

Corporate Background

Alpha Cancer Technologies Inc., (ACT) is a private clinical stage biotechnology company with Immunotherapy and Immuno-Oncology products under development. The company's drug products use proprietary recombinant human alpha fetoprotein (AFP). In nature AFP is an immune regulatory protein involved in protecting the fetus from attack by the mother's immune system and is a carrier protein known for diverting and transporting nutrients from the mother to the embryo via AFP receptors which are found exclusively on rapidly growing fetal cells. AFP receptors are also found on most cancer cells and immune system suppressor cells but are absent on normal cells.

Immunotherapy - the company has now requested a Pre-IND (PIND) meeting with FDA to enter Phase II clinical trials in Myasthenia Gravis (MG) (Orphan Drug Designation from the FDA) followed by Phase II clinical trials in Inflammatory Bowel Disease (IBD/Crohn's/Colitis) with extensions to Hashimoto Disease and Multiple Sclerosis (MS). ACT-101 (AFP) has been shown to be exceptionally safe in clinical trials in over 300 patients.

Immuno-Oncology - AFP can deliver chemotherapy to over 80% of solid and liquid cancer cells and Myeloid Derived Suppressor cells (MDSCs) on a targeted basis providing greater efficacy with significantly reduced toxicity – a safe and targeted immuno-oncology platform.

Celgene (Merger announced with Bristol-Myers Squibb January 3, 2019) has invested US\$10.5 million and now owns a 15% equity stake in ACT with no other commercial rights.

The company's platform technologies have a significantly mitigated risk profile in every area of development and an expedited clinical development path.

Compelling Rationale – Potential Game Changer

Immunotherapy Platform – It is well-known that many autoimmune diseases in women go into remission during pregnancy and there is a strong correlation between the level of AFP in mother's blood and the decrease in the symptoms of her disease.

Myasthenia Gravis (MG) – In a study conducted at George Washington University in the Experimental model of chronic MG a dose of 1 mg/day for 14 days significantly reduced the mean clinical scores at the end of treatment compared with the control, indicating a decrease in MG disease severity ($p=0.0125$). There was also a significant reduction in acetylcholine receptor (AChR)-specific immunoglobulin G (IgG) and IgG subclasses IgG1, IgG2a and IgG2. Analysis of the neuro-muscular junction (NMJ) showed preservation of the AChR in the rats treated with ACT-101, consistent with a decrease in antibody-mediated damage of the AChR as reflected in a significantly lower concentration of IgG at the NMJ, and significantly decreased membrane attack complex (MAC) deposition compared to the control group. There were no changes in the T or B cell populations with ACT-101 treatment, suggesting that ACT-101 does not have a general immunosuppressive effect.

Inflammatory Bowel Disease (IBD) – A request for a pre-IND meeting with FDA will be submitted in the coming months following the completion of the final clinical trial design by leaders in IBD – Robarts Clinical Trials. Previously, in a randomized placebo controlled clinical study in patients with inflammatory bowel disease (IBD – Crohn's/Colitis) using AFP extracted from human fetal tissue, AFP was highly effective in reducing inflammation and producing remission in patients who were unresponsive to standard therapies. Study summary is below:

- Randomized placebo-controlled study in patients with IBD (78 patients - 56 with colitis, 22 with Crohn's)
- Disease duration of 5-15 years with radiological evidence of disease
- Patients were treated with 4 microg/kg of AFP daily (10 Crohn's-IM and 28 colitis - IV) 40 with placebo for 30 days
- After 30 days 100% of AFP-treated patients had definite improvement in their clinical symptoms
- Laboratory parameters returned to normal (Hemoglobin, albumin, IGA, IGM, decrease in CD71+ cells, etc.). 47% of patients gained weight of up to 12 kg. 30% of Crohn's and 32% of colitis patients had complete restoration of normal bowel movements and no symptoms of disease. Endoscopy confirