PA-149

DOMMINO-1: A Phase II, Open-Label, Multicenter Study of Inobrodib in Combination With Pomalidomide and Dexamethasone in Patients With Relapsed or Refractory Multiple Myeloma

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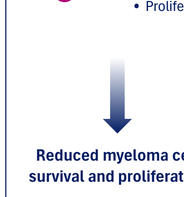
DOMMINO-1 is prospectively evaluating a first-in-class oral p300/CBP-targeted combination in pomalidomide-refractory RRMM previously treated with bispecific TCE therapy

INTRODUCTION

- Patients with RRMM who progress after T-cell redirecting therapies, including bispecific TCEs, have limited effective treatment options and poor outcomes
- Contemporary salvage therapies after T-cell redirecting therapies have demonstrated response rates of <30%, with a median PFS of ~4 months[1]
- New treatment options, with mechanisms distinct from T-cell-redirecting therapy and established therapeutic classes, are needed in this setting
- Inobrodib (CCS1477) is a first-in-class, potent, selective, orally bioavailable inhibitor of the bromodomains of the closely related histone acetyltransferases p300 and CBP
- Preclinical studies reported synergistic anti-myeloma activity with immunomodulatory drugs, including pomalidomide, which was associated with enhanced suppression of *IRF4*, a key oncogenic driver in MM[2]

WHY TAKE InoPd FORWARD?

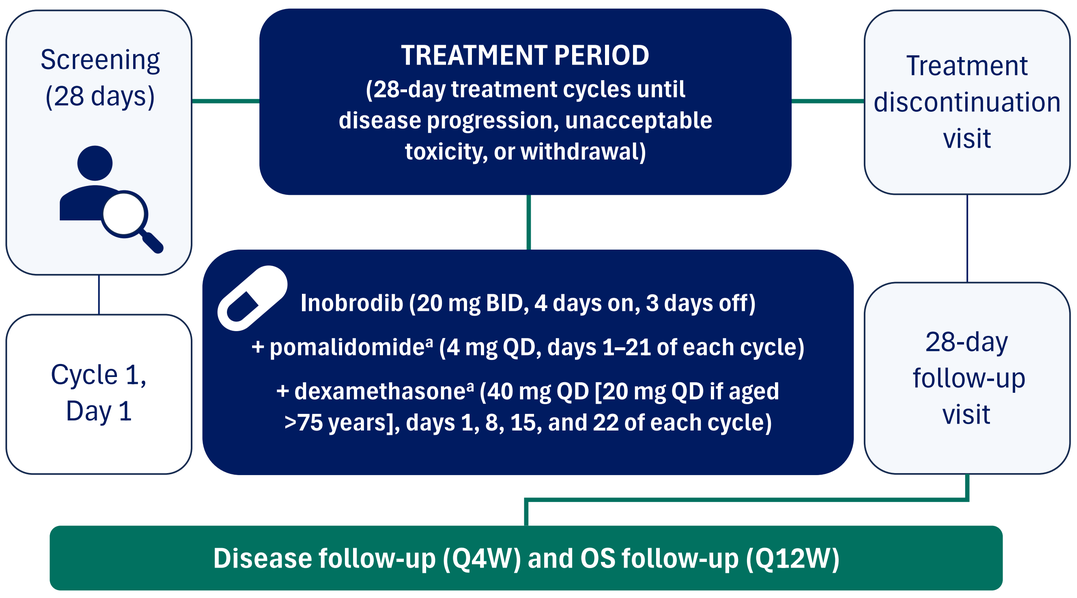
67% ORR at the selected optimal 20-mg inobrodib dose in prior phase I/II experience[3]



DOMMINO-1 STUDY DESIGN

Global, multicenter, open-label, phase II

100 patients will be enrolled to achieve 90 patients in the efficacy-evaluable population



[a]Pomalidomide and dexamethasone will be administered per standard of care.

