Protheragen

Protheragen Inc.

An Armed Oncolytic Viral for the Treatment of Refractory Cancers

with Stable Structural and Biological Traits

Overview

Drug Name	BS001
Description	BS001 is an armed oncolytic virus, derived from an attenuated herpes simplex virus type 2 (HSV-2) viral strain, engineered to selectively replicate within tumors and to express the granulocyte macrophage colony-stimulating factor (GM-CSF). It is being developed as an intratumoral treatment for several oncological indications. BS001 is in phase III development stage as a third- or later-line treatment for advanced/metastatic melanoma, and in phase II for advanced bladder carcinoma relapsed and metastasized after prior radiotherapy/immunotherapy. In addition, it is undergoing early clinical evaluation as a non-first-line treatment or an adjuvant treatment for other advanced/metastatic cancers.
Drug Modality	Oncolytic virus
Indication	Melanoma, bladder carcinoma, pancreas cancer, and other solid tumors
Product Category	Cancer immunotherapy
Mechanism of Action	Direct tumor cell lysis and the expression of GM-CSF to trigger and potentiate antitumor immune responses
Status	Phase 3
Patent	Granted

Collaboration Opportunity

Protheragen Inc. is actively seeking partnership for BS001. Potential collaboration can be strategic alliance, licensing, or marketing agreement.

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Drug Modality

Armed Oncolytic Virus

Based on proprietary oncolytic virus technology platform, BS001 is constructed derived from the wild-type HSV-2 strain HG52. BS001 is a genetically engineered oncolytic virus with deletion of ICP34.5 and ICP47 and insertion of hGM-CSF. In the construction of BS001, the ICP34.5 neurovirulence gene is deleted to attenuate the toxicity and enhance tumor selectivity. Because the ICP34.5 gene renders host cells unable to turn off protein synthesis upon viral infection, therefore ICP34.5 inactivation renders the HSV unable to replicate in normal cells. However, ICP34.5-deficient HSV can still replicate in cancer cells due to a defect in the shut-off response of cancer cells. Therefore, BS001 selectively amplifies in tumor cells. The function of the ICP47 gene is to antagonize the transporter protein of the host cell associated with antigen presentation. Deletion of the ICP47 gene helps present tumor associated antigens and promote the oncolytic activity.

Indication

Refractory Cancers

BS001 is in clinical development for the treatment of advanced/metastatic melanoma, bladder, liver and pancreatic cancer, and recurrent central nervous system tumors.
Melanoma is a highly aggressive, therapy-resistant malignant tumor that originates in melanocytes. According to data from the Surveillance, Epidemiology, and End Results (SEER) program, the five-year survival rate for patients with metastatic melanoma in the United States from 2005-2011 was just 16%. The Globocan data showed that approximately 325,000 incident cases of skin melanoma cases were diagnosed globally in 2020. Moreover, if 2020 rates continue, the burden from melanoma could increase to 510,000 new cases by 2040.
Bladder cancer is the tenth most frequently diagnosed cancer worldwide. The global prevalence of bladder cancer is approximately 1.65 million. Bladder cancers can be divided into muscle-invasive and non-muscle-invasive types and subdivided into low- and high-grade tumors, depending on their malignant potential. Approximately 75% of patients are diagnosed with non-muscle-invasive bladder cancer, which has a variable prognosis.
The pancreas is a dual-function gland with both endocrine and exocrine components. The vast majority of

pancreatic cancers arise in the exocrine glands and ducts, which together account for more than 95% of the cells in the pancreas. Pancreatic cancer is the deadliest of all malignancies, with a five-year survival rate of less than 10%. It is currently the seventh leading cause of cancer mortality worldwide. According to the Globocan data, 495,773 individuals were newly diagnosed with pancreatic cancer worldwide in 2020. The American Cancer Society estimates that in 2022, there will be approximately 62,210 new cases of pancreatic cancer.

Mechanism of Action

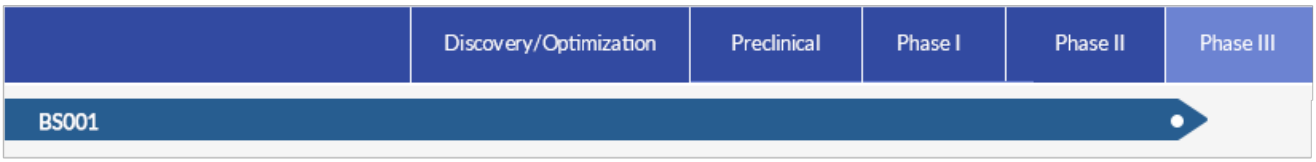
Direct Tumor Cell Lysis and GM-CSF Expression

BS001 is a genetically engineered oncolytic herpes simplex virus type 2 designed to selectively amplify in tumor cells and express GM-CSF. Deletion of the ICP34.5 neurovirulence gene in the virus reduces viral toxicity and enhances tumor selectivity. Removal of ICP47 gene facilitates the presentation of tumor-associated antigens and promotes the oncolytic activity of the virus. Therefore, BS001 is able to selectively infect tumor cells and replicate itself. The intratumoral replication of BS001 leads to multiplication, lysis of the infected cancer cell and spread to adjacent cancer cells. The danger signals generated by virus-infected cells can generate immune costimulation, thereby overriding immunosuppression and reversing tolerance within the tumor microenvironment. In addition, GM-CSF expressed by BS001 can promote the activation, maturation and migration of immune cells to enhance the immune response to cancer cells.

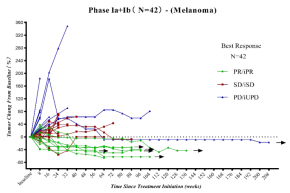
Status

The Status of BS001

BS001 is in phase III development as a third-line or later treatment for advanced/metastatic melanoma. It is in phase II development for advanced bladder cancer relapsed and metastasized after previous radiotherapy/immunotherapy. In addition, BS001 is being evaluated in early clinical trials as a non-first-line treatment for advanced/metastatic liver and pancreatic cancer, as well as an adjuvant treatment for high-grade non-muscle-invasive bladder cancer and recurrent central nervous system tumors.



Data



Tumor Change from Baseline

In the phase Ib clinical study, 22 eligible subjects were evaluated, showing an overall trend of changes in target lesions compared to the baseline period.

Phase Ia + II Study of BS001 for Patients with Melanoma	
1 year survival rate	94.40%
Median overall survival	≥ 24.8 months in follow-up
Median overall survival of Ia	28.9 months in follow-up
Longest survival period	52.8 months in follow-up

Improved Survival Rate

BS001 oncolytic virotherapy showed a favorable safety profile and demonstrated durable antitumor activity in patients with melanoma.

* For more data, please contact us.

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