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Developing Cancer Immunotherapies

ASX Announcement

Imugene Presents New PD1-Vaxx Data at the 2022 World Conference on Lung Cancer

Sydney, Australia, 8 August 2022: Imugene Limited (ASX:IMU), a clinical stage immuno-oncology company, announces new data from non-small cell lung cancer patients in the Phase I IMPRINTER trial has been presented as a poster presentation at the IASLC 2022 World Conference on Lung Cancer (WCLC 2022) taking place in-person and online from 6-9 August 2022 in Vienna, Austria, and follows this announcement.

The title of the presentation is "Phase 1: IMU-201 (PD1-Vaxx), a B-Cell Immunotherapy as Monotherapy or in Combination with Atezolizumab, in Adults with Non-Small Cell Lung Cancer". Professor Michael Boyer M.D., MBBS, FRACP, PhD, Chris O'Brien Lifehouse Hospital presented the poster in person.

Imugene MD & CEO Leslie Chong said: "Phase 1 trials are generally designed to look for safety, tolerability and early response signals to determine the optimal dose for further development. I am encouraged that we are seeing positive signals with correlative biomarker data at such an early stage of our PD1-Vaxx Phase I trial and we are now progressing to the Phase 1b combination studies in treatment naïve patients."

"It's particularly gratifying to have followed a patient in the trial for over 18 months where their tumour burden has been reduced to zero. For such a late-stage patient, having a chemo-free alternative could mean a very real difference to their quality of life, she added".

Four patients were in the 10 µg/dose cohort (one patient achieved a CR), 6 patients in 50 µg/dose cohort (two patients achieved SD), and 4 patients in the 100 µg/dose cohort (one patient achieved PR and two patients achieved SD).

Exploratory biomarker data indicates that IMU-201 is immunogenic and stimulates a sustained, antibody response. Importantly, by week 6, antibodies to IMU-201 were generated and sustained at high titers during treatment with 100 µg PD1-Vaxx. There was a dose dependent increase in antibody production in patients receiving the 100 µg dose.

Taken together, these data support further evaluation of IMU-201 in NSCLC. Next steps are to evaluate immune mediated response to IMU-201 and to combine with the check point inhibitor, atezolizumab.

Full study details can also be found on clinicaltrials.gov under study ID: NCT04432207

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About Imugene (ASX:IMU)

Imugene is a clinical stage immuno-oncology company developing a range of new and novel immunotherapies that seek to activate the immune system of cancer patients to treat and eradicate tumours. Our unique platform technologies seek to harness the body's immune system against tumours, potentially achieving a similar or greater effect than synthetically manufactured monoclonal antibody and other immunotherapies. Our product pipeline includes multiple immunotherapy B-cell vaccine candidates and an oncolytic virotherapy (CF33) aimed at treating a variety of cancers in combination with standard of care drugs and emerging immunotherapies such as CAR T's for solid tumours. We are supported by a leading team of international cancer experts with extensive experience in developing new cancer therapies with many approved for sale and marketing for global markets.

Our vision is to help transform and improve the treatment of cancer and the lives of the millions of patients who need effective treatments. This vision is backed by a growing body of clinical evidence and peer-reviewed research. Imugene is well funded and resourced, to deliver on its commercial and clinical milestones. Together with leading specialists and medical professionals, we believe Imugene's immuno-

oncology therapies will become foundation treatments for cancer. Our goal is to ensure that Imugene and its shareholders are at the forefront of this rapidly growing global market.

Release authorised by the Managing Director and Chief Executive Officer

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Phase 1: IMU-201 (PD1-Vaxx), a B-Cell Immunotherapy as Monotherapy or in Combination with Atezolizumab, in Adults with Non-Small Cell Lung Cancer

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Introduction

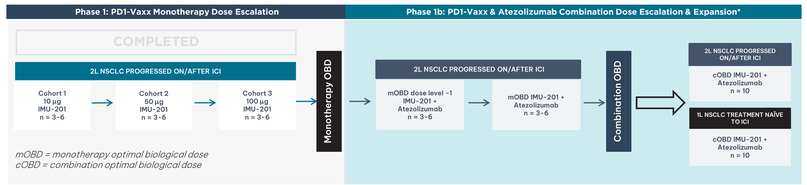
Therapies with monoclonal antibodies targeting PD-1 and its ligands are associated with positive clinical outcomes and have revolutionized cancer treatment. However, patients treated with PD-1/PD-L1 blockade may develop a primary or secondary resistance to therapy (Sharma, 2017). Contrary to monoclonal antibodies, chimeric B-cell cancer vaccines have the advantage of producing polyclonal B-cell antibodies that can potentially induce memory B- and T-cell responses while reducing immune evasion and suppression. The hypothesis is that a polyclonal induced B cell antibody response will be more effective or as effective with improved safety over current monoclonal antibody therapy. IMU-201 (PD1-Vaxx) is being developed using an active immunization approach to treat cancers that over express PD-L1 by inducing the production of anti-PD-1 antibodies utlising a peptide epitope designed to stimulate polyclonal antibodies against PD-1 (Kaumaya, 2020). Here we present preliminary data from the ongoing Phase 1 study (NCT04432207).

