ¹⁷University of Hull, ¹⁸University of Lincoln, ¹⁹University of Northampton, ²⁰University of Northumbria, ²¹University of Salford, ²²University of Sheffield, ²³University of Stirling, ²⁴University of Strathclyde, ²⁵University of Sunderland, ²⁶University of Teesside, ²⁷University of Trier, ²⁸University of Ulster, ²⁹University of Westminster, ³⁰University of Winchester, ³¹University of Worcester, ³²University of York

Background

The introduction of trastuzumab has dramatically changed outcomes in patients with human epidermal growth factor receptor 2 positive (HER2+) cancer. However, primary or acquired resistance to trastuzumab has been increasingly recognized as a major obstacle in the clinical management of this disease. Combination of anti-HER2 antibodies with other immunotherapies is likely to improve the quantity and quality of responses. BI-1607 is a human monoclonal antibody (mAb) targeting FcyRIIB (CD32b) with antagonistic function capable of blocking the inhibitory function of FcyRIIB on immune effector cells. BI-1607 has been engineered to not a glycan in position N297C in the constant domain (Fc), and thus cannot interact with FcγRIIIb through its Fc. Given its high specificity and affinity for FcyRIIB, BI-1607 blocks other antibodies binding to FcyRIIB. As a result, BI-1607 is expected to shift tumor cells cancer antibodies (here anti-HER2) to selectively engage activating FcγRIIb, thus augmenting FcγRIIb-dependent therapeutic activity (ADCC, ADCP).

Tumor-associated macrophages express high levels of FcγRIIb and are a major target of BI-1607 in the tumor microenvironment. This concept was demonstrated in preclinical in vivo models showing increased efficacy of the combination therapy with the mutated surrogate of BI-1607 and an anti-HER2, an anti-cytotoxic T lymphocyte-associated protein 4 (CTLA-4), and an anti-CD137 (Hv100) in compared to monotherapy. It is important to note that BI-1607 will have no single-agent activity. Instead, its clinical use will be in combination with other immunotherapies and tumor-killing antibodies such as trastuzumab. Preclinical data indicate the combination retains the efficacy of anti-HER2 therapy with lower doses of anti-HER2, as well as increased efficacy also in HER2-low tumors.

The choice of trastuzumab as the combination agent in this trial was based on promising preclinical studies, a recognized need for additional options for those patients who do not respond or only respond to trastuzumab, and promising results from the newly approved Fc-engineered anti-HER2 mAb margetuximab. Ultimately, if shown to be safe and effective in combination with trastuzumab, BI-1607 can also be used in combination with other cytotoxic or immunomodulatory antibodies for cancer treatment.



Methods

This is a Phase 1/2a, first-in-human, open-label, multi-center, dose-escalation, consecutive-cohort study of BI-1607 in combination with trastuzumab in subjects with HER2+ advanced solid tumors. Phase 1 aims to assess safety and tolerability and to determine the MTD of BI-1607 in combination with trastuzumab.

Phase 2a will explore efficacy in RP2D of BI-1607 in combination with trastuzumab in two separate expansion cohorts:

- a) in subjects with locally advanced or metastatic HER2+ breast cancer and
- b) in subjects with HER2+ metastatic gastric or gastroesophageal junction adenocarcinoma.

Eligible patients must have a HER2+ locally advanced unresectable or metastatic solid tumors and have received standard of care or be intolerant to standard of care anti-HER2 therapy with progressive disease after the last line of treatment.

Patients are treated with BI-1607 in combination with trastuzumab once every 3 weeks. After first disease assessment at week 4, patients with progressive disease (PD) are discontinued from treatment, while patients with stable disease (SD), partial response (PR), or complete response (CR) may continue treatment for up to 2 years.

Phase 1

As of November 9th 2023, 11 patients have been treated at doses ranging from 100 to 1000 mg. All patients have tolerated the treatment well with no serious adverse events related to BI-1607 observed (SAEs). Adverse reactions (AR) of lower grade in the 100 mg cohort, 2 patients experienced grade 1-2 ARs. All patients experienced grade 1-2 ARs. All patients experienced grade 1-2 ARs. All patients experienced grade 1-2 ARs.

