Precision oral medicines with enhanced therapeutic index

Corporate Presentation

Jan 2024

Jubilant Therapeutics: A precision oral therapeutic company focused on oncology

Differentiated Pipeline

JBI-802: coREST inhibitor/Dual epigenetic modulator for synergistic anti-tumor activity in ET/ MPN plus related tumors

JBI-778: brain penetrant PRMT5i with differentiated safety, focused on synthetic lethality and spliceosome mutations

2 IND track programs: PD-L1i brain penetrant; PAD4i in oncology/autoimmune

Improved Therapeutic Index

TIBEO (**T**herapeutic **I**ndex and **B**rain **E**xposure **O**ptimization) discovery engine

Validated with proven track record of partnerships: Lengo – Blueprint

Near-Term Catalysts

JBI-802: Preliminary human proof of principle achieved to support further development in ET/MPN and other hematologic malignancies with neuroendocrine tumors as upside; Early Phase II data by mid-2024

JBI-778: IND approved; Phase I initiation in spliceosome mutated tumors in 1Q 2024

Healthy Financial Position

Continuing support from parent co.; diversifying investor base for growth

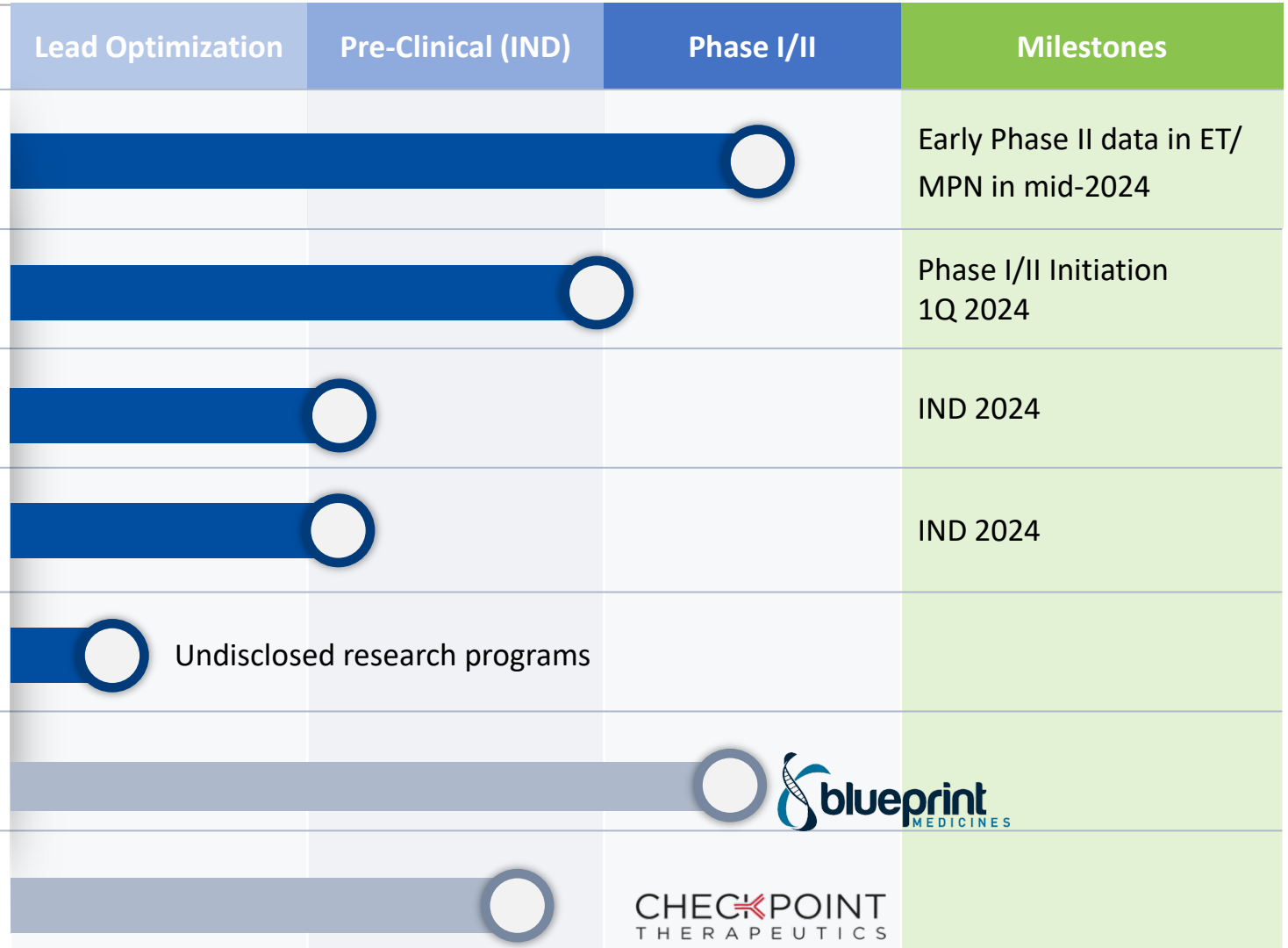
Company has a cost optimized operating model with a focus on value creation

Wholly owned assets; opportunities to maximize partnership to get non-dilutive funding

JUBILANT THERAPEUTICS

Broad Pipeline of Differentiated Assets with Improved Therapeutic Index

Program	Mechanism	Indications	Milestones
JBI-802	coREST Inhibitor/ Epigenetic Modulating Agent	ET/MPN and neuro endocrine tumors	Early Phase II data in ET/ MPN in mid-2024
JBI-778	PRMT5 Inhibitor Brain Penetrant	Spliceosome mutated tumors	Phase I/II Initiation 1Q 2024
JBI-2174	PD-L1 Inhibitor Brain Penetrant	Brain tumor and metastases	IND 2024
JBI-1044	PAD4 Inhibitor	Oncology and auto-immune disease	IND 2024
Other	Various	Various	
EGFR[1,*]		Oncology	
BRD4[*]		Oncology	



- [1]Blueprint Medicines acquired Lengo Therapeutics (Frazier Healthcare entity) for $250M in cash plus $215M in milestone payments
- *Economic rights reside with Jubilant Therapeutics' parent company

Experienced Management

Jubilant Tx Management Team

Syed Kazmi, PhD., MBA
President and CEO

Luca Rastelli, PhD
CSO

Jeremy Barton, MD
Interim CMO

Shyam Pattabiraman
CFO

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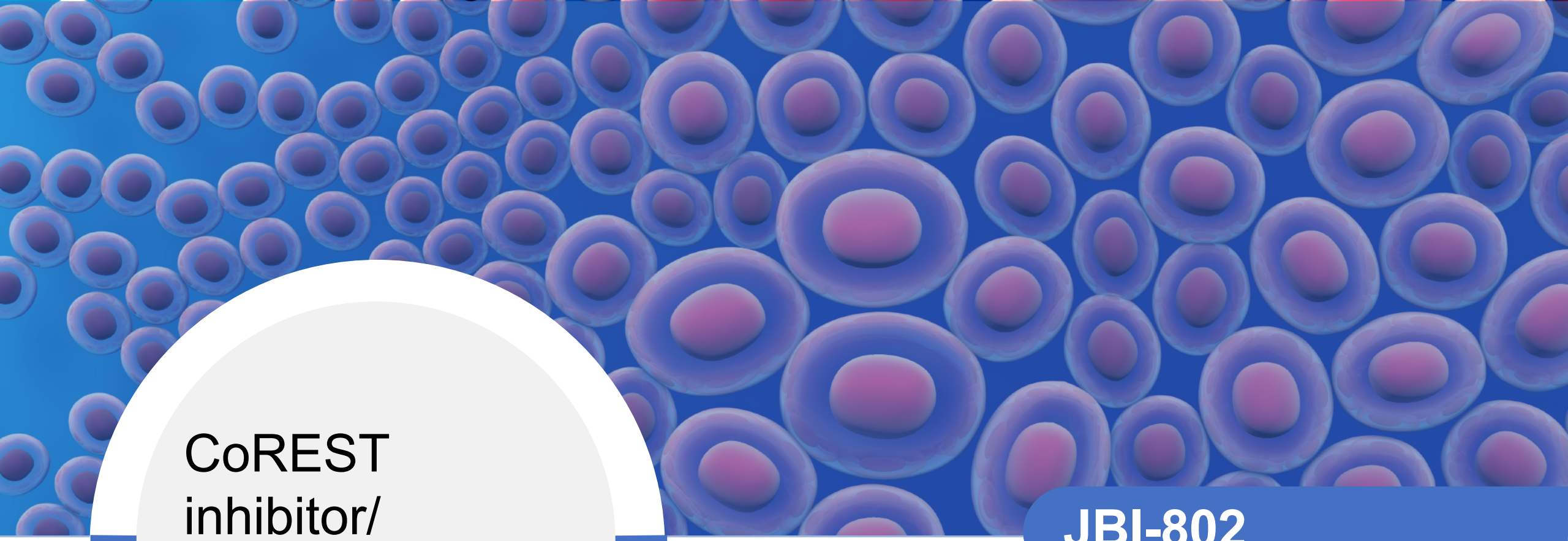

JBI-802

CoREST inhibitor/ Epigenetic Modulating Agent

JBI-802 Highlights: Breakthrough in Epigenetic Therapy of REST-driven tumors

MOA	Novel, oral, potent and selective dual inhibitor of both LSD1 and HDAC6 in low nM range; Targeting stem cell modulation with LSD1; Modulation of immune suppression by inhibition of HDAC6 with 75-100x selectivity
Differentiation	First in class mechanism of inhibiting two epigenetic targets in CoREST complex: Unique pharmacophore leading to faster clearance and better therapeutic index
Clinical opportunities	ET/MPN, MDS, AML, SCLC and neuroendocrine cancer as a monotherapy Potential for combination with checkpoint inhibitors in multiple tumors with IO resistance
Efficacy	Synergistic anti-tumor activity, superior vs either target alone. Enhanced anti-tumor activity in combination with an immune checkpoint inhibitor
Safety	Favorable safety profile with no significant safety concerns or accumulation
Milestones	IND accepted by FDA, Phase I proof of principle achieved, early Phase II data expected mid-2024

JBI-802 Phase I data suggests therapeutic potential in sensitizing immunotherapy resistant tumors and in ET/MPN with thrombocytosis

- 11 patients enrolled, last patient ongoing
- Dose-proportional increases in exposure across cohorts, correlation between exposure and the on-target effects of platelet decrease, as expected based on the well-known LSD1 inhibitors MOA
- 10mg dose is safe, with no platelet decrease and shows biological activity
- 2/2 NSCLC, both IO resistant, patients showed tumor-related symptoms improvements and 1 had confirmed PR. This patient has STK11 mutation, known to induces resistance to IO
- 3 patients have tumor-related symptoms improvements, all of these 3 patients had NO negative effect on platelets
- **Distribution of drug to tissue/tumor might explain activity without toxicity and unique opportunity in NSCLC with STK11 and/or liver metastasis, resistant to IO treatment**
  - *"The anti-tumor activity seen in NSCLC patients is remarkable given the poor prognosis based on their genetic and metastatic pattern. The 10 mg dose of JBI-802 was well-tolerated without any clinically significant adverse effects and the initial clinical data suggest a good therapeutic index for JBI-802" – Dr. Starodub, The Christ Hospital, Cincinnati*
- **Dose dependent platelet decrease shows that JBI-802 is pharmacologically active and represents Proof of Principle in hematological malignancies like Essential Thrombocythemia (ET) and other MPN/ MDS characterized by thrombocytosis**

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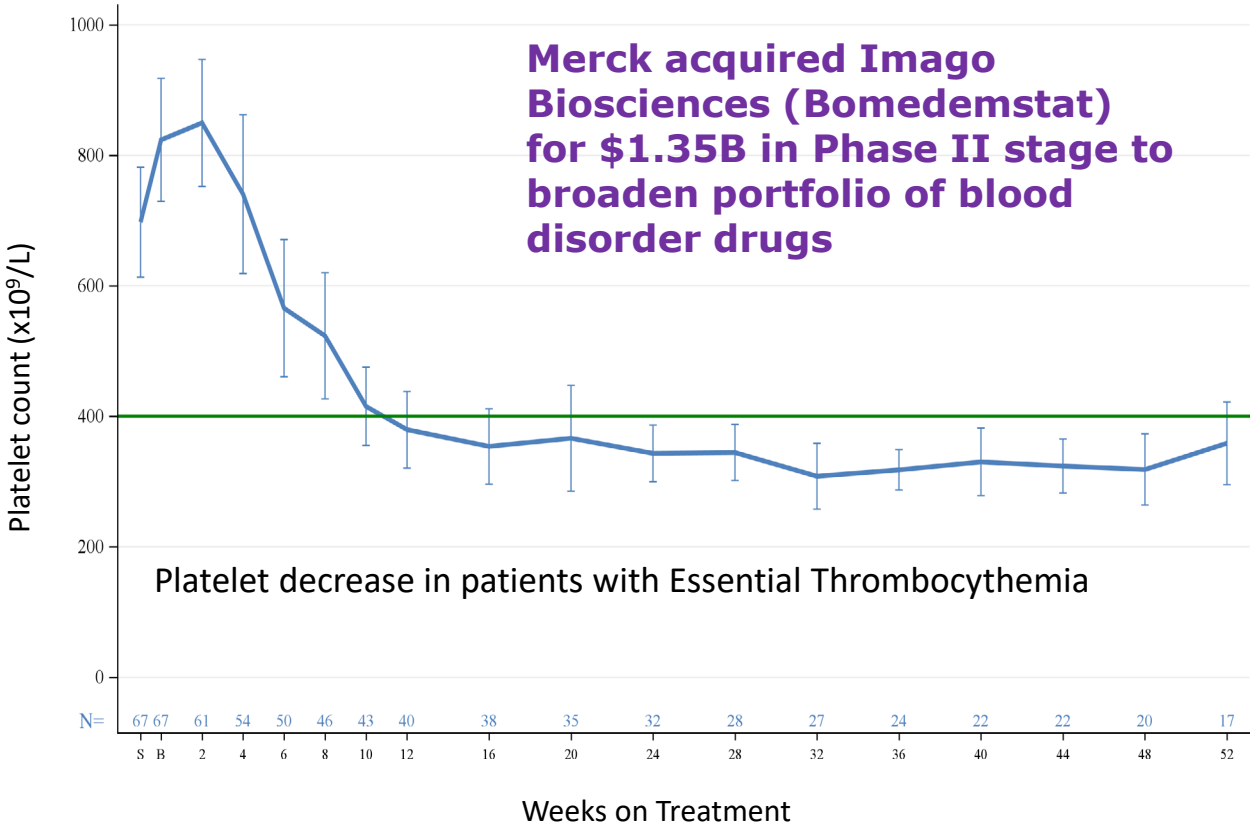
Leveraging LSD1 in Megakaryocytes for the treatment of Essential Thrombocythemia (ET)