DOMMINO-1 AT A GLANCE

- **Global, multicenter, open-label, phase II**
- **100 patients will be enrolled to achieve 90 patients in the efficacy-evaluable population**
- **Oral InoPd (inobrodib + pomalidomide + dexamethasone)**
- **Primary endpoint: ORR by ICR (IMWG criteria)**
- **Study sites in the UK and the US**

RATIONALE: TARGETING THE IRF4 AXIS

Inobrodib (CCS1477): Targeting the p300/CBP–IRF4 Axis in Multiple Myeloma[3,4]

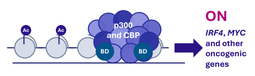
Bromodomain inhibition displaces p300 and CBP from chromatin, suppresses *IRF4* transcription, and complements the activity of pomalidomide

1. INOBRODIB: p300 AND CBP BROMODOMAIN INHIBITION

Inobrodib selectively binds the bromodomains of p300 and CBP and displaces them from chromatin, blocking transcriptional co-activation of oncogenic programs

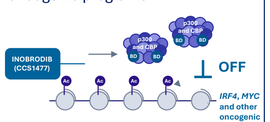
WITHOUT INOBRODIB

p300 and CBP are recruited to chromatin through transcription factor interactions, supporting oncogenic transcription



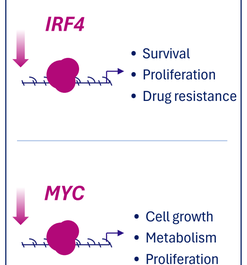
WITH INOBRODIB

Inobrodib binds the p300 and CBP bromodomains and displaces p300 and CBP from chromatin, reducing transcriptional co-activation of oncogenic programs



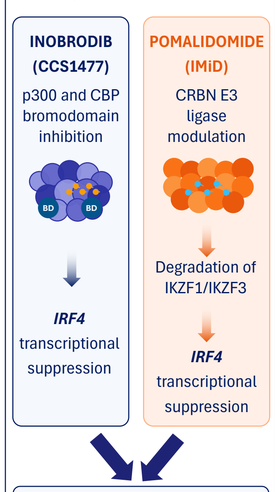
2. TRANSCRIPTIONAL REPROGRAMMING

Loss of p300 and CBP at target loci leads to reduced transcription of key oncogenic drivers, particularly *IRF4* and *MYC*, resulting in impaired myeloma cell survival and proliferation



3. COMPLEMENTARY ACTIVITY WITH POMALIDOMIDE

Inobrodib and pomalidomide suppress the IRF4 program through complementary mechanisms, resulting in enhanced anti-myeloma activity



Ac Acetylation · BD Bromodomain · p300 and CBP · ⊥ Inhibition

WHO IS THIS STUDY FOR?

KEY INCLUSION CRITERIA[a]

- ≥18 years of age
- Relapsed or refractory MM (IMWG criteria)
- Refractory to pomalidomide
- Refractory or intolerant to ≥1 proteasome inhibitor
- Refractory to ≥1 anti-CD38 mAb
- Previously treated with an approved bispecific TCE
- ECOG PS 0–2
- Adequate hematologic, renal, and hepatic function[b]

KEY EXCLUSION CRITERIA[a] (SELECTED)

- Use of investigational agent, chemotherapy, immunotherapy, or anticancer agent from a previous clinical study within the shorter of 14 days or 5 half-lives of first dose
- mAb therapy, such as anti-CD38 mAbs, within 14 days prior to first dose
- Bispecific antibody (or other TCE) or ADC within 30 days prior to first dose
- Active or unresolved clinically significant infections
- Active malignancies (other than MM) within 24 months
- Concomitant use of strong CYP3A4 inducers/inhibitors or interacting herbal supplements

[a]Other protocol-defined inclusion/exclusion criteria may apply.

[b]Adequate hematologic and renal function defined as hemoglobin level ≥8.0 g/dL, platelet count ≥75 × 10^9/L, absolute neutrophil count ≥1.0 × 10^9/L, and creatinine clearance ≥30 mL/min.