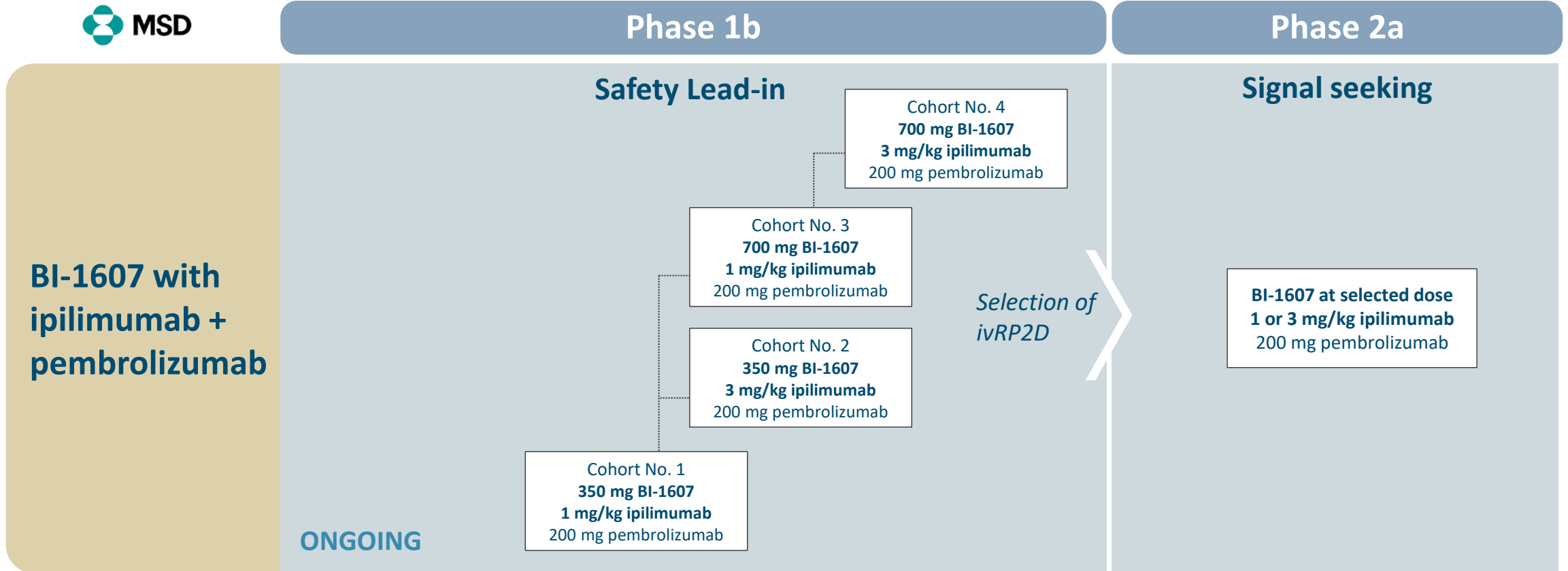
BI-1607 exhibits non-linear pharmacokinetics in line with expectations for a therapeutic antibody. Effective half-life in the therapeutic dose range is approximately 2 weeks. Dose levels of 500 mg and above are expected to achieve full target coverage throughout the three weekly dose intervals, which was confirmed by observed receptor occupancy data.

As trastuzumab-containing therapies may carry a risk for QTc-prolongation, the potential effect of BI-1607 was explored through population-pharmacokinetics. No positive correlation between BI-1607 serum concentration and QTcP or heart rate was found. This further supports the combination of BI-1607 and trastuzumab as a safe combination. Additional exposure-safety analysis of various exposure metrics is in progress. No statistically significant correlation to dose, such as a potential correlation to infusion duration.

BI-1607 was tolerated well in heavily pretreated patients with advanced solid tumors. Disease control was observed in 4/11 evaluable patients who had previously received standard of care anti-HER2 therapy with progressive disease after the last line of treatment. Pharmacokinetic and premonoclonal data showed identification of a wide weak dose range can be achieved.