Platelet decrease in patients with Essential Thrombocythemia

U.S. ET Market Opportunity for 2nd Line (2L)

80 – 100k
ET Prevalent Population (U.S.)[1]

40 – 50k
50% of patients on cytoreductive therapy[2]

8 – 12.5k
20 – 25% sub-optimal / intolerant to HU[3,4]

LSD1 inhibition blocks MEP-platelet pathway, so it decreases both in tumor and normal cells

Source: 1) Imago Biosciences 2) American Journal of Hematology, Vol. 91, No. 4, April 2016, 3) Blood. 2017;130(17):1889-1897. 4) Journal of Clinical Oncology 2017 35:15_suppl, e18565-e18565

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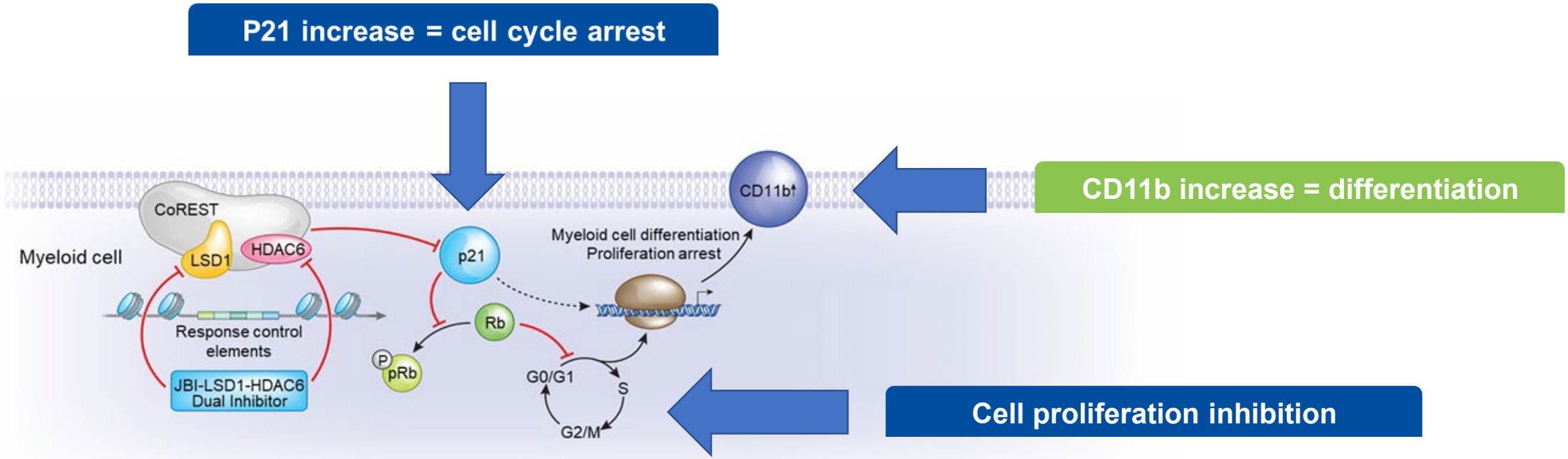
How and Why JB-802 is superior to Bomedemstat in Essential Thrombocythemia?

- **JBI-802 is able to induce faster reduction of platelets (within ~10 days* compared to ~10 weeks**)**
  - JBI-802 induces p21, resulting in deeper proliferation arrest (100% vs 60%) and deeper differentiation
  - It also induces apoptosis as opposed to only growth arrest (these properties are also the basis for JBI-802's activity beyond ET)
- **JBI-802 does not induce Dysgeusia in patients* (compared to 55% incidence**)**
  - JBI-802 volume of distribution in humans is ~20x less than Bomedemstat, so exposure outside blood compartment (likely responsible for Bomedemstat's high incidence of Dysgeusia and other constitutional toxicities) is very limited outside of certain organs like liver
- **JBI-802 does not induce Anemia in patients and in animals* (compared to 16% incidence**)**
  - JBI-802 inhibits not only LSD1, which induces block of MEP differentiation, common precursors of both platelet and erythrocytes, but also HDAC6
  - HDAC6 inhibition is able to stimulate the differentiation of the MEP precursors to form mature erythrocytes to avoid anemia

**JBI-802 Phase I trial – basket tumor patients **Bomedemstat Phase II trial – ET patients*

JBI-802 CoREST inhibition induces tumor cell differentiation and growth arrest



JBI-802 shows deeper increase in differentiation and inhibition of proliferation than Bomedemstat

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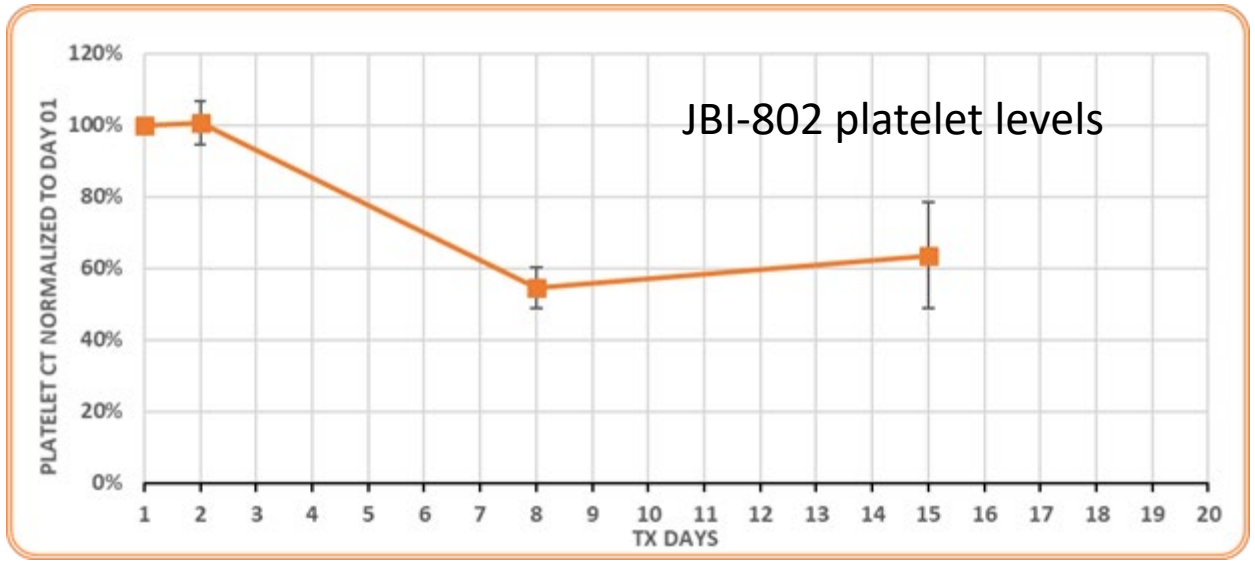
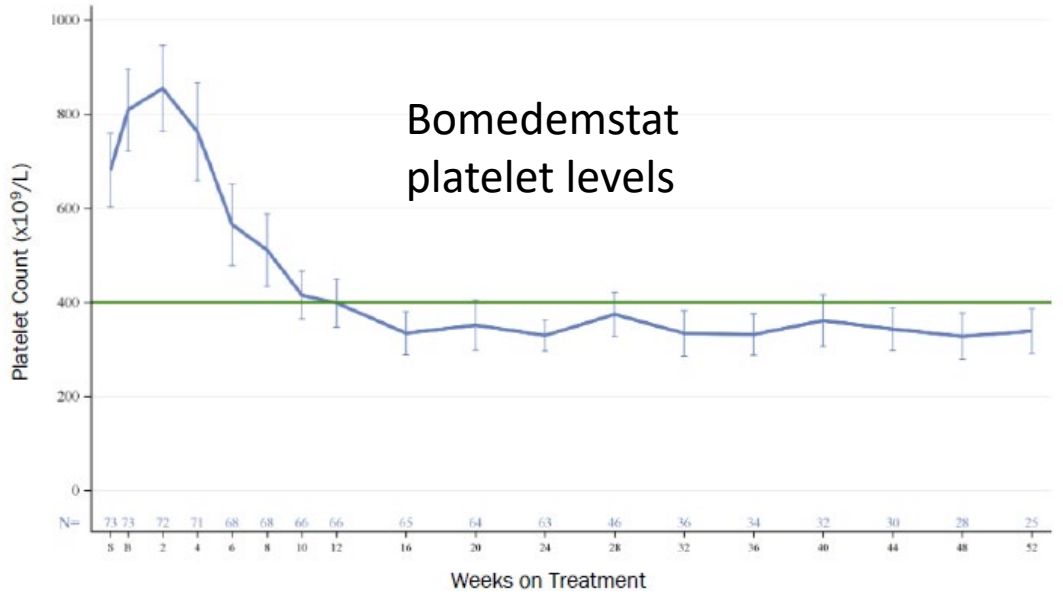
Human proof of principle for JBI-802 with faster onset of clinical activity than Bomedemstat





- Preliminary human data confirms that JBI-802 can induce dose dependent decrease in platelets without effect on erythroid parameters – Proof of Principle for treatment of disease with elevated platelets like ET
- JBI-802 appears to have superior efficacy and induce platelet decrease much faster than Bomedemstat

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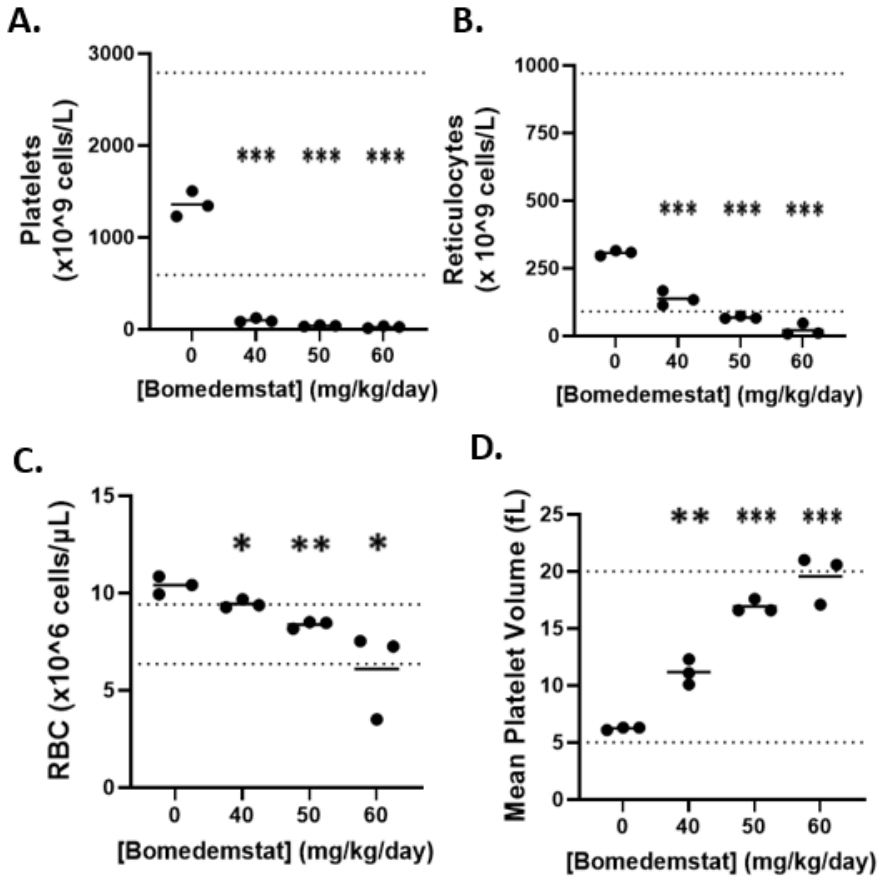
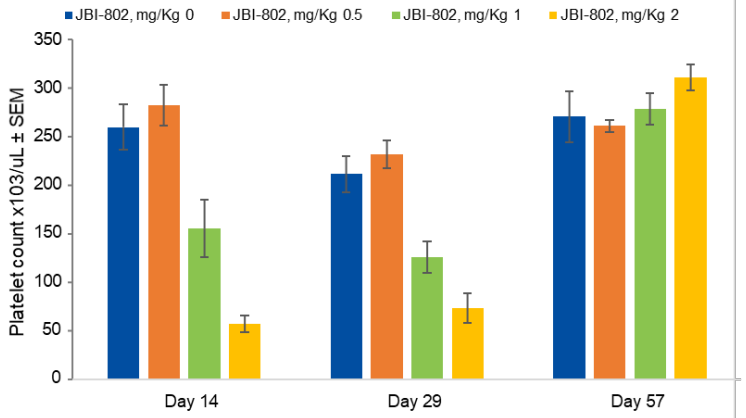
JBI-802 contrary to Bomedemstat has no impact on RBC in animal species