DOMMINO-1 TODAY

(as of September 2, 2026)

- **31 / 31** Sites activated (10 UK | 21 US)
- **50 / 100** Patients enrolled
- **10** Patients screening
- **On track for completion by the end of 2026**

LEADING ENROLLING SITES

(as of September 2, 2026)

1. University of Pennsylvania
2. Emory University
3. Levine Cancer Institute
4. The Royal Marsden NHS FT
5. Moffitt Cancer Center

With thanks to all participating investigators and site teams.

STUDY DESIGN & STATISTICAL ANALYSIS PLAN

SAMPLE SIZE & DESIGN

- 100 patients will be enrolled to obtain 90 patients in the efficacy-evaluable population for the primary analysis
- Bayesian optimal phase II dual-criterion design based on the primary endpoint of ORR

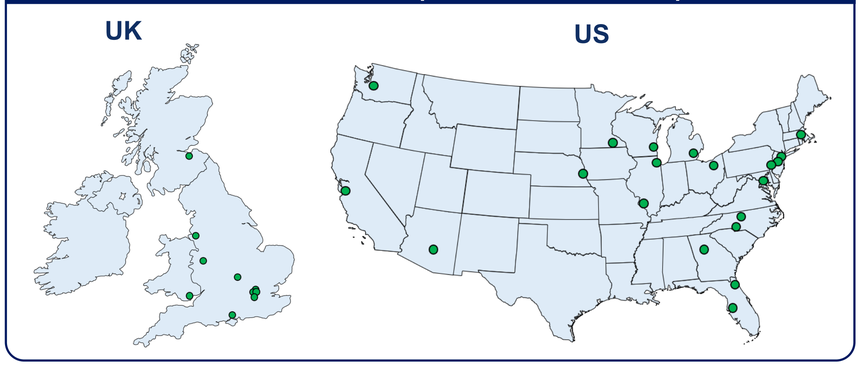
ANALYSIS SETS

- Efficacy-evaluable set (primary)
- Full analysis set
- Safety set
- PK analysis set

KEY ANALYSIS DETAILS

- Primary endpoint: ORR with responses assessed by ICR per IMWG criteria, with exact 95% confidence intervals
- Secondary time-to-event endpoints (DOR, PFS, OS) analyzed using the Kaplan–Meier method
- Futility analysis: ~3 months after 36 efficacy-evaluable patients enrolled
- Primary ORR data cut: ~3 months after last efficacy-evaluable patient enrolled

STUDY LOCATIONS (31 ACTIVATED SITES)



FURTHER INFORMATION ABOUT DOMMINO-1 (NCT07096778)

For more information about DOMMINO-1, please visit ClinicalTrials.gov (NCT07096778) or scan the QR code. This trial is actively enrolling patients.

REFERENCES

1. Costa LJ, et al. *Leukemia.* 2025;39(3)543–54.
2. Nicosia L, et al. *Cancer Cell.* 2023;41(12):2136–53.
3. Joseph N, et al. Presented at the EHA 2026 Congress (Poster PS1883).
4. Nicosia L, et al. Presented at IMS 2023 (Poster PA-195).

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ABBREVIATIONS

Ac, acetylation; **ADC**, antibody-drug conjugate; **BD**, bromodomain; **BID**, twice daily; **CBP**, CREB-binding protein; **CRBN**, cereblon; **DOR**, duration of response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **ICR**, independent central review; **IKZF1/3**, Ikaros family zinc finger 1/3; **IMiD**, immunomodulatory imide drug; **IMWG**, International Myeloma Working Group; **InoPd**, inobrodib plus pomalidomide and dexamethasone; **IRF4**, interferon regulatory factor 4; **mAb**, monoclonal antibody; **MM**, multiple myeloma; **NHS FT**, National Health Service Foundation Trust; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **PK**, pharmacokinetic; **Q4W**, every 4 weeks; **Q12W**, every 12 weeks; **QD**, once daily; **RRMM**, relapsed or refractory multiple myeloma; **TCE**, T-cell engager.

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