ASCEND ASN-002 PROGRAM OVERVIEW

Corporate Overview

Ascend is a cancer immunotherapy company developing medicines to treat primary, recurrent and metastatic cancers. Cancers are made up of many different cell types that influence and regulate the tumour microenvironment promoting tumour growth. Ascend’s strategy focuses on targeting these key cells and altering the host microenvironment from one that supports tumour growth to one that results in cancer eradication. The company applies a number of different technologies and approaches utilizing viral vectors, and delivery systems that can be conjugated to deliver biologicals and small molecule (immune modulators, kinase inhibitors or chemotherapeutics) payloads. We believe that applying a combination chemotherapy and immunotherapy (chemo-immunotherapy) approach has the potential to materially improve clinical outcomes.

Ascend is developing proprietary treatments for breast cancer and basal cell carcinoma (skin cancer). These products have generated results supportive of safety and clinical benefit and also address major clinical needs.

- **ASN-002** has been developed as an injectable skin cancer treatment. It has undergone Phase I/II clinical studies in 64 patients showing that the product was safe, well tolerated, and generated favourable clinical outcomes.
- **ASN-004** is a vaccine developed for breast cancer. A prototype version of the treatment was studied in more than 10 clinical trials and 100 patients, and showed encouraging clinical results.

### ASN-002 - Skin Cancer

- Basal cell carcinoma (BCC) is the most common form of skin cancer, and the most common form of cancer in the US, Australia and Europe.
- Surgery is the main treatment option for BCC, but for an estimated 500,000 patients, surgery is not a good clinical option.
- Non-surgical alternatives are lacking for nodular BCC.
- ASN-002 is directly injected into the BCC tumour to stimulate an immune response which destroys the cancer.
- Phase 2 clinical trial evaluating ASN002 in nBCC commenced in Q3, 2015 at multiple clinical sites in Australia (Brisbane and Melbourne).

### ASN-004 - Breast Cancer

- ASN-004 is an improved version of a vaccine and platform developed at Melbourne’s Burnet Institute.
- Treatment can address breast cancer which afflicts over 500,000 individuals in the US, Western Europe and Japan.
- Predecessor to ASN-004 studied in a series of investigator-led clinical trials by the Burnet Institute in Australia and Overseas over a 15-year period.
- Study found eight out of 15 patients (53%) in placebo group had cancer recurrence compared to one out of 16 (6%) in the treated group at the 10-year mark.
- ASN-004 can potentially be used to treat patients in over a dozen different types of other cancers.
ASN-002 is an adenovirus (a type of cold-virus) engineered to produce Interferon-γ. It is also able to induce local expression of Type I interferons as a consequence of the innate response to the adenoviral infection. IFN-γ is a potent immunomodulatory, antiviral, and anti-proliferative cytokine that has potent anticancer activity. IFN-γ can directly inhibit human tumor cell growth and can induce apoptosis in susceptible cancer cell types. Extensive experiments in a range of animal cancer models suggest that endogenous IFN-γ may be involved in immune surveillance of tumors via a combination of lymphocyte-mediated responses, direct actions on tumor cells, and inhibition of tumor angiogenesis. 
In spite of the broad range of biological effects conferred by Interferon–γ, many cancer cells are resistant to the direct cytotoxic program initiated by this cytokine. However, recent progress has shed light on how resistant cancer cells can be rendered susceptible to Interferon–γ – to a powerful form of necrotic cell death called “necroptosis.” Ascend is currently evaluating chemotherapeutic agents that can unmask the necroptosis pathway when combined with ASN-002. We believe that this chemo-immunotherapeutic approach has real prospects to further improve clinical outcomes in solid cancers and may be particularly effective in cancers that have already shown clinical benefit from the immunomodulatory effects of IFN-γ alone.

Clinical Experience

Cutaneous Lymphoma

ASN-002 has demonstrated impressive clinical responses in two types of Cutaneous Lymphomas.

<table>
<thead>
<tr>
<th></th>
<th>Complete Response</th>
<th>Partial Response</th>
<th>Total Response Rates</th>
</tr>
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<tbody>
<tr>
<td>Cutaneous T cell Lymphoma</td>
<td>15.6% (5)</td>
<td>25.0% (8)</td>
<td>40.6% (13)</td>
</tr>
<tr>
<td>Cutaneous B cell Lymphoma</td>
<td>52.6% (10)</td>
<td>31.6% (6)</td>
<td>84.2% (16)</td>
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Numbers in brackets represents numbers of patients - total of 51 evaluable (19 CBCL and 32 CTCL) patients from two studies and 29 responding patients. Complete Response represents total regression of tumor & Partial Response represents a 50% regression.

Advanced Melanoma

A 23% Complete Response and a 46% Overall response rate was observed in Advanced Melanoma patients treated with ASN-002 in combination with T cell therapy.
Commercial Objectives for ASN-002

The current clinical development objectives of Ascend is to demonstrate the clinical benefit of ASN-002 in the dermatological oncology settings and the company has commenced Phase 2 studies in nodular basal cell carcinoma.

Ascend also believes that ASN-002 can be more broadly applied in a number of other solid cancer settings with the potential for significant clinical benefit in patients with locally advanced or recurrent cancers. There have been many studies documenting the encouraging clinical prospects of IFN-γ presumably based solely on the immunomodulatory potential of the cytokine. In many of these cancers, locally advanced and recurrent cancer are still major clinical challenges as the cancer recurs in as many as one quarter to one third of patients following surgery. In the majority of these cases, they recur in the region of the original primary cancer and lead to severe morbidity. Once the cancer has recurred and/or metastasized, the patient is generally considered incurable. Palliative surgery is difficult and disfiguring, and further radiation therapy is not generally beneficial for more than a few months.

Ascend believes that there is a significant clinical opportunity for a chemo-immunotherapeutic strategy utilizing ASN-002 to address locally advanced/recurrent disease in a number of cancers.

Current Clinical Trial

A Study of the Efficacy and Safety of ASN-002 in Adult Patients with Low-risk Nodular Basal Cell Carcinoma (ASN-002-001).


References


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