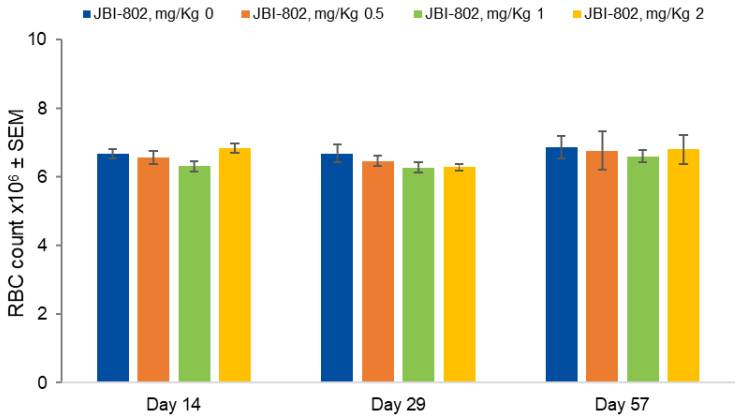
Bomedemstat RBC Modulation: Dose dependent decrease



JBI-802 Platelet Modulation: dose dep decrease



JBI-802 RBC Modulation: no effect



Toxicological experiments confirm JBI-802 ability to decrease platelet levels but no effect on RBC

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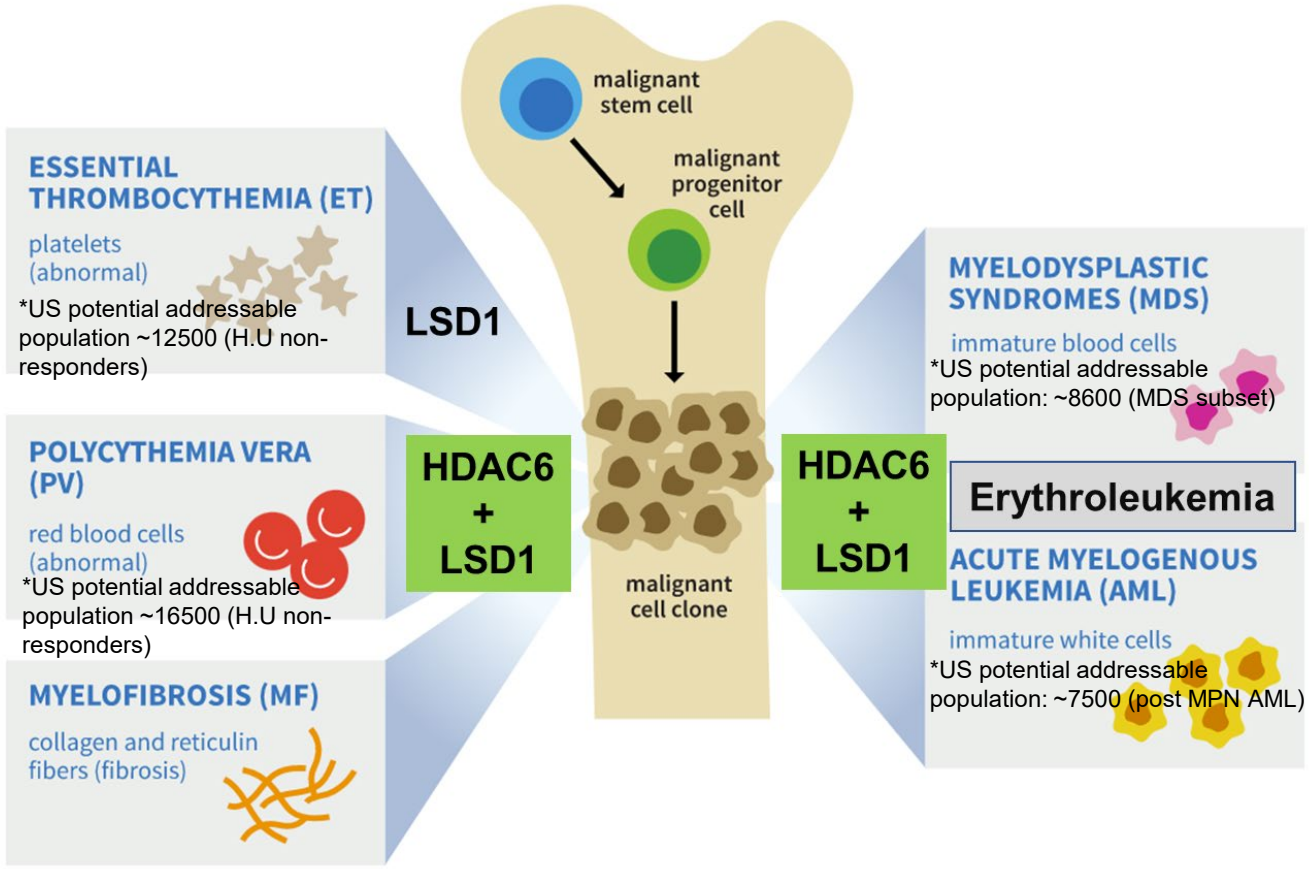
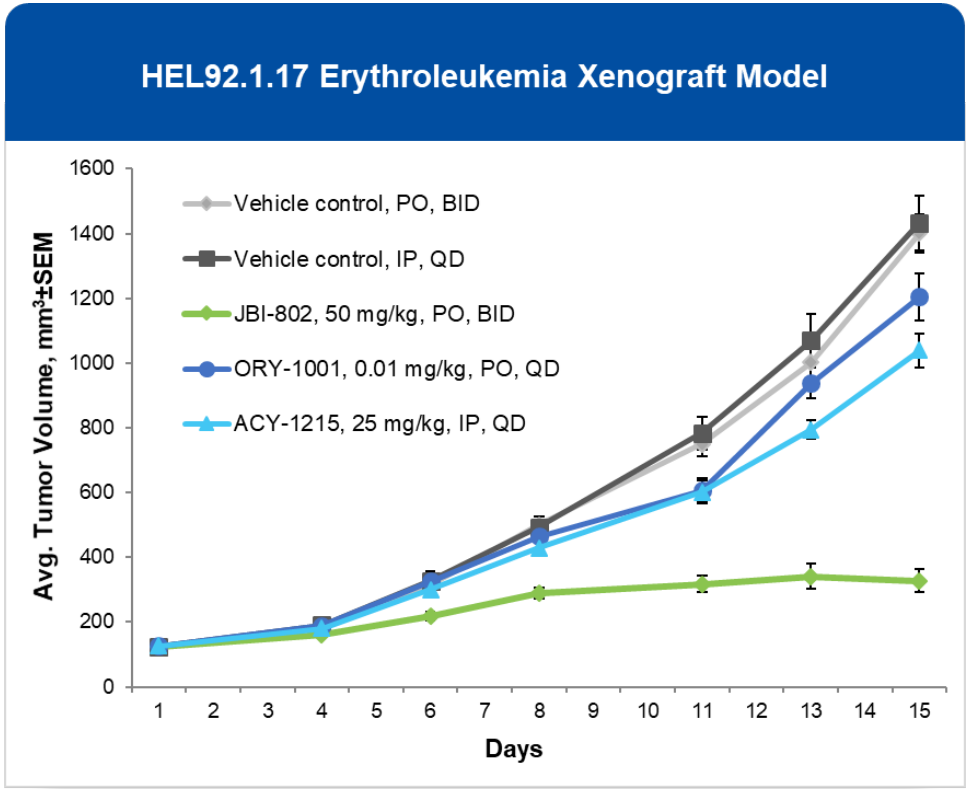
The Dual inhibition LSD1+HDAC6 expands potential beyond ET



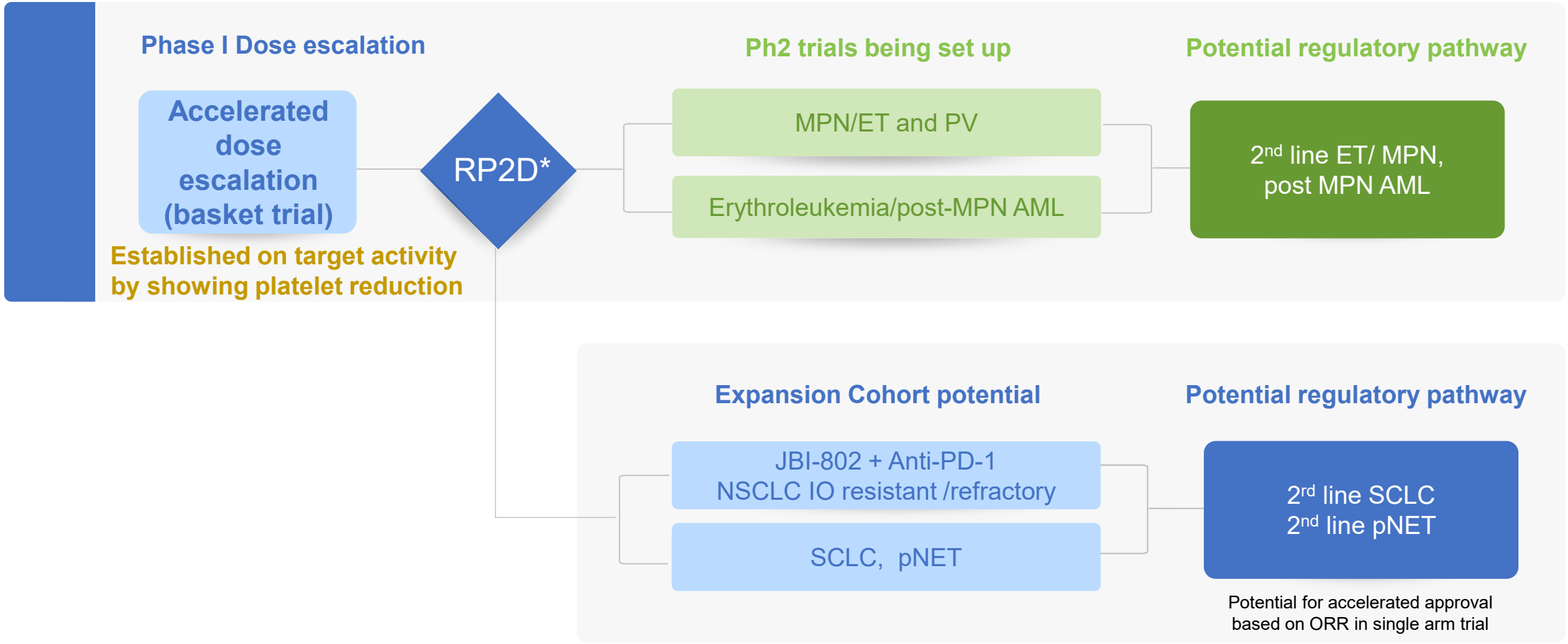


JBI-802 has better efficacy than LSD1i or HDAC6i alone in achieving tumor regression

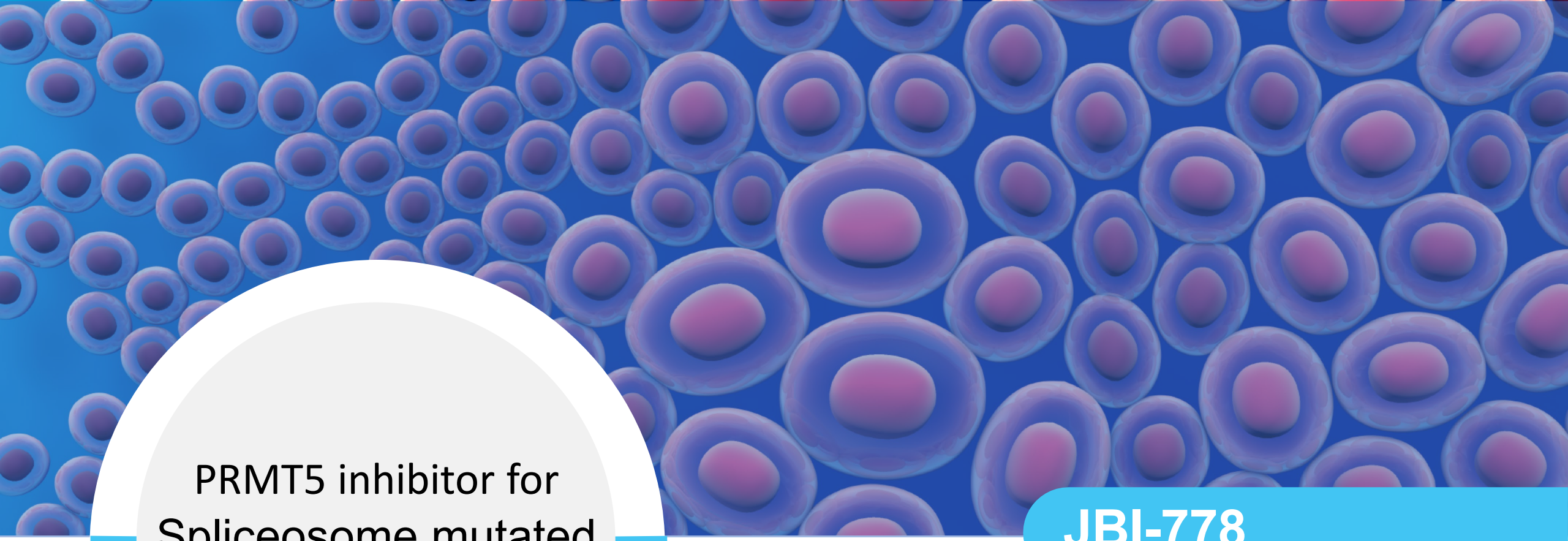
JBI-802: Clinical Trial for ET+ (MPN and MDS/MPN with thrombocytosis)

Study	Heme Study
Phase:	Phase 1/2
Geography:	Australia
Number of patients:	30 Essential Thrombocythemia (ET):~20 other MPN ~10
Indications:	ET+ , where + is patient with MPN and MPN/MDS and MPNu or MPN-BP or MPN-AP with thrombocytosis
Number of clinical sites:	5
CRO finalization:	Q1 FY2024
First Patient In (FPI):	Q2 FY2024 (*to be finalized with CRO*)
Patient enrollment duration:	12-15 months
Treatment / Follow up:	52 weeks
# of cycles	Treatment duration: 28 days • *Average treatment duration is anticipated to be ~52 weeks/patient*

