May 12, 2022

# Announcement of the early termination of a phase II clinical trial of the cancer peptide vaccine GRN-1201 in the United States and Top-line data

**Tokyo, Japan - May 12, 2022**/ -- BrightPath Biotherapeutics (TSE Growth 4954) announced that the Company decided to discontinue its Phase II clinical trial of cancer peptide vaccine GRN-1201 in combination with the anti-PD-1 antibody, pembrolizumab, in patients with non-small cell lung cancer in the United States. The current key top-line data are reported in this release.

The study was planned to enroll 64 cases. However, as the global pandemic of COVID-19 infection became more serious after 2020, clinical sites shifted medical resources to acute care and outpatient clinics for infectious diseases, and patients hesitated to visit the hospital, resulting in many clinical trials being delayed. In addition, pembrolizumab monotherapy was the standard therapy for the current study population (non-small cell lung cancer patients with PD-L1 expression in more than 50% of cancer cells: estimated to be about 20%) when the study was initiated, but at present the combination of pembrolizumab and chemotherapy has become a major standard therapy for the indication. As a result, patient enrollment has been considerably delayed compared to the original plan, and as of May 12, 2022, the cumulative number of patients enrolled in the study was only 20, which is about 30% of the original plan.

On the other hand, as the study has been conducted for a long term and the clinical results could be observed as an open-label study, which enabled us to understand that it would be difficult to properly evaluate for GRN-1201 using the study protocol originally designed.

- The current ORR, the primary endpoint, is comparable to that of single-agent pembrolizumab, but PFS and OS, which are more appropriate to evaluate the clinical efficacy, possibly indicate that combination of pembrolizumab and GRN-1201 is superior to single-agent pembrolizumab.
- Even in non-PR cases, all the three cases evaluated as SD have reached a survival time of greater than 70 weeks, suggesting durable clinical benefit.

Consequently, OS and/or PFS, not ORR, are considered appropriate as the primary endpoint.

In addition, the combination of pembrolizumab with chemotherapy is considered the major

standard therapy for the study indication and does not limit the eligibility to the patients with PD-L1 expression of 50% or higher. Thus, high level PD-L1 expression is no longer needed to limit the use of GRN-1201.

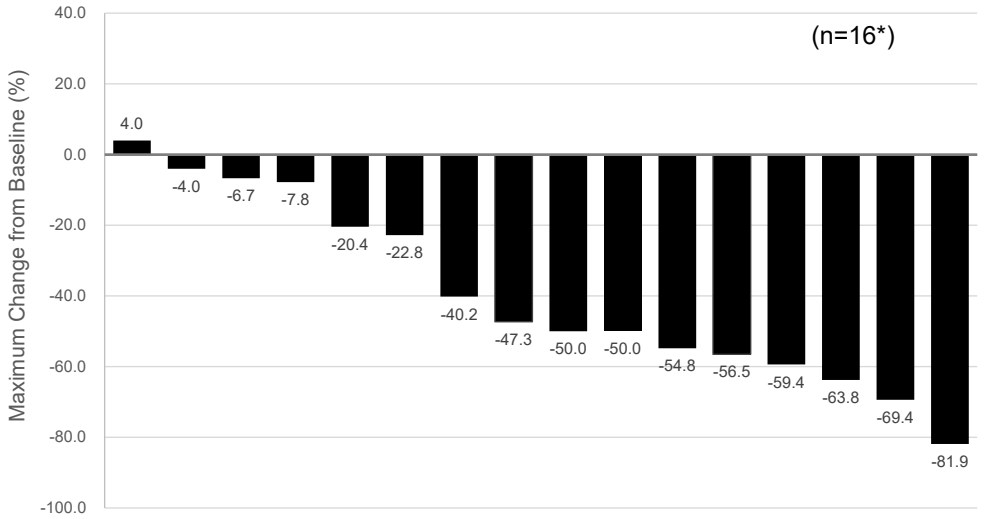
Thus, we considered that it would be more appropriate to re-plan the endpoints and eligibility requirements and to re-start a study rather than to continue with the current indication and study protocol.

The combination of pembrolizumab and GRN-1201 did not appear to increase the frequency of Grade 3 or higher treatment-related AEs compared to pembrolizumab alone based on published historical data, so it is anticipated that GRN-1201 can be added to the existing combination therapy of pembrolizumab and chemotherapy or others without any additional severe trAEs. We believe it is possible to incorporate GRN-1201 into a clinical trial of various designs.

Top-line data of this clinical trial are as follows.

