# Phase 1/2 study of PRO1160, a CD70-directed antibody-drug conjugate, in patients with advanced solid tumors and hematologic malignancies

ProfoundBio

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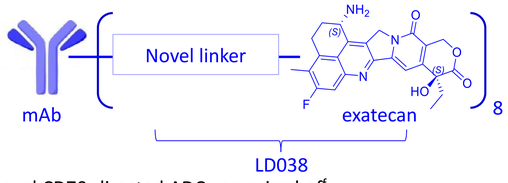
## Background and Rationale

- CD70 is a tumor surface antigen that is highly expressed in many hematological and solid malignancies and only transiently expressed on activated T and B cells and mature DCs
- CD70 facilitates immune evasion and tumor progression via its interaction with CD27 and downstream signaling pathways
- CD70 is expressed heterogeneously in the majority of renal cell carcinoma (RCC), non-Hodgkin lymphoma (NHL), and nasopharyngeal carcinoma (NPC)

| Disease | % CD70 positive |
|---|---|
| RCC[a,b,c,d] | 70-87% |
| Clear cell[c,d] | 82-93% |
| Papillary[c,d] | 50-67% |
| Chromophobe[c,d] | 0% |
| NPC[e] | 80% |
| NHL[a,b,d] | 60-77% |
| DLBCL[d] | 84% |
| FL[d] | 77% |
| MCL[d] | 67% |

DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; MCL=mantle cell lymphoma

## PRO1160 Structure

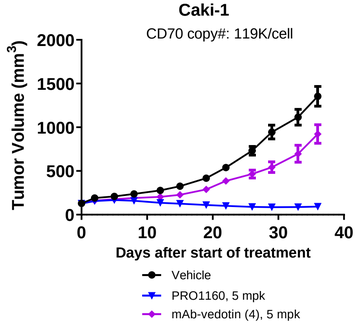



- PRO1160 is a novel CD70-directed ADC comprised of[f]:
  - Human monoclonal antibody specific for CD70
  - Protease-cleavable proprietary hydrophilic linker
  - Topoisomerase 1 inhibitor payload, exatecan (with the linker and payload collectively known as LD038
- In preclinical studies, PRO1160 Is stable in plasma and retains the PK properties and bioactivity of the unconjugated parent antibody

## Preclinical Efficacy

Robust activity in preclinical models of CD70-positive malignancies

- PRO1160 produced sustained tumor regression in the Caki-1 CDX model following repeat-doses
- Markedly improved efficacy compared to the vedotin-based comparator

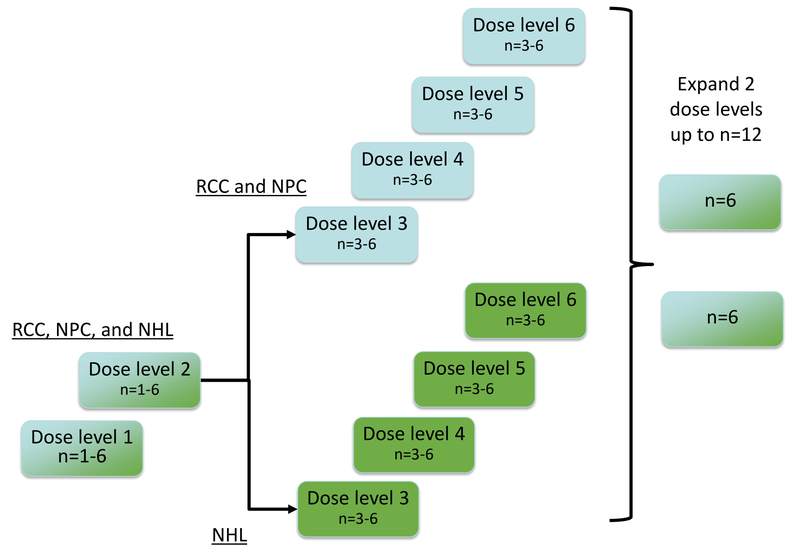



## Study Design

- PRO1160-001 is an actively enrolling, first-in-human, open-label, multicenter study enrolling subjects from the US, with future enrollment in China planned
- CD70 is retrospectively tested
- PRO1160 is administered IV on Day 1 of a 21-day cycle and may be continued until disease progression, unacceptable toxicity, or other reason for treatment discontinuation

### Part A: Dose escalation and dose level expansion

- Dose-escalation in multiple tumor types
- Dose escalation may proceed separately for RCC/NPC and NHL, due to differences in prior therapies that may lead to different recommended Phase 2 doses (RP2D)




### Part B: Tumor-specific cohort expansion

| RCC | NPC | NHL |
|---|---|---|
| n=20 | n=20 | n=20 |

MTD=maximum tolerated dose NHL=non-Hodgkin lymphoma; NPC=nasopharyngeal carcinoma; RCC=renal cell carcinoma; RP2D=recommended Phase 2 dose

## Study Objectives

| | |
|---|---|
| **Primary** | • Evaluate the safety and tolerability of PRO1160 in patients with locally advanced and/or metastatic solid tumors<br>• Identify the MTD if reached, and the RP2D of PRO1160 in patients with locally advanced and/or metastatic solid tumors |
| **Secondary** | • Assess the antitumor activity of PRO1160<br>• Assess the PK of PRO1160 |
| **Exploratory** | • Assess the immunogenic potential of PRO1160<br>• Assess biomarkers related to response, toxicity, PK/PD, and resistance to PRO1160 |

## Study Population

**Key Inclusion Criteria**

- Adults with histologically or cytologically confirmed metastatic or unresectable malignancy of one of the following types:
  - RCC (clear cell or papillary subtypes)
  - NPC
  - NHL (diffuse large B-cell lymphoma, mantle cell lymphoma, and follicular lymphoma)
- Previously received all therapies known to confer clinical benefit
- Measurable disease per RECIST 1.1 (RCC/NPC) or Lugano classification (NHL)
- Willing to provide pre-treatment tumor specimen (archival or fresh biopsy) for CD70 testing

**Key Exclusion Criteria**

- Prior CD70-directed therapy
- History of another malignancy within 3 years
- Known active central nervous system (CNS) metastases
- HIV infection, active hepatitis B or hepatitis C infection

## Study Status

- PRO1160-001 is actively enrolling at US sites
- Sites in China are in the activation phase

**www.clinicaltrials.gov identifier: NCT05721222**

## References

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