Clinical development: focused on hematologic malignancies with neuroendocrine tumors as upside



MPN: Myeloproliferative neoplasms *SCLC: Small cell lung cancer*
pNET: pancreatic Neuroendocrine tumors *ET: Essential Thrombocythemia* *PV: Polycythemia vera*



PRMT5 inhibitor for Spliceosome mutated tumors

JBI-778

JBI-778 Highlights: Brain penetrant PRMT5i active in both MTAP+/- and spliceosome mutated tumors

MOA	Substrate competitive, SAM co-operative inhibitor of PRMT5 Synthetic lethality demonstrated in cell lines and patient cells with spliceosome mutation
Differentiation	Orally available across species with excellent brain penetration Equally potent both in MTAP WT and MTAP null tumors in-vitro and in-vivo Spliceosome mutation based patient selection
Clinical opportunities	MTAP+/- and spliceosome mutated tumors
Efficacy	Robust anti-proliferative activity across MTAP-WT and MTAP null cell lines In vivo efficacy shown in MTAP mutant models (H460), including in the brain (orthotopic U87) and in MTAP wt model Z138 >> potent than GSK
Safety	Well tolerated in the 28-day GLP toxicity in Rat and Dog (No anemia and changes in platelet observed at the highest dose supported by lack of effect on HSC; No mortality or morbidity observed)
Milestones	IND approved, drug product available Clinical trial initiation in 1Q 2024 in EGFR mutated NSCLC, IDHmutated high grade Glioma, ACC

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How JBI-778 is different from other PRMT5 inhibitors

Differentiation	**SAM Competitive** Pfizer, Prelude, J&J	**MTA Cooperative** Tango, Mirati, Amgen	**JBI-778** **Substrate competitive/ SAM cooperative, Spliceosome selective, Brain penetrant**
MoA	Block the binding of SAM cofactor shared among many other methyltransferases	Stabilizes MTA bond to PRMT5 which is increased in MTAP-deficient tumor Gives opportunity for patient selection and reduction in toxicity	• Target substrate site and stabilize SAM bond to PRMT5 giving high biological selectivity • High and balanced brain penetration gives opportunity in primary tumors as well as brain metastases
Issues	• Blocking a non-selective cofactor could explain non-tolerable toxicity • Limited patient selection strategy	• MTAP deficiency is present in ~10% patients and not applicable to brain since MTA is metabolized in brain	• Address safety issue of 1st generation • Targets broad patient population irrespective of MTAP status • Spliceosome-based patient selection (mutually exclusive from MTAP)
Stage	Phase I/II but terminated due to toxicity and limited efficacy	Phase I/II	IND approved; Phase I/II in 1Q 2024

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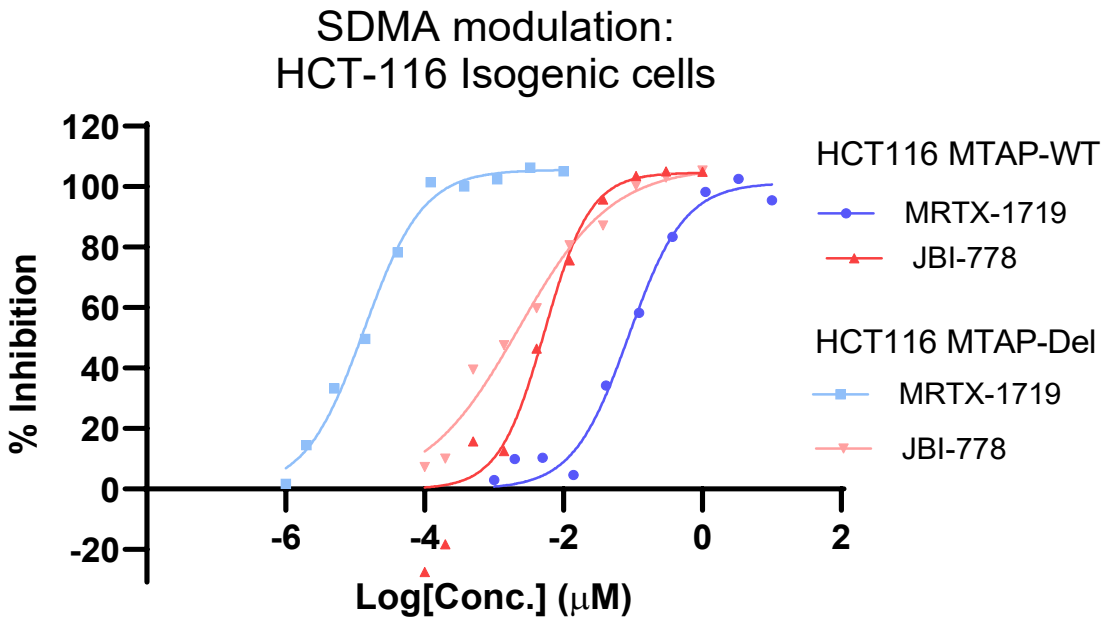
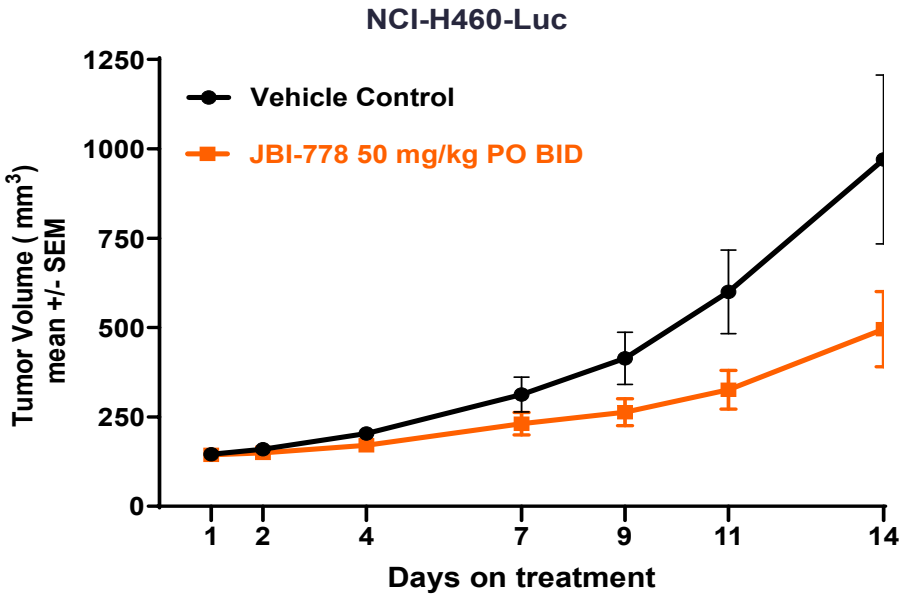
JBI-778 but not MRTX equally potent in MTAP null and WT in-vitro and in-vivo





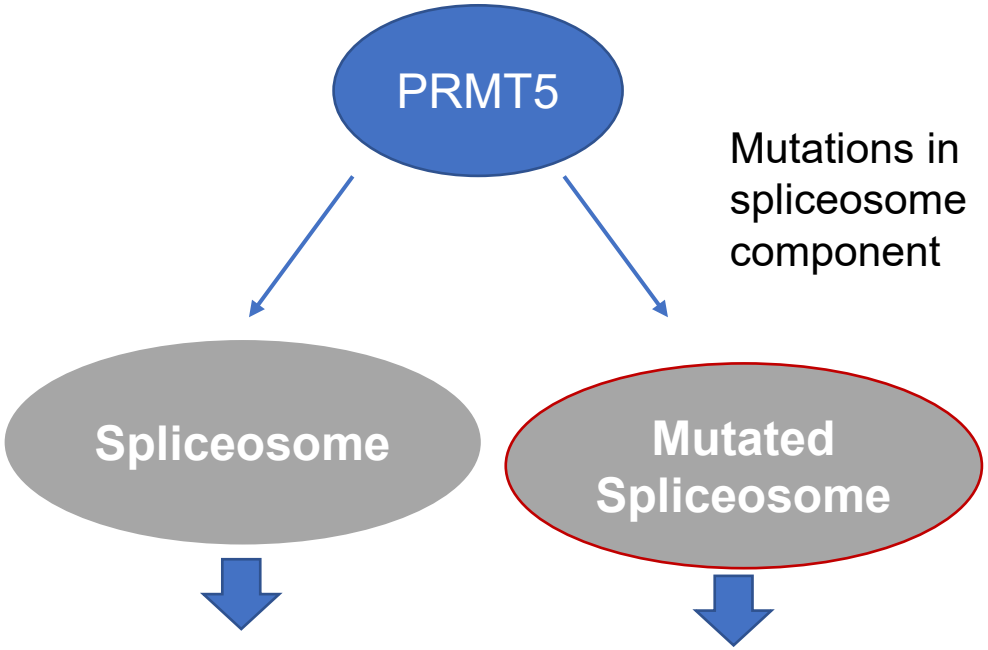
MRTX1719 is only active in MTAP-null cells
JBI-778 is equipotent in MTAP-WT and null cells

JBI-778 is active in-vivo in a MTAPwt lung cancer (and in a MTAP null model U87mg)

Source: Jubilant study

Spliceosome mutations create synthetic lethality with PRMT5 inhibition

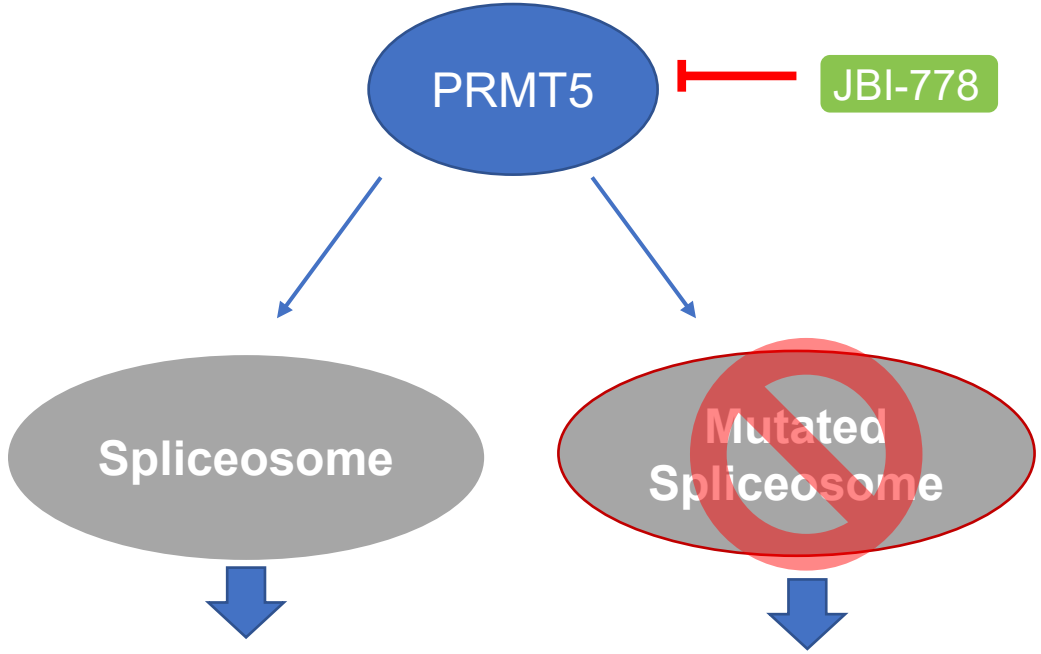
PRMT5 is required for spliceosome activity



Normal cell with fully spliced mRNA

Cancer cell with partially spliced mRNA that increase tumorigenesis

PRMT5 inhibition inactivates splicing



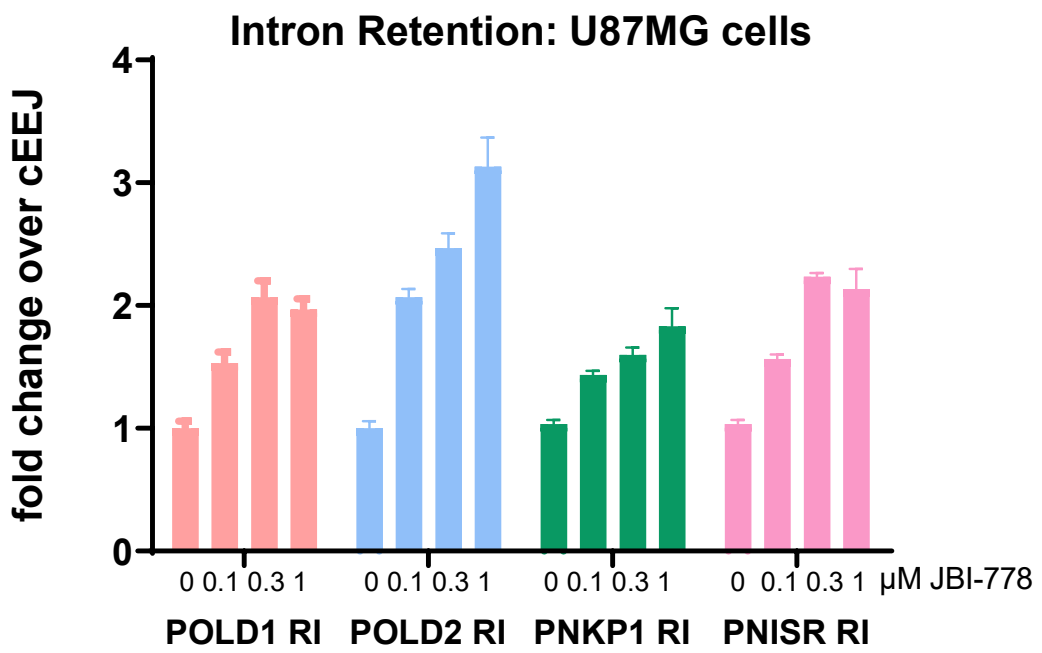
ALIVE normal cell less sensitive to PRMT5 inhibition