Given the encouraging results observed in this heavily pre-treated patient population, the activity of BI-1607 in combination with trastuzumab and other monoclonal antibodies is being explored in a Phase 2a study.

BI-1607 PHASE 1B/2A CLINICAL STUDY DESIGN



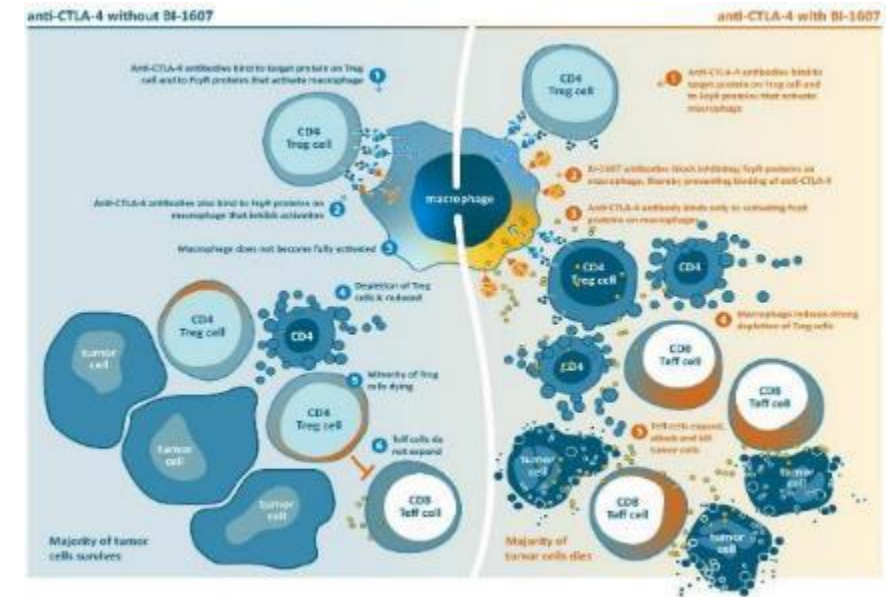
WHAT'S NEXT?

First Phase 1b data BI-1607 + ipilimumab + pembrolizumab H2 2025E

BI-1607: POSITIVE CLINICAL PHASE 1 DATA, **TRIPLET STUDY** ONGOING

Phase 1b/2a ongoing since Dec 2024

- Evaluating safety and anti-tumoral activity
- 2 dose levels of **BI-1607** with 2 dose levels of **ipilimumab (anti-CTLA-4)** (1 and 3 mg/kg) in combination with 200 mg flat dose of **pembrolizumab***
- Patients with unresectable or **metastatic melanoma**, previously treated with anti-PD-1/L1
- Includes an exploratory part assessing **lower doses of anti-CTLA-4**



Preclinical studies indicate that a triple combination regimen including BI-1607 could allow the use of **lower doses of ipilimumab**, potentially achieving increased tolerability and higher efficacy.

BEST CLINICAL RESPONSES IN LEAD PROGRAMS BI-1808 AND BI-1206

(cut-off DEC 2024)

BI-1808 single agent

1 CR in Ovarian Cancer
1 PR in GIST
9 patients with SD
26 evaluable patients

CTCL cohort:

3 PR
1 patient with SD
4 evaluable patients

BI-1910 single agent

6 patients with SD
12 evaluable patients

BI-1206 + rituximab in NHL

SC formulation:

2 CR
3 PR
3 patients with SD
9 evaluable patients

IV formulation:

5 CR
1 PR
6 patients with SD
17 evaluable patients

BI-1206 SC + rituximab + acalabrutinib in NHL

1 CR
1 PR
2 evaluable patients

BI-1206 + pembrolizumab in solid tumors

1 CR
1 PR
8 patients with SD
24 evaluable patients

CR = complete response PR = partial response SD = stable disease



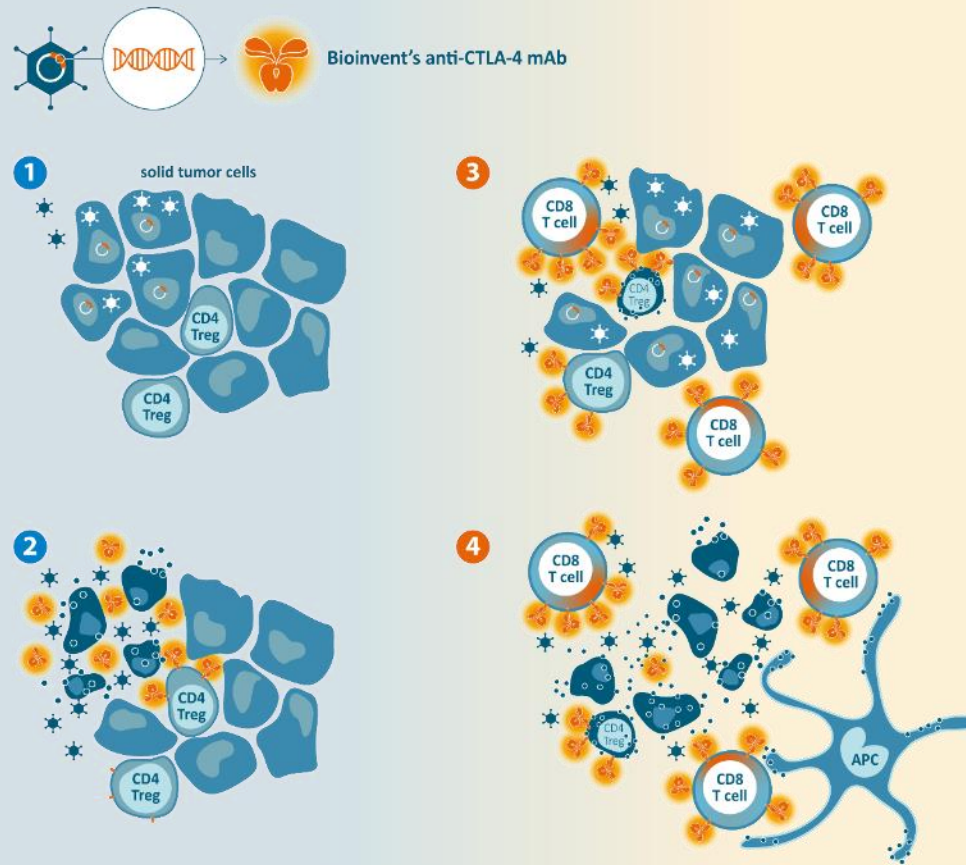
ANTI-CTLA-4

ONCOLYTIC VIRUS BT-001

BT-001: PHASE 1/2A ONGOING

50/50 PARTNERSHIP WITH TRANSGENE TO DEVELOP NEXT GENERATION ONCOLYTIC VIRUSES

mAbs and oncolytic virus attack the solid tumor together



Oncolytic virus & anti-CTLA-4 antibody combination elicits stronger antitumor response & targeted expression of anti-CTLA-4 antibody to improve safety profile

Journal for
Immunotherapy of Cancer

Vectorized Treg-depleting α CTLA-4 elicits antigen cross-presentation and CD8⁺ T cell immunity to reject 'cold' tumors

Monika Semmrich,¹ Jean-Baptiste Marchand,² Laetitia Fend,² Matilda Rehn,¹ Christelle Remy,² Petra Holmkvist,¹ Nathalie Silvestre,² Carolin Svensson,¹ Patricia Kleinpeter,² Jules Deforges,² Fred Junghus,¹ Kirstie L Cleary,³ Mimoza Bodén,¹ Linda Mårtensson,¹ Johann Foloppe,² Ingrid Teige,¹ Eric Quéméneur,² Björn Frendeus^{1,3}

To cite: Semmrich M, Marchand J-B, Fend L, et al. Vectorized Treg-depleting α CTLA-4 elicits antigen cross-presentation and CD8⁺ T cell immunity to reject 'cold' tumors. *Journal for Immunotherapy*