Study Design

The IMPRINTER (IMU.201.101) study is an ongoing open-label dose escalation study of IMU-201 as monotherapy (Phase 1) or in combination with atezolizumab (Phase 1b) for patients with PD-L1 expressing non-small cell lung cancer (NSCLC). **Figure 1** shows the study design.

All patients enrolled in Phase 1 of the study must have previously received an immune checkpoint inhibitor (ICI) and experienced disease progression. Patients enrolled in Phase 1b of the study are either ICI naïve or have previously received an ICI containing regimen and progressed on or after this treatment. The primary objective is to evaluate the safety and tolerability of IMU-201 as monotherapy or in combination with atezolizumab and identify the optimal biological dose (OBD). The secondary objective is to evaluate the efficacy of IMU-201 as monotherapy or in combination with atezolizumab. The exploratory objective is to evaluate humoral and cellular immunogenicity data, including IMU-201 and PD-1 specific antibodies (IgG, IgM), vaccine-specific cytokine levels, and regulatory and effector T and B cells.

Figure 1. Study Design



Method

In Phase 1: IMU-201 is administered by intramuscular (IM) injection on Days 1, 15, 29, 64, and every 63 days subsequently until end of treatment. Dose-limiting toxicity (DLT) assessment is completed after 29 days on treatment. Tumor evaluation is conducted every 42 days according to RECIST 1.1 until progression or discontinuation.

In Phase 1b: IMU-201 is administered by intramuscular (IM) injection on Days 1, 15, 29, 57, and every 56 days subsequently until end of treatment. Atezolizumab 840mg is administered every 2 weeks starting at day 15 until end of treatment. Tumor evaluation is conducted every 42 days according to RECIST 1.1 until progression or discontinuation.

In this Phase 1/1b study key eligibility criteria include:

- Histologically confirmed NSCLC tumor stage IIIB (not eligible for definitive treatment) or IV. (3 major types of NSCLC are acceptable including squamous, adenocarcinoma, and large cell carcinoma)
- Age of at least 18 years
- Life expectancy of at least 12 weeks in the opinion of the Investigator
- Zubrod/Eastern Cooperative Oncology Group (ECOG) score performance status 0-1
- Prior treatment criteria:
  - Phase 1: Progressed on prior PD-1 / PD-L1 containing regimen
  - Phase 1b: Treatment naïve or progressed on prior PD-1/ PD-L1 containing regimen
- PD-L1 expression criteria:
  - Phase 1: TPS/TC ≥ 50% or IC ≥ 10% (testing by 22C3, SP142, or SP263). Patients with PD L1 TPS/TC < 50% or IC < 10% expression may be included with agreement of Sponsor
  - Phase 1b: IMU-201 + atezolizumab, TPS/TC ≥ 50% or IC ≥ 10% (testing by 22C3, SP142, or SP263)
- At least one measurable lesion as defined by Response Evaluation Criteria In Solid Tumors (RECIST) 1.1 criteria.

Demography

Baseline characteristics of the patients in Phase 1 are summarised in **Table 1.**

Table 1: Baseline Characteristics

	PD1-Vaxx 10 µg N=4	PD1-Vaxx 50 µg N=6	PD1-Vaxx 100 µg N=4
Median age, years (range)	70 (46-76)	75 (51-89)	73.5 (56-85)
Age ≥ 65 years, n (%)	3 (75)	4 (67)	3 (75)
Sex, male, n (%)	3 (75)	5 (83)	3 (75)
Sex, female, n (%)	1 (25)	1 (17)	1 (25)
Race, n (%)			
Asian	0 (0)	0 (0)	1 (25)
White	4 (100)	6 (100)	3 (75)
Prior ICI therapy			
Atezolizumab	1	1	
Durvalumab		1	
Nivolumab	1		1
Pembrolizumab	1	4	3
Tislelizumab	1		

Safety Results

Safety data from patients in Phase 1 are shown in **Table 2** and **Table 3.**

Table 2: Adverse Events ≥ Grade 3 Regardless of Attribution (n=14)

Adverse Event *	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	Total n (%)
Acute kidney injury	1 (7)			1 (7)
Bile duct obstruction	1 (7)			1 (7)
Cerebrovascular accident		1 (7)		1 (7)
Immune-mediated pneumonitis			1 (7) **	1 (7)
Non-cardiac chest pain	1 (7)			1 (7)
Pneumonia	1 (7)			1 (7)

* Data cut-off 22Jun2022. Highest grade reported.
** Grade 5 event occurred after patients withdrew from the study.