DEAD tumor cell due to PRMT5 inhibition blocking most mRNA

Adapted from Jensen-Pergakes et al., MCT, 2022

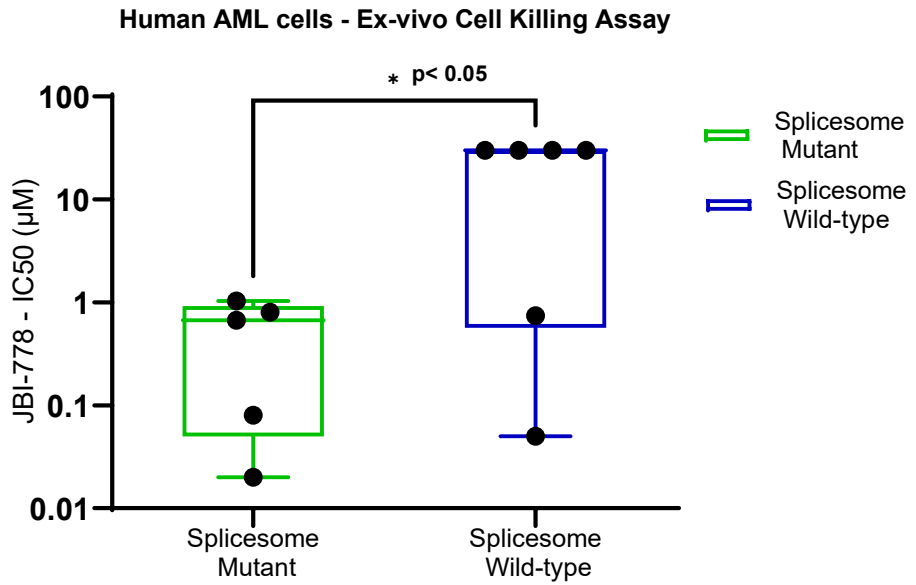
JBI-778 highly sensitive for spliceosome mutated tumors

PRMT5 Inhibition increases intron retention



Spliceosome mutations result in intron retention, leading to translation of non-functional proteins and cell death

Spliceosome mutated patient cells sensitive to PRMT5 Inhibition



JBI-778 is more potent against Spliceosome mutated patient cells (Jubilant data by Champions Oncology)

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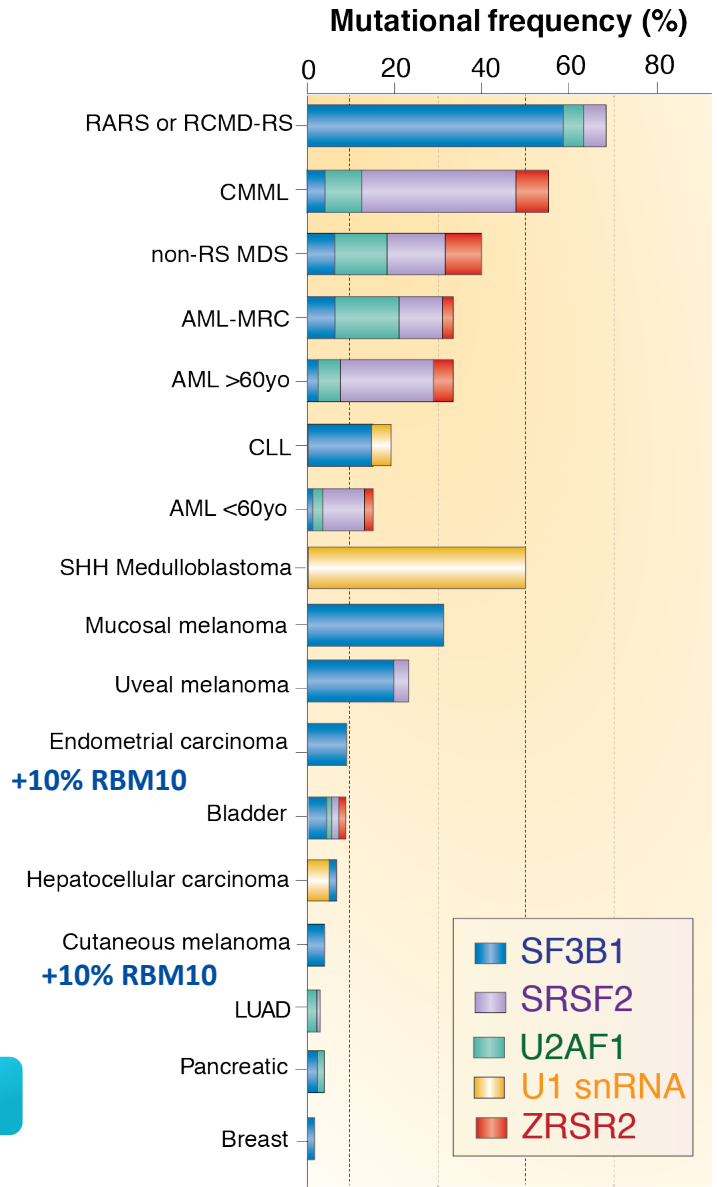
JBI 778 has a broad market opportunity: patient selection based either on spliceosome mutations or alternatively MTAP deletion



Spliceosome mutated liquid and solid tumors

50-80% of MDS and myeloid malignancies

Almost everyone ≥ 50 years old with a SF mutation developed AML

10-15% CLL patients

50% SHH-medulloblastomas

20-30% non-cutaneous melanoma

20-30% Bladder and Lung when including RBM10

MTAP deficient tumors

Table 2. MTAP deficiency in hematologic malignancies

Tumor type	MTAP deficiency (frequency)	Reference
Adult T-cell leukemia	15/94	22, 23
B-lineage ALL	36/227	24, 25
T-cell acute leukemaia	28/45	26
Diffuse large cell lymphoma	6/16	27
Mantle cell lymphoma	8/52	28

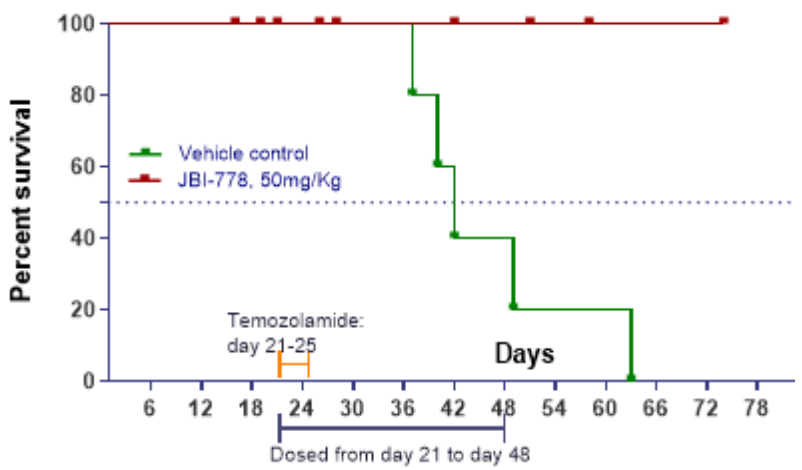
Table 1. MTAP deficiency in solid tumors

Tumor type	MTAP-deficiency (frequency)	Reference
Mesothelioma	64/95	4
Pancreatic cancer	91/300	5
Osteosarcoma	11/40	7, 8
Chondrosarcoma	7/14	9
Soft tissue sarcoma	8/21	10
Gliomas	9/12	11
Gastrointestinal stromal tumors	25/146	12
Endometrial cancer	7/50	13
Esophageal carcinoma	25/114	14
Chordoma	12/30	15
Biliary tract cancer	10/28	16
Metastatic melanoma	8/14	17
Non-small cell lung cancer	9/50	18
Breast cancer (loss of heterozygosity)	19/119	30

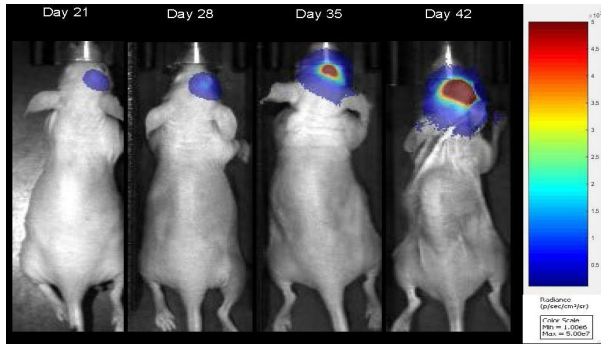
LUAD=Lung adenocarcinoma

JBI-778 optimized brain penetration increase survival in glioblastoma model

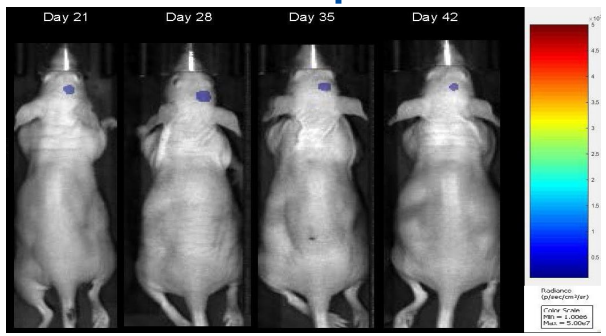
Survival Plot: U87MG Orthopedic Study



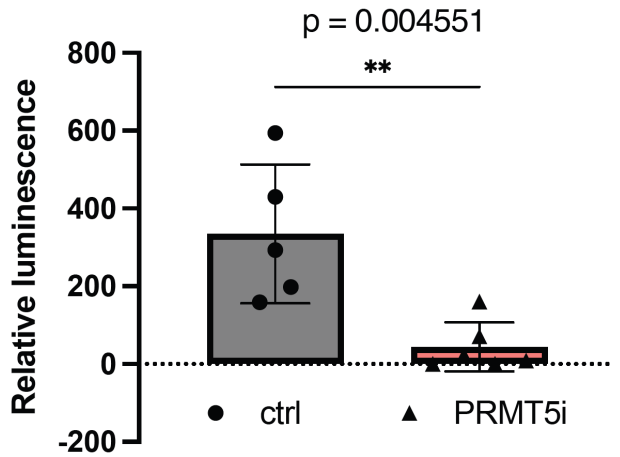
Vehicle control



JBI-778-50mpk BID



JBI-778 treatment results in much less tumor burden on 005 GBM



GBM 005 animal model is among the best representation of the human glioblastoma tumor available

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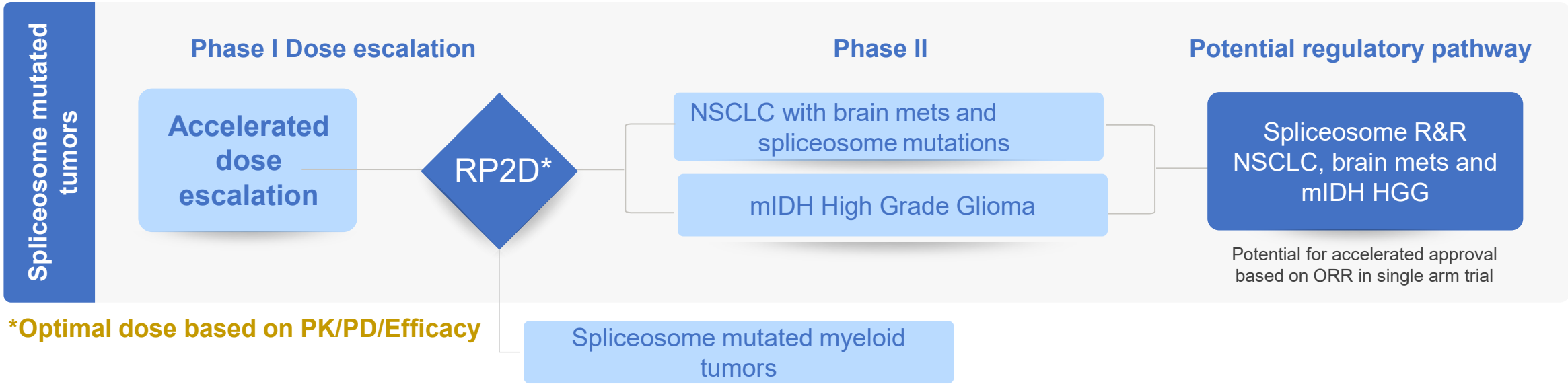
JBI-778 clinical development strategy



Dose escalation component

- Recruiting tumor patients with high spliceosome mutation frequency

Spliceosome mutated myeloid tumors: MDS, MDS/MPN (CMML), AML
NSCLC: Non-small cell lung cancer