ABSTRACT
Background Immune checkpoint blockade (ICB) is a clinically proven concept to treat cancer. Still, a majority of patients with cancer including those with poorly immune infiltrated 'cold' tumors are resistant to currently available ICB therapies. Cytotoxic T lymphocyte-

intratumoral VV_{eat}- α CTLA-4 synergized with α PD-1 to reject cold tumors.
Conclusion Our findings demonstrate in vivo proof of concept for spatial restriction of Treg depletion-optimized immune checkpoint blocking, vectorized α CTLA-4 as a highly effective and safe strategy to target CTLA-4. A

Winner of the 2022 JITC Best Oncolytic and Local Immunotherapy Paper Award



PROMISING BT-001 PHASE 1 COMBINATION DATA AT ESMO 2024

Clinical responses in 2/6 refractory patients when given in combination with pembrolizumab

Phase 1/2a open-label, multicenter, dose-escalation study of BT-001 Part B presented at ESMO September 2024

- BT-001 induces tumor regression in patients who failed previous anti-PD(L)-1 treatment
- In a patient with a heavily pretreated leiomyosarcoma, BT-001 was able to modulate the tumor microenvironment, turning a “cold” tumor to “hot”, enhancing the potential of T cell infiltration and a shift to PD(L)-1 positivity
- Early signs of efficacy with clinical responses observed with BT-001 in combination with KEYTRUDA® (pembrolizumab), in 2 of 6 patients who failed previous treatment

transgene
BioInvent

Initial clinical results of BT-001, an oncolytic virus expressing an anti-CTLA4 mAb, administered as single agent and in combination with pembrolizumab in patients with advanced solid tumors

S. Champier¹, C. Lebbe², J.-F. Barain³, A. Italiano⁴, M. Sakka⁵, C. Spring-Gissel⁶, N. Stojkovic⁷, M. Brandely⁸, A. Sadrouti⁹, A. Ropenga¹⁰, M. Semerich¹¹, A. McAllister¹², M. Chisamore¹³ and P. Cassier⁹

¹Oncology Department (DTEP), Gustave Roussy - Cancer Campus, Villejuif, France; ²Dermatology Dept., Hôpital Saint Louis AP-HP Paris, France; ³King Albert 2 Cancer Institute, US Louvain Saint-Louis, Woluwe-Saint-Lambert, Belgium; ⁴Early Phase Trials Unit, Institute Bergonié Centre Regional de Lutte Contre le Cancer, Bordeaux, France; ⁵Transgene SA, Brach-Defontaine, France; ⁶Bioinvent International AG, Lund, Sweden; ⁷Merck & Co., Inc., Rahway, NJ, USA; ⁸Medical Oncology Department, Centre Leon Berard, Lyon, France

BACKGROUND

- Intratumoral (IT) administration of an oncolytic virus has been shown to induce local systemic antitumor effects through direct tumor cell killing and adaptive cytotoxic T cell response.
- BT-001 is an oncolytic vaccinia virus with enhanced replication selectivity in tumor cells and genetically engineered to express GM-CSF and a novel full-length anti-CTLA4 mAb.
- BT-001 showed strong antitumor activity in various murine tumor models, including immunologically “cold” tumors with enhanced activity when combined with an anti-PD-1 agent.
- BT-001 (I) is a first-in-human dose-escalation trial to evaluate safety, tolerability, and antitumor activity of IT injections of BT-001 alone and in combination with intravenous pembrolizumab in patients with advanced/metastatic solid tumors.