Table 3: Adverse Events Assessed As Related to Study Drug in All Patients (n=14)

Adverse Event *	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	Total n (%)
Cough	1 (7)					1 (7)
Decreased appetite	1 (7)					1 (7)
Diarrhoea	1 (7)					1 (7)
Dyspnoea	1 (7)					1 (7)
Fatigue	1 (7)	1 (7)				2 (14)
Immune-mediated pneumonitis		1 (7)			1 (7) **	2 (14)
Injection site erythema	2 (14)					2 (14)
Injection site pain	5 (36)					5 (36)
Injection site tenderness	3 (21)					3 (21)
Muscle twitching	1 (7)					1 (7)
Myalgia upper extremities	1 (7)					1 (7)
Pruritus	1 (7)					1 (7)
Stomatitis	1 (7)					1 (7)

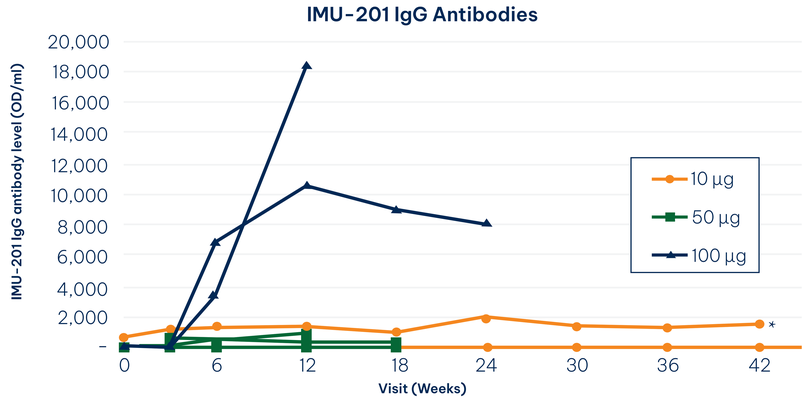
* Data cut-off 22Jun2022. Highest grade reported.
** Grade 5 event occurred after patients withdrew from the study.

- No DLTs were observed
- Treatment was well tolerated with most adverse events reported as grade 1 and not requiring medical intervention
- Adverse events reported as related to study treatment were mainly injection site related and were low grade and manageable
- Two events of immune-mediated pneumonitis, one in the 50µg/dose cohort and one in the 100µg/dose cohort. Both patients were withdrawn from the study

Biomarker Results

Phase 1 exploratory biomarker of IMU-201 antibody production is shown in **Figure 2.**

Figure 2: IMU-201 Antibody Development in Phase 1



- By week 6, antibodies to IMU-201 were generated and sustained at high titers during treatment with 100 µg PD1-Vaxx
- There was a dose dependent increase in antibody production in patients receiving the 100 µg dose
- *One patient in the 10 µg cohort exhibited anti-IMU 201 antibody at baseline, believed to be cross reactivity with the assay with prior nivolumab treatment

Tumor Response Results

- Four patients were in the 10 µg/dose cohort, 6 patients in 50 µg/dose cohort, and 4 patients in the 100 µg/dose cohort
- In the 10 µg/dose cohort, one patient achieved a CR
- In the 50 µg/dose cohort, two patients achieved SD
- In the 100 µg/dose cohort, one patient achieved PR and two patients achieved SD
- Three patients remain on study

Conclusion

IMU-201 was generally safe and well tolerated. The potential for immune related adverse events requires evaluation of additional patients. IMU-201 monotherapy has shown an anti-tumor effect. Exploratory biomarker data indicates that IMU-201 is immunogenic and stimulates a sustained, antibody response. Taken together, these data support further evaluation of IMU-201 in NSCLC. Next steps are to evaluate immune mediated response to IMU-201 and to combine with the check point inhibitor, atezolizumab.

Reference

P. Sharma, et al., Primary, Adaptive, and Acquired Resistance to Cancer Immunotherapy. Cell. 2017 Feb 9;168(4):707-723.

P.T.P Kaumaya, et al., Immunogenicity and antitumor efficacy of a novel human PD-1 B-cell vaccine (PD1-Vaxx) and combination immunotherapy with dual trastuzumab/pertuzumab-like HER-2 B-cell epitope vaccines (B-Vaxx) in a syngeneic mouse model. Oncoimmunology. 2020 Oct 1;9(1):1818437.