IND clearance by FDA and ready to initiate FIH clinical study

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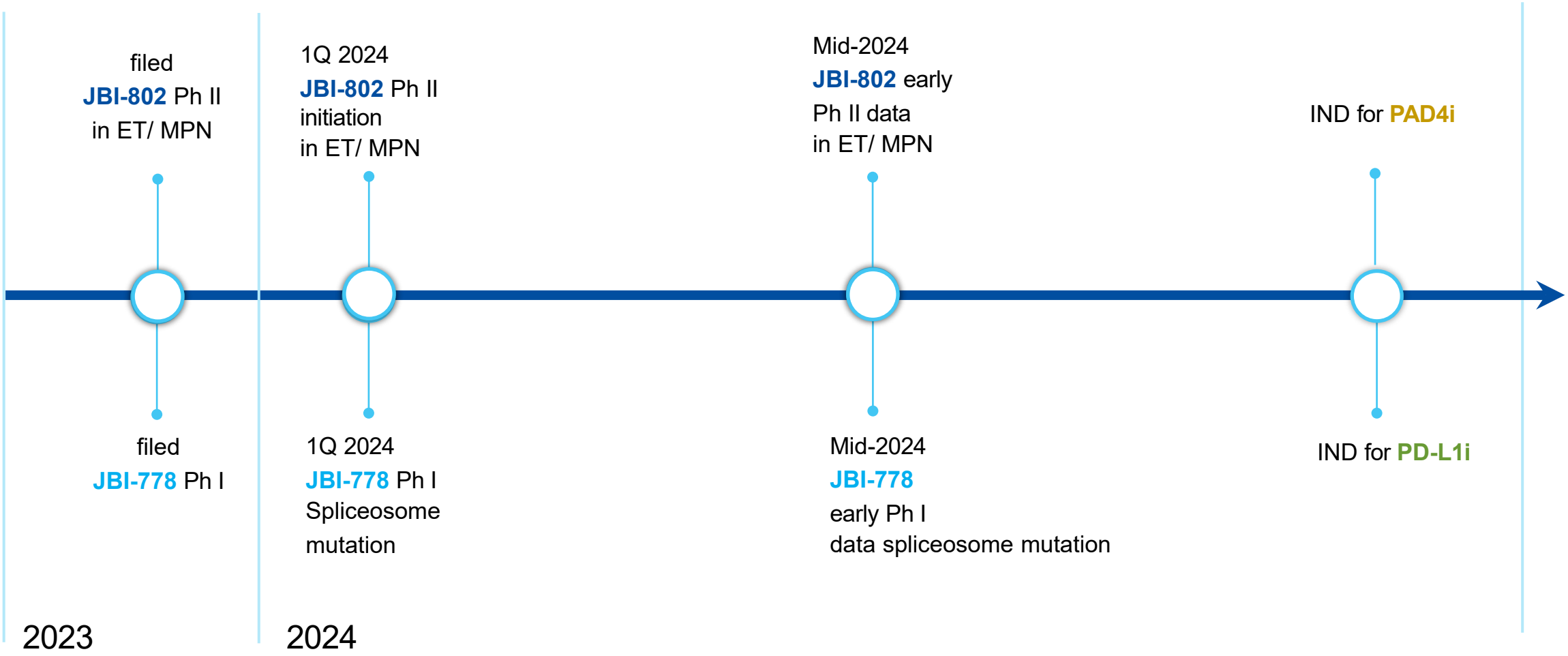
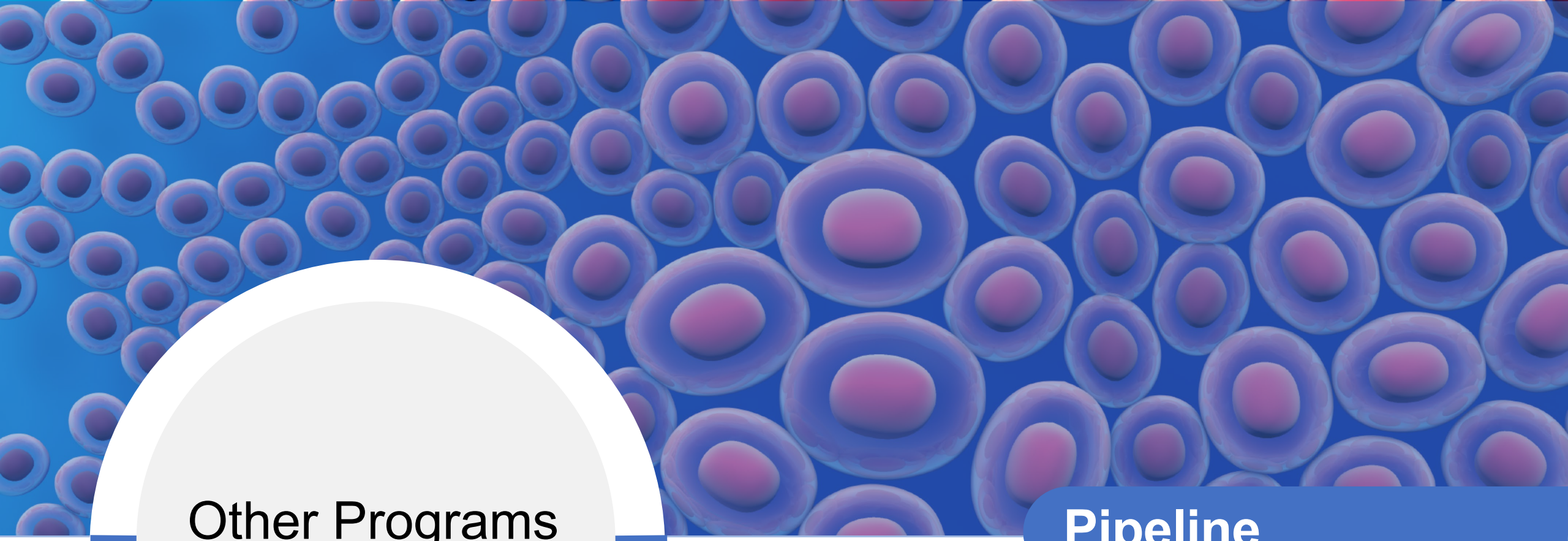
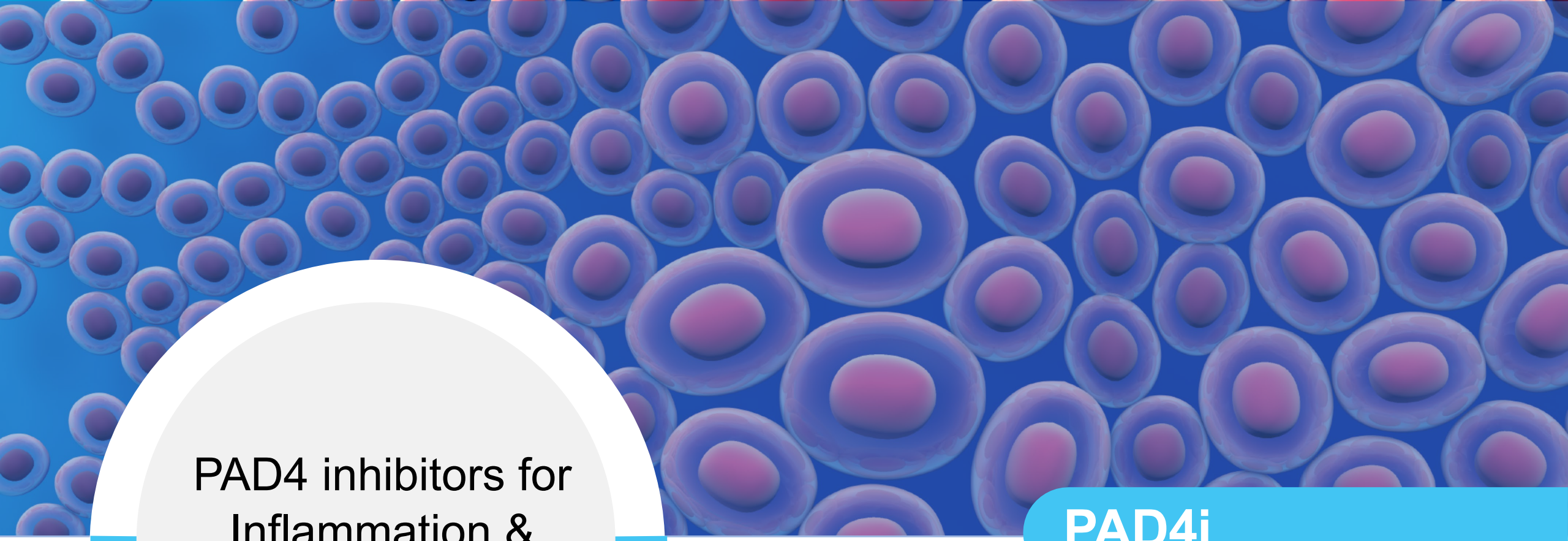
Upcoming Milestones and Catalysts





Other Programs

Pipeline



PAD4 inhibitors for Inflammation & Oncology

PAD4i

PAD4 Inhibitor Highlights: First in class for autoimmune and cancer

Current Status	Clinical candidate identified with **optimized therapeutic margin** to address acute and chronic autoimmune indications
Differentiation	First-in-class PAD4 inhibitors with mechanism of action affecting broad range of diseases **No observed immune suppression** unlike JAK-2 and TNF-α
Clinical opportunities	RA, psoriasis, fibrosis, high unmet niche inflammatory indications like hidradenitis suppurativa (HS) and antibody associated vasculitis (AAV) Liver mets in colorectal and pancreatic cancer using PAD4 induced MPO as biomarker
Efficacy	Therapeutic activity observed in multiple disease models including cancer, RA and other autoimmune/inflammation models including diabetic wound healing and psoriasis
Safety	14 day toxicology studies: Well tolerated with acceptable therapeutic margin with no observed immune suppression including absence of neutropenia, thrombocytopenia and leukopenia. 28 days pilot toxicology ongoing
Milestone	Potential IND filing in 2H 2024

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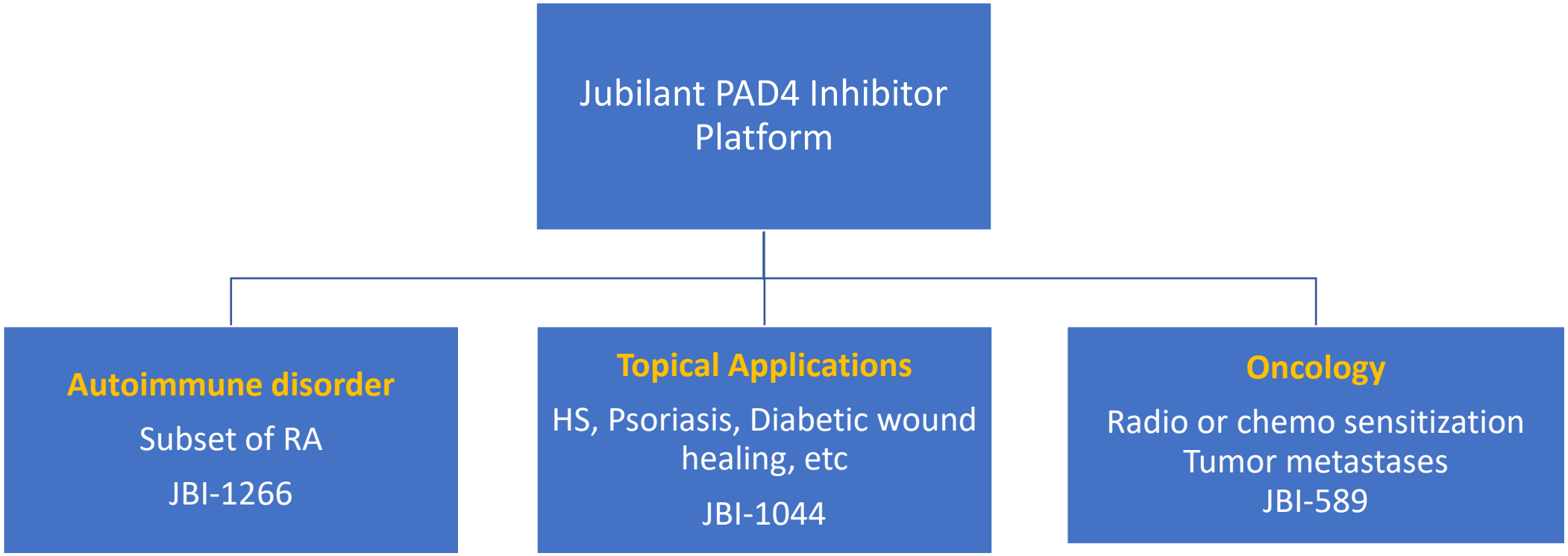
Jubilant PAD4 platform: Multiple molecules designed for distinct purposes



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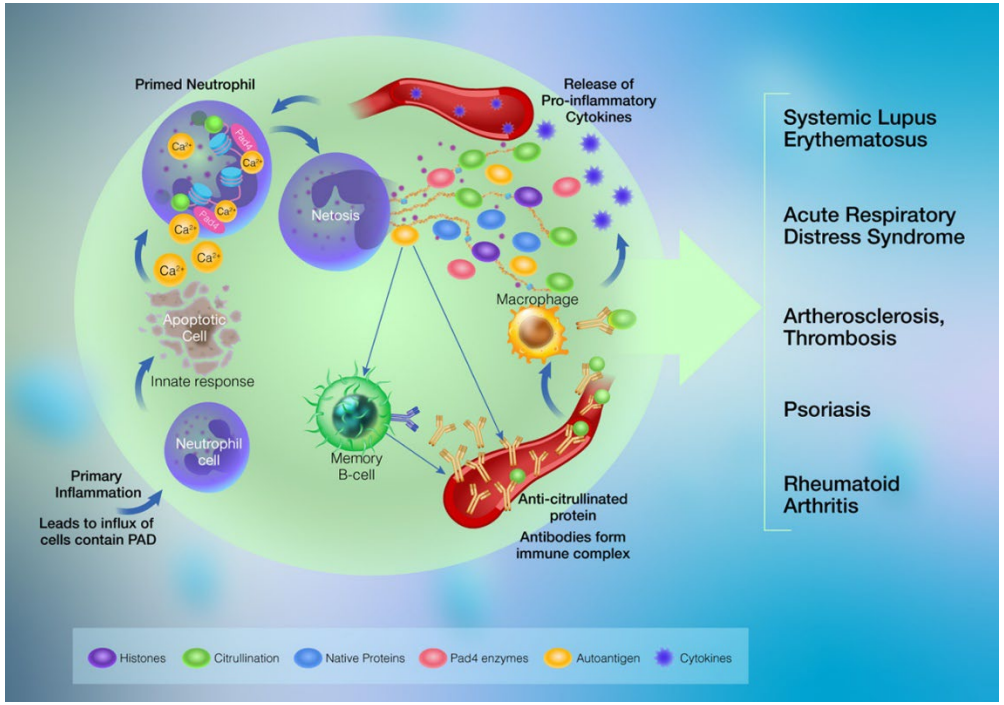
PAD4: A Breakthrough target in the Autoimmune field

PAD4 dispensable in human

Contrary to all other targets in Autoimmune disease PAD4 deletion/inhibition **does not give immunosuppression**