RESULTS

- A total of 24 patients received IT injections of BT-001 every 3 weeks as monotherapy (Part A) at doses of 10⁷ pfu/ml (cohort 1, n=8), 10⁸ pfu/ml (cohort 2, n=8) or 10⁹ pfu/ml (cohort 3, n=8), or combined to 200 mg of IV pembrolizumab (Part B) at the dose of 10⁷ pfu/ml (n=8).
- Treatment was administered until disappearance of all measurable lesions (for BT-001), confirmed disease progression per RECIST, or unacceptable toxicity (for BT-001 and pembrolizumab), for a maximum of 24 months.
- Translational analyses were performed in part A, and consisted of:
 - Virus detection by qPCR in 11 tumor biopsies at baseline and on Day 5 or 10, 2, 4, 6, 8, 10, 14, 16, 18, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, 104, 108, 112, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 160, 164, 168, 172, 176, 180, 184, 188, 192, 196, 200, 204, 208, 212, 216, 220, 224, 228, 232, 236, 240, 244, 248, 252, 256, 260, 264, 268, 272, 276, 280, 284, 288, 292, 296, 300, 304, 308, 312, 316, 320, 324, 328, 332, 336, 340, 344, 348, 352, 356, 360, 364, 368, 372, 376, 380, 384, 388, 392, 396, 400, 404, 408, 412, 416, 420, 424, 428, 432, 436, 440, 444, 448, 452, 456, 460, 464, 468, 472, 476, 480, 484, 488, 492, 496, 500, 504, 508, 512, 516, 520, 524, 528, 532, 536, 540, 544, 548, 552, 556, 560, 564, 568, 572, 576, 580, 584, 588, 592, 596, 600, 604, 608, 612, 616, 620, 624, 628, 632, 636, 640, 644, 648, 652, 656, 660, 664, 668, 672, 676, 680, 684, 688, 692, 696, 700, 704, 708, 712, 716, 720, 724, 728, 732, 736, 740, 744, 748, 752, 756, 760, 764, 768, 772, 776, 780, 784, 788, 792, 796, 800, 804, 808, 812, 816, 820, 824, 828, 832, 836, 840, 844, 848, 852, 856, 860, 864, 868, 872, 876, 880, 884, 888, 892, 896, 900, 904, 908, 912, 916, 920, 924, 928, 932, 936, 940, 944, 948, 952, 956, 960, 964, 968, 972, 976, 980, 984, 988, 992, 996, 1000.
- Tumor response was assessed by the investigator using RECIST v1.1 on Day 1 (week 0), 15 (week 1), 21 (week 2), 28 (week 3), 35 (week 4), 42 (week 5), 49 (week 6), 56 (week 7), 63 (week 8), 70 (week 9), 77 (week 10), 84 (week 11), 91 (week 12), 98 (week 13), 105 (week 14), 112 (week 15), 119 (week 16), 126 (week 17), 133 (week 18), 140 (week 19), 147 (week 20), 154 (week 21), 161 (week 22), 168 (week 23), 175 (week 24), 182 (week 25), 189 (week 26), 196 (week 27), 203 (week 28), 210 (week 29), 217 (week 30), 224 (week 31), 231 (week 32), 238 (week 33), 245 (week 34), 252 (week 35), 259 (week 36), 266 (week 37), 273 (week 38), 280 (week 39), 287 (week 40), 294 (week 41), 301 (week 42), 308 (week 43), 315 (week 44), 322 (week 45), 329 (week 46), 336 (week 47), 343 (week 48), 350 (week 49), 357 (week 50), 364 (week 51), 371 (week 52), 378 (week 53), 385 (week 54), 392 (week 55), 399 (week 56), 406 (week 57), 413 (week 58), 420 (week 59), 427 (week 60), 434 (week 61), 441 (week 62), 448 (week 63), 455 (week 64), 462 (week 65), 469 (week 66), 476 (week 67), 483 (week 68), 490 (week 69), 497 (week 70), 504 (week 71), 511 (week 72), 518 (week 73), 525 (week 74), 532 (week 75), 539 (week 76), 546 (week 77), 553 (week 78), 560 (week 79), 567 (week 80), 574 (week 81), 581 (week 82), 588 (week 83), 595 (week 84), 602 (week 85), 609 (week 86), 616 (week 87), 623 (week 88), 630 (week 89), 637 (week 90), 644 (week 91), 651 (week 92), 658 (week 93), 665 (week 94), 672 (week 95), 679 (week 96), 686 (week 97), 693 (week 98), 700 (week 99), 707 (week 100).