# Assessment of Tumor Size

As of 6 May 2022

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Best Response | PD | SD | SD | SD | SD | SD | PR | PR | PR | PR | PR | PR | PR | PR | PR | PR |
| Overall Response | PD | NE | SD | SD | SD | PD | PR | NE | PR | PD | PR | NE | PR | PR | PR | PR |

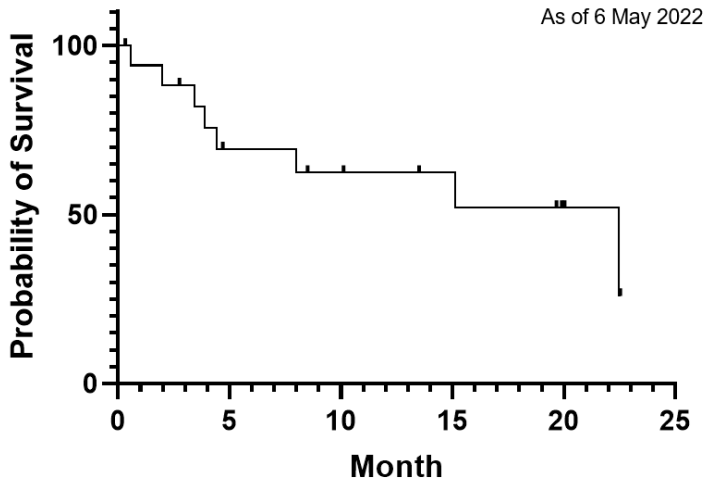
* This analysis was performed using the data from patients who have at least one post-baseline imaging evaluation for tumor response

# Progression Free Survival

| | PFS Median (M) | 12M PFS Rate | Number of subjects | Number of events(%) |
|---|---|---|---|---|
| Pembro-monotherapy Keynote-024 *[1,2,3] | 7.7 | 48% | 154 | 126 (82%) |
| Pembro-monotherapy Keynote-042 *[4,5] | 7.1 | 37% | 299 | 221(74%) |
| **GRN-1201 +Pembro** | **22.5** | **62%** | **19** | **8 (42%)** |

TPS ≥ 50% for Keynote-042

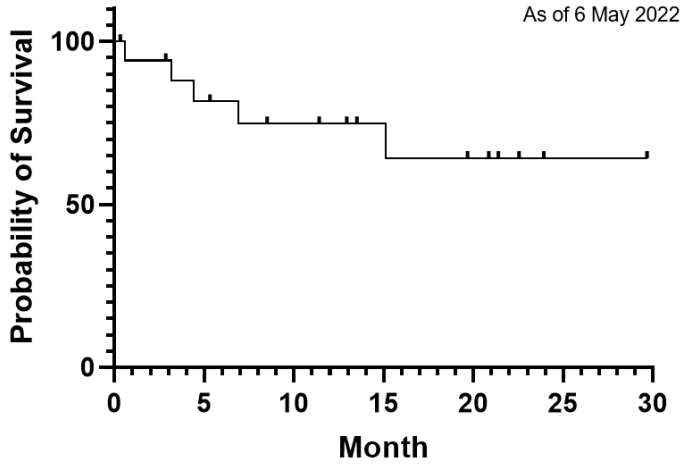
As of 6 May 2022



# Overall Survival

| | OS Median (M) | 12M Survival Rate | 24M Survival Rate | Number of subjects | Number of events(%) |
|---|---|---|---|---|---|
| Pembro-monotherapy Keynote-024 *[1,2,3] | 26.3 | 70% | 52% | 154 | 103 (67%) |
| Pembro-monotherapy Keynote-042 *[4,5] | 20 | 64% | 45% | 299 | 157 (53%) |
| **GRN-1201 + Pembro** | Not reached | 75% | 64% | 19 | 5 (26%) |

TPS ≥ 50% for Keynote-042




Reference:
*1 J Clin Oncol, 2021 Jul 20;39(21):2339-2349
*2 J Clin Oncol, 2019 Mar 1;37(7):537-546
*3 NICE; Pembrolizumab for untreated PD-L1 positive metastatic non-small-cell lung cancer [ID990] Committee Papers
*4 Lancet, 2019 May 4;393(10183):1819-1830
*5 MSD K.K.

# Safety and Tolerability

- No major safety issues
  - GRN-1201 in combination with pembrolizumab did not appear to increase the number of patients experiencing ≥ Grade 3 treatment-related adverse events relative to pembrolizumab as a single agent.
  - No patient discontinued due to GRN-1201-related adverse events.

**About BrightPath:**

BrightPath Biotherapeutics is a clinical-stage biopharmaceutical company focused on immuno-oncology and dedicated to improving treatment and clinical outcomes for patients through cancer vaccine, therapeutic antibodies, and cell therapy that harness the immune system to fight cancer.

BrightPath's clinical-stage products include iPS-NKT(unmodified induced pluripotent stem cell-derived NKT therapy), BP2301(HER2-targeted CAR-T) and GRN-1201(four shared tumor associated antigen-based peptide cancer vaccine).

BrightPath has several potentially first-in-class and best-in-class preclinical candidates in immunomodulatory antibodies and a novel personalized neoantigen vaccine platform.

For more information, visit https://www.brightpathbio.com/english/index.html

**Forward-Looking Statements:**

This news release contains forward-looking statements that are based on the current expectations and beliefs of BrightPath. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements. BrightPath cautions that these forward-looking statements do not guarantee our future financial results but involve risks and uncertainties that could cause actual results to differ materially from those discussed in the forward-looking statements. These forward-looking statements speak only as of the date of this press release and BrightPath assumes no duty to update forward-looking statements, except as may be required by law.

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