- PAD4 catalyzes citrullination, a modification that converts an arginine in a protein into the amino acid citrulline
- DNA damage-induced apoptosis and Neutrophil Extracellular Trap (NET)-formation (NETosis), a neutrophil defense mechanism against microbial infection
- Autoimmune disease due to antibodies are produced against key proteins that have been citrullinated (ACPA)
- Inhibition or genetic deletion of PAD4 in neutrophils inhibits citrullination as well NETosis

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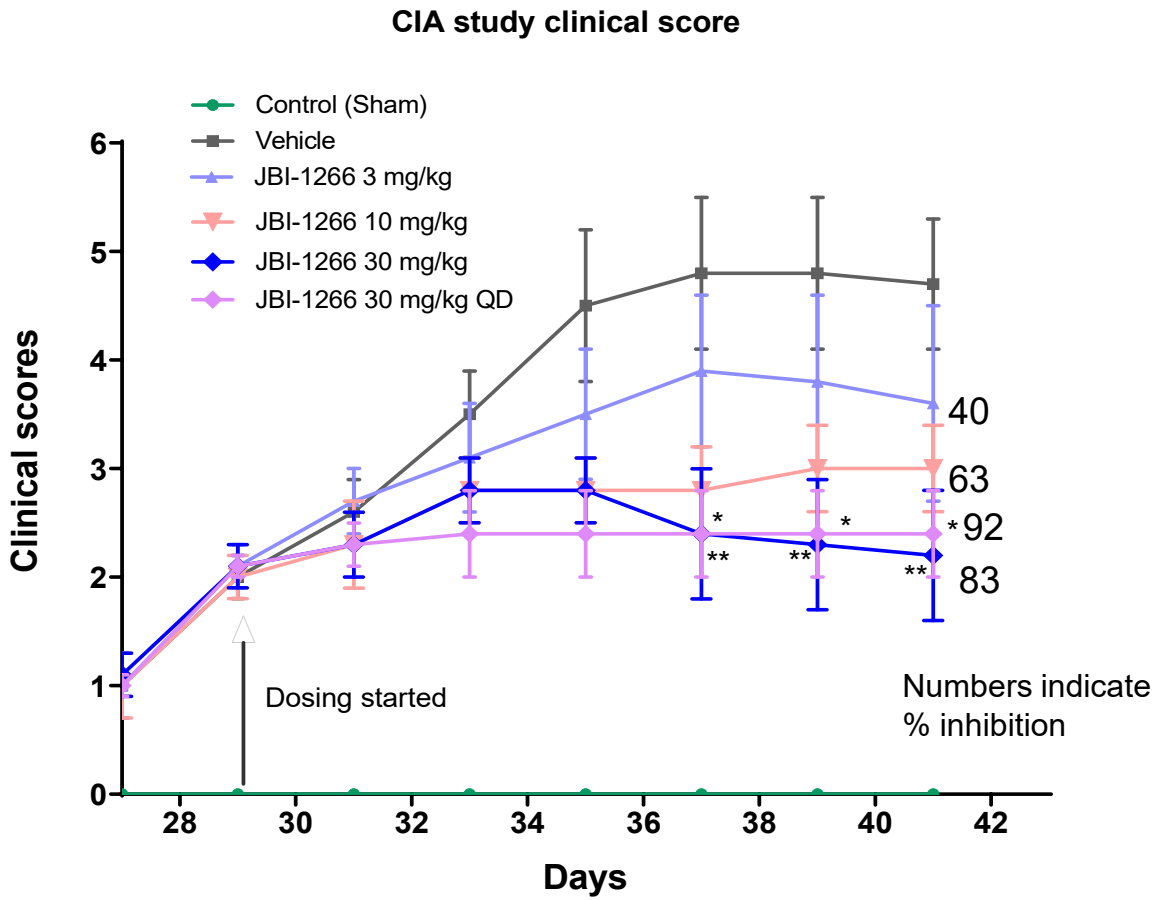
JBI-1266 showed excellent efficacy in CIA RA model and good safety margin

- Orally available novel, small molecule inhibitor complies with the rule of five
- Unique Mechanism of action: modulation of citrullination and NETosis
- Selective against PAD4 and does not inhibit other isoforms
- Excellent efficacy demonstrated in collagen induced arthritis model by oral route of administration
- Efficacy has also been demonstrated in psoriasis, diabetic wound healing and atopic dermatitis models
- Clean in CEREP safety panel, cardiac profiler and AMES negative
- 14- Repeat dose toxicity in rat clearly demonstrate acceptable safety margin
- 28 days pilot toxicology ongoing

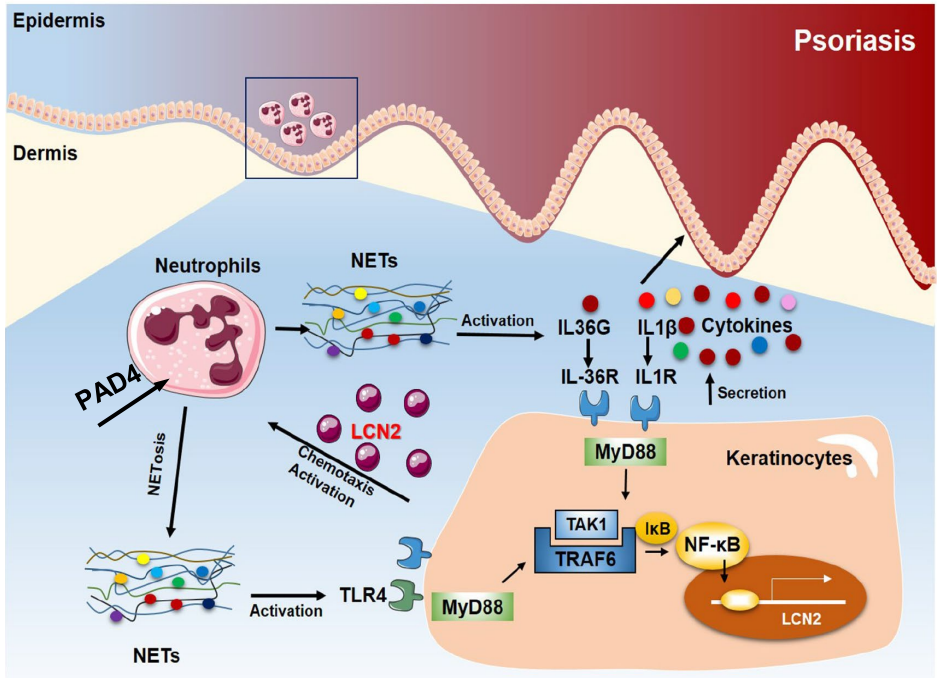


All the tested doses of JBI-1266 are efficacious; ED_{50} is ~10 mg/kg

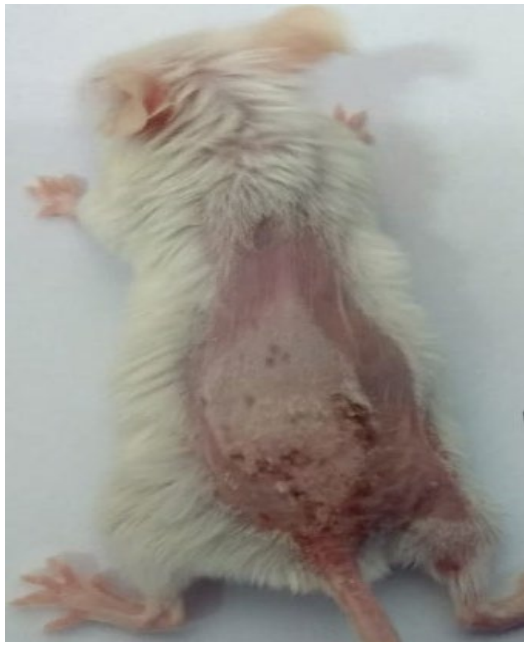
Note: Study done @ Eurofins; LPS induction was not used

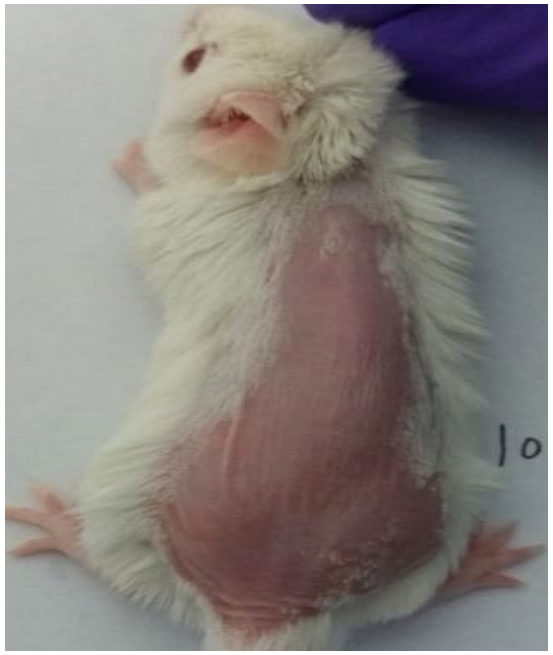
JBI-1044 showed excellent efficacy in Imiquimod induced psoriasis-Topical model

Model of the NETs-TLR4/IL-36R-keratinocyte amplification loop in psoriasis



Imiquimod Day 9 **JBI-1044-500μg**





- Psoriasis is a common chronic immune-mediated disease
- Psoriatic skin lesions have enhanced amount of NETs
- Amount of NETs correlates well with disease severity
- PADs, especially PAD4 plays an important role in NETosis
- Targeting PAD4 to inhibit NETs formation has been shown to be protective in IMQ-induced psoriasis

Shao et al., 2019; Sung-Hu et al., 2016

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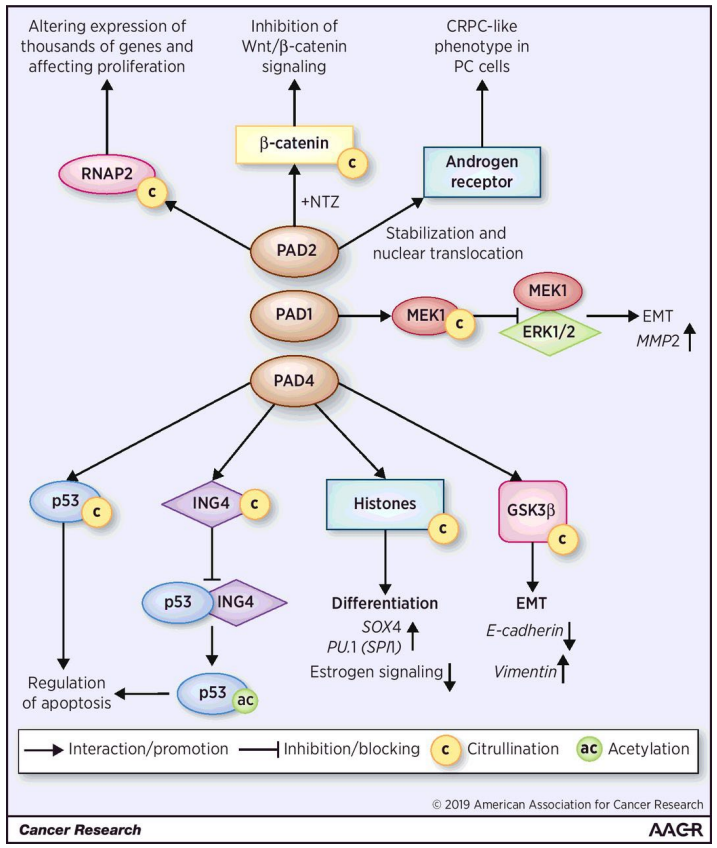
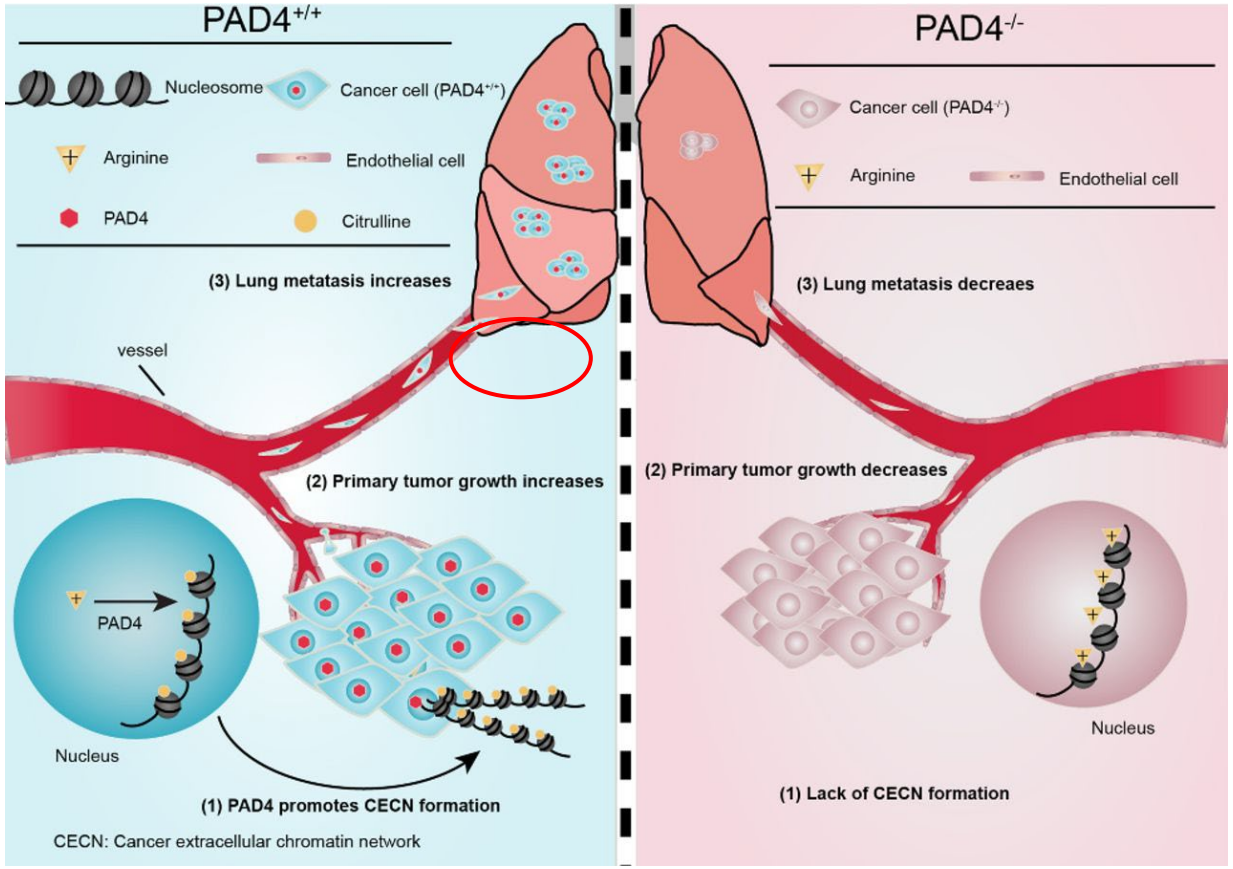
Accumulating data reveals role for PAD4 in cancer





