# A Phase Ib/II Study to Assess the Safety and Efficacy of PM8002 (Anti-PD-L1 x VEGF-A Bispecific Antibody) in Combination with Nab-Paclitaxel for First Line Treatment of Locally Advanced or Metastatic Triple-Negative Breast Cancer

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## Background

### Triple-negative breast cancer(TNBC)

- TNBC, the degree of malignancy is higher and more aggressive than other breast cancer type, with poor prognosis.
- There remains an urgent need for additional treatment options for TNBC patients (pts) as a first-line therapy.
- This is a single arm, Phase Ib/II study (NCT05918133) to evaluate the efficacy and safety of PM8002 in combination with nab-paclitaxel as a first-line therapy for TNBC pts.

### PM8002

- PM8002 is a bispecific antibody targeting both PD-L1 and VEGF-A containing two humanized anti-PD-L1 VHHs fused to the c-terminus of an anti-VEGF-A IgG (see right).
- Results of Phase I dose-escalation showed that PM8002 was well-tolerated in patients with solid tumors who were dosed from 1 mg/kg to 45 mg/kg (presented at SITC2022; poster #725).
- Results of Phase Ib/IIa dose-expansion showed encouraging antitumor activity and good safety in patients with advanced solid tumors (presented at ASCO2023; poster #414802).


## Method

**Key Eligibility Criteria**

- Patients with locally advanced or metastatic TNBC who have not received prior systemic treatment for TNBC;
- Age ≥ 18 years;
- ECOG score 0-1;
- Adequate organ function.

**Open label, Single arm study**
**PM8002+Nab-paclitaxel**
**PM8002 20mg/kg**
- On days 1 and 15 of 28-day cycle
**Nab-paclitaxel 100 mg/m²**
- On days 1, 8 and 15 of 28-day cycle

**Disease progression/ unacceptable toxicity**

**Primary endpoint:** Objective Response Rate (ORR) assessed by investigators per RECIST1.1, the incidence and severity of Treatment-Related Adverse Events (TRAEs) graded according to NCI-CTCAE v5.0.
**Secondary endpoint:** Progression Free Survival(PFS), Disease Control Rate (DCR).

## Results

### Patients

- As of October 08, 2023, 42 pts had been enrolled and received at least 1 dose of PM8002 combined with nab-paclitaxel (Table 1).

*Table 1. Baseline Characteristics*

| Patient Characteristics (n=42) | |
|---|---|
| **Median age, years (Q1, Q3)** | 53.5 (41.0, 60.0) |
| Sex, n (%) | |
| Male | 0 |
| Female | 42 (100.0) |
| ECOG PS, n (%) | |
| 0 | 19 (45.2) |
| 1 | 23 (54.8) |
| Number of metastatic sites, n (%) | |
| 0-2 | 18 (42.9) |
| ≥ 3 | 24 (57.1) |
| Liver metastasis, n(%) | |
| Yes | 16(38.1) |
| No | 26(61.9) |
| Brain metastasis, n(%) | |
| Yes | 2(4.8) |
| No | 40(95.2) |
| Paclitaxel treatment,n(%) | |
| Yes | 14(33.3) |
| No | 28(66.7) |

### Efficacy

**Antitumor activity observed in pts**

At the data cut-off date:

- Median duration of exposure was 6.9 months (range: 2.0-10.3 months).
- 42 pts had at least 1 response evaluation.
- 26 pts remained on treatment.
- The ORR was 78.6% (32 PRs and 1 CR), with 29 objective responses occurring at the patient's first evaluation. The confirmed ORR was 71.4% . The ORR of PD-L1 CPS < 1 and PD-L1 CPS≥1 were 76.9% and 80.0%,respectively.
- Median and progression free survival (PFS) was 9.2 months (95% CI: 8.5, --). The mPFS of PD-L1 CPS < 1 and PD-L1 CPS≥1 were 7.4 months (95%CI:5.7, --) and 9.2 months( 95%CI:8.5, --),respectively.
- The DCR was 95.2%.
- Median duration of response (DOR) was 7.2 months (95% CI:5.5, --).