CONCLUSIONS

IT administration of BT-001 in combination with pembrolizumab showed promising early signs of efficacy with documented radiological responses in 20 patients. The trial is still ongoing to further evaluate BT-001 in the dose of 10⁷ pfu/ml, combined with pembrolizumab (cohort 2), in a patient with heavily pretreated leiomyosarcoma. BT-001 treatment in combination with pembrolizumab seemed to not be the major immunomodulator for the tumor microenvironment with a high T cell infiltration and a shift to PD(L)-1 positivity.

ACKNOWLEDGMENTS

The authors wish to thank all patients, clinicians, caregivers and technical staff involved in the project.

TRIAL INFORMATION

Trial sponsored by TRANSGENE, 400 Boulevard Gonthier d'Andemach - Parc Chenevierre - CS20268 - 67405 Illkirch Graffenstaden Cedex - France. This trial is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

TRANSLATIONAL ANALYSES

A. Tumor biopsy analyses (part A)

B. WT Intratumoral collection of anti-CTLA4

C. Anti-vaccinia virus neutralizing antibodies (parts A and B)

Biological fluids analysis (part A)

PD(L)-1 resistant melanoma

Metastatic leiomyosarcoma

CONCLUSIONS

IT administration of BT-001 in combination with pembrolizumab showed promising early signs of efficacy with documented radiological responses in 20 patients. The trial is still ongoing to further evaluate BT-001 in the dose of 10⁷ pfu/ml, combined with pembrolizumab (cohort 2), in a patient with heavily pretreated leiomyosarcoma. BT-001 treatment in combination with pembrolizumab seemed to not be the major immunomodulator for the tumor microenvironment with a high T cell infiltration and a shift to PD(L)-1 positivity.

BT-001: PHASE 1/2A OPEN-LABEL, MULTICENTER, DOSE-ESCALATION STUDY

Ongoing phase

Phase 1A Dose Escalation

BT-001 IT (18 pts)
Metastatic/advanced solid tumors
3 doses

COMPLETED

Phase 1B Dose Escalation

BT-001 IT + Pembrolizumab (12 pts)
Metastatic/advanced solid tumors
RDPB

ONGOING

Phase 2a Expansion Cohorts

BT-001 IT + Pembrolizumab
Tbd: Soft tissue sarcoma, Merkel cell carcinoma, Melanoma, Triple negative breast cancer, Non-small cell lung cancer
RDPB

PLANNED

Main Eligibility Criteria

- 1 injectable lesion 25-50mm in diameter
- ECOG 0-1
- Failed or not eligible for standard of care

Participating Countries

- France, Belgium
- IND approved in US





KEY CATALYSTS 2025

EXPECTED KEY CLINICAL MILESTONES 2025

TNFR2 platform

mid-2025

YE2025

BI-1808

in solid tumors/TCL

Single agent Ph 2a
additional data

Ph 2a data with
pembrolizumab

BI-1910

in solid tumors

Ph 1 single agent data
Ph 1 data with pembro

FcyRIIB platform

BI-1206

in NHL

Ph 2a data with rituximab
+ acalabrutinib

BI-1206

in solid tumors

Ph 1 data with
pembrolizumab

BI-1607

in solid tumors

Ph 1b data with
pembrolizumab +
ipilimumab



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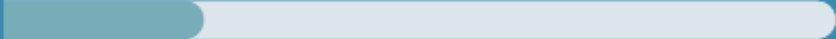




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EXTERNAL PIPELINE (MARCH 2025)

BIOINVENT'S OUT-LICENSING AGREEMENTS FOR PROJECTS IN CLINICAL DEVELOPMENT

Program	Target	Primary indication	Phase 1	Phase 2	Phase 3	Market	Partner
MT-2990	anti-IL33	Vasculitis (ANCA)					Mitsubishi Tanabe
Mezagitamab (TAK-079)	anti-CD38	Primary Immune Thrombocytopenia					Takeda
Orticumab	anti-ApoB100	Cardiovascular					Abcentra
DS-1055	anti-GARP	Solid tumor					Daiichi-Sankyo
HMI-115	anti-PRLR	Alopecia					Hope Medicine/Bayer

BioInvent's external projects are a seal of excellence for the quality of the company's research and development capabilities.