- NETs were shown to stimulate cancer cell adhesion, migration, and invasion in-vitro
- PAD4 inhibition can therefore reduce both primary tumor growth and the formation/growth of metastasis as shown genetically in breast and NPC cells

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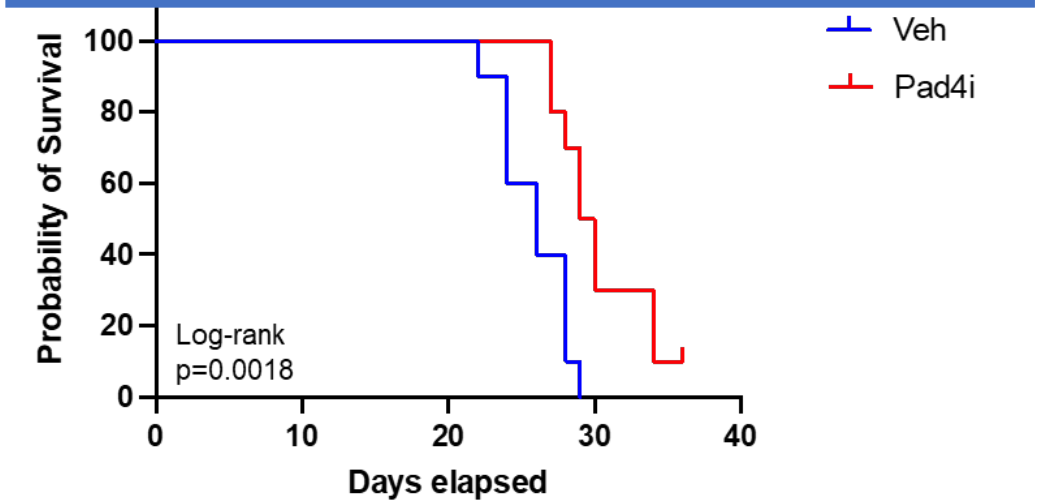
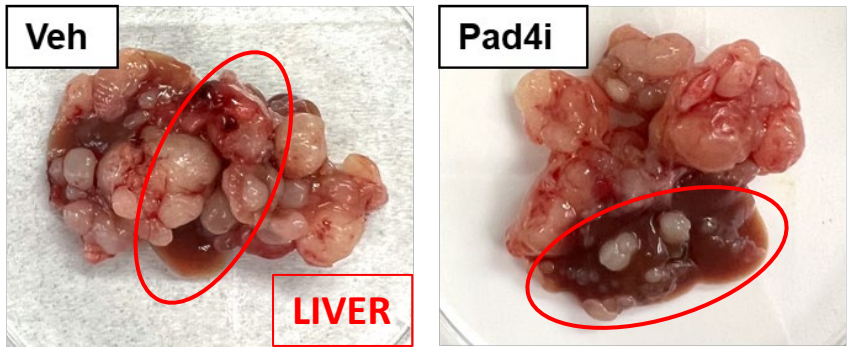
JBI inhibitors confirms role of PAD4 in multiple models of metastatic cancer

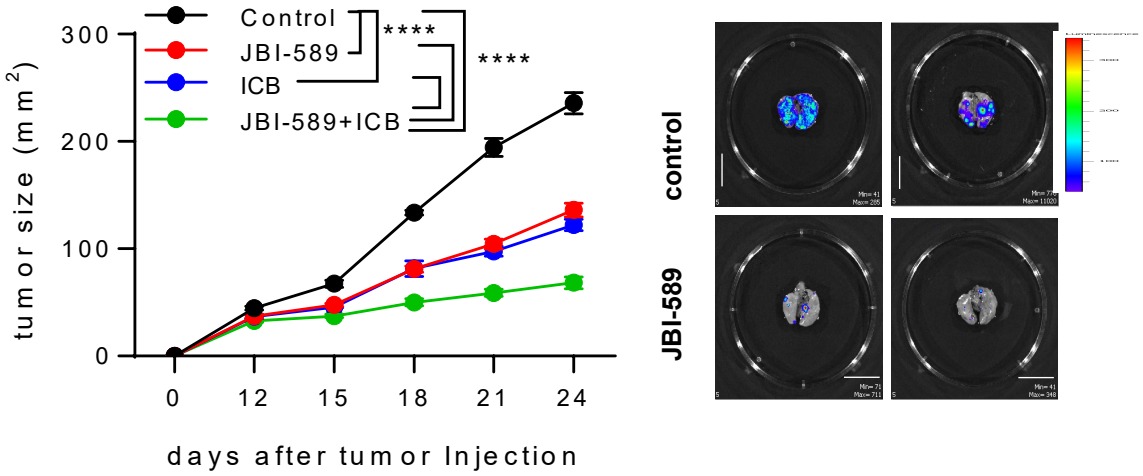
Metastatic pancreatic cancer to liver



MC38 splenic injection ($2x10^5$ cells)

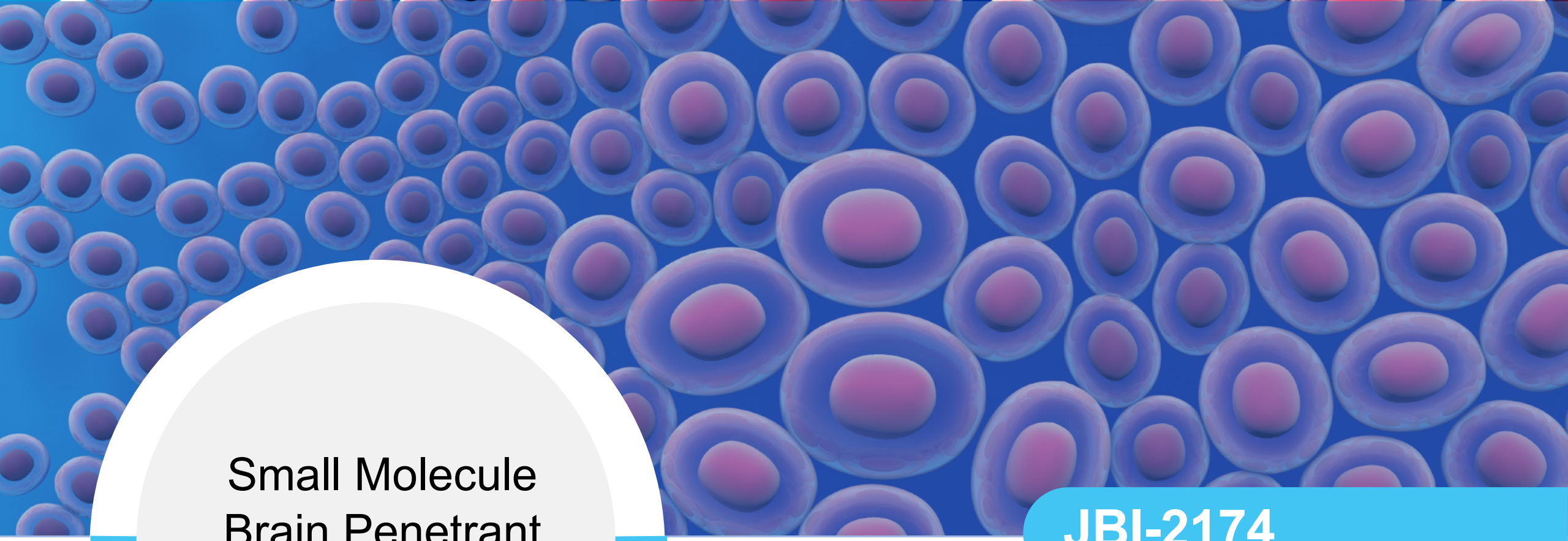


Metastatic lung cancer



JBI-589 slows the growth of the primary tumor and completely abolishes the formation of lung metastasis

Cancer Res (2022) 82 (19): 3561–3572.
https://doi.org/10.1158/0008-5472.CAN-21-4045



JBI-2174

Small Molecule
Brain Penetrant
PDL-1 inhibitor

Oral Brain Penetrant and Gut-restrictive PD-L1 Inhibitor

MOA	Oral, highly selective PD-L1 inhibitors to address organ specific bio-distribution and long-term maintenance therapy
Differentiation	Uniquely targets brain tumors to achieve efficacy in tumors resistant to approved anti-PD1/PDL-1 Second series targets GI to achieve superior efficacy vs non targeted anti-PD1/PDL-1 Short term exposure and oral dosing - opportunity for long-term maintenance therapy
Clinical opportunities	GBM and brain metastases and GI tumors like non-dMMR/MSI-H CRC, liver cancer and stomach cancer remain underserved by immuno-checkpoint antibodies
Efficacy	Multiple leads showed robust anti-tumor activity comparable to anti-PD-L1 antibodies Lead optimization ongoing to select development candidates
Safety	Well tolerated at efficacious doses in 14-day repeat dose NHP study. Clean profile in other safety screening
Milestone	Potential IND filing in 2H 2024

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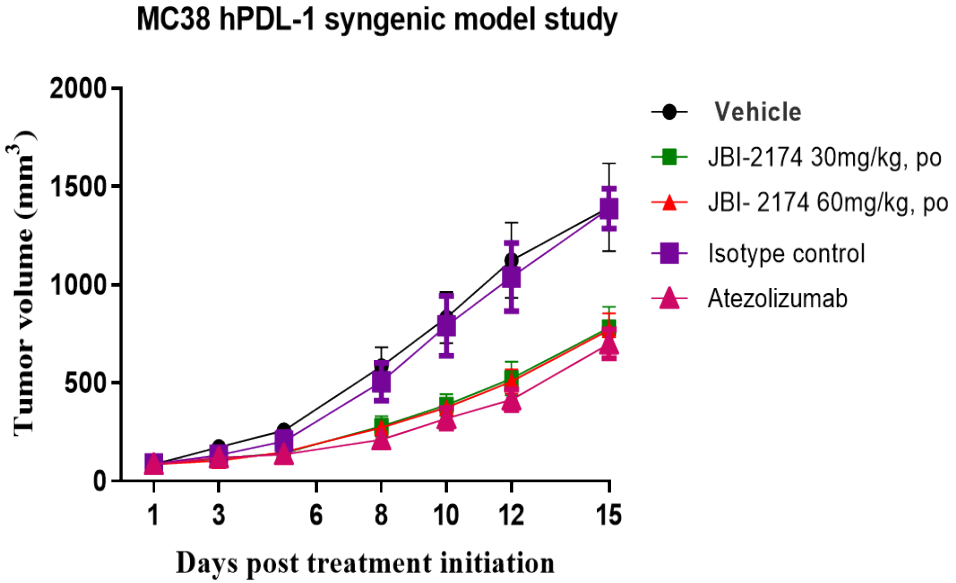
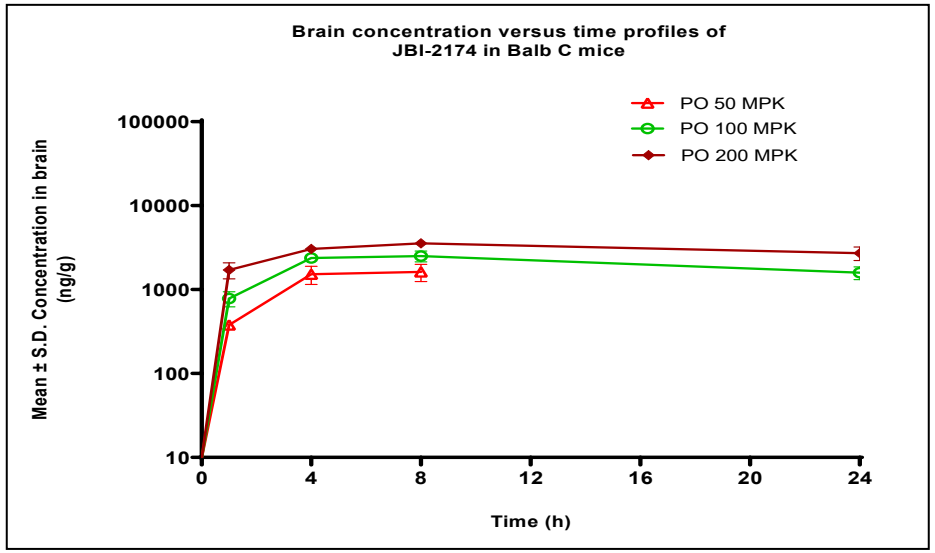
JBI-2174 efficacy comparable to Anti-PD-L1-ab





Sustained and excellent brain exposure

- **Well tolerated in repeat dose toxicity study in NHP**
  - Body weight: No test article-related changes in body weight was observed.
  - Clinical pathology: No test article-related changes in hematology, coagulation, and serum chemistry were noted at any dose Level.
  - Necropsy: No gross lesions were noted
  - No changes in histopath observed in all doses

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