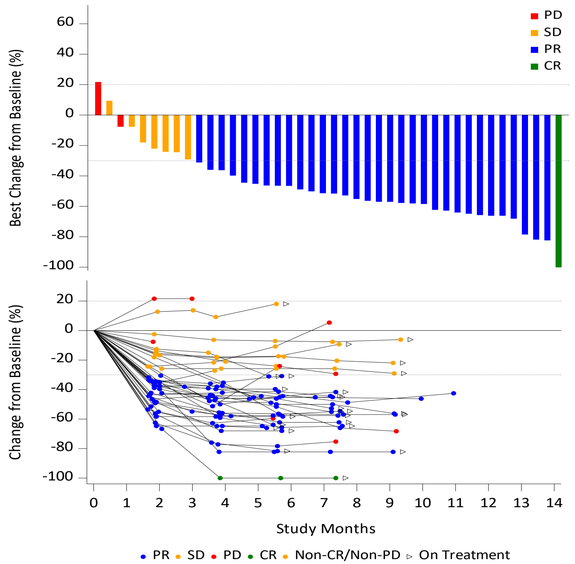
*Table 2. Efficacy Outcomes of Evaluable Patients*

| Response | Efficacy Evaluation Population ITT (n=42) |
|---|---|
| ORR, % (95% CI) | 78.6(63.2,89.7) |
| Confirmed ORR ,%, (95% CI) | 71.4(55.4,84.3) |
| DCR, % (95% CI) | 95.2(83.8,99.4) |
| On treatment (n) | 26 |
| Median duration of Exposure, month (min, max) | 6.9(2.0,10.3) |
| mPFS, month(95% CI) | 9.2(8.5,--) |
| Median TTR ,Month(95% CI) | 1.9(1.8,2.0) |
| mDOR, month (95% CI) | 7.2(5.5,--) |
| 6 months PFS Rate, % (95% CI) | 88.1(74.4,96.0) |
| 6 months DOR Rate, % (95% CI) | 84.8(68.1,94.9) |

*Table 3. Efficacy Outcomes in Subgroups According to PD-L1 CPS Status at Baseline*

| CPS | n(%) | ORR | mPFS,month(95%CI) |
|---|---|---|---|
| <1 | 13(31.0) | 76.9% | 7.4(95%CI: 5.7, --) |
| ≥1 | 25(59.5) | 80.0% | 9.2( 95%CI:8.5, --) |
| ≥10 | 9(21.4) | 100% | 9.2( 95%CI:5.5, --) |
| UK | 4(9.5) | 75.0% | --( 95%CI:1.81, --) |
| ITT | 42 | 78.6% | 9.2( 95%CI:8.5, --) |

*Figure 1. Waterfall & Spider Plots of all Efficacy Evaluable Patients*




### Safety

- Any-grade and grade ≥3 treatment-related adverse events (TRAEs) of the combination regimen occurred in 100% and 38.1% pts, respectively (Table 4).
- Serious adverse events (SAEs) occurred in 11.9% pts.
- TRAEs leading to discontinuation occurred in 2.4% pts.
- The most common TRAEs (≥10% of pts) were neutropenia (85.7%), leukopenia (76.2%), anemia (71.4%), alopecia (47.6%), proteinuria (40.5%) and hypertriglyceridemia (38.1%).

*Table 4. Overview of TRAEs of the combination regimen*

| Categories | n (%) | | | |
|---|---|---|---|---|
| All TRAEs | 42(100) | | | |
| ≥3 TRAEs | 16(38.1) | | | |
| SAEs | 5(11.9) | | | |
| TRAEs leading to discontinuation | 1(2.4) | | | |
| **TRAE ≥ 10%** | **Grade, n (%)** | | | |
| | **All** | **3** | **4** | **5** |
| Neutropenia | 36(85.7) | 6(14.3) | 1(2.4) | 0 |
| Leukopenia | 32(76.2) | 5(11.9) | 0 | 0 |
| Anemia | 30(71.4) | 1(2.4) | 0 | 0 |
| Alopecia | 20(47.6) | 0 | 0 | 0 |
| Proteinuria | 17(40.5) | 0 | 0 | 0 |
| Hypertriglyceridemia | 16(38.1) | 2(4.8) | 0 | 0 |

## Conclusions

**PM8002 combined with nab-paclitaxel showed encouraging antitumor activity regardless of PD-L1 status and good safety profile as a first-line therapy for TNBC patients.**
**This phase II study is still ongoing with near-term plans to enter phase III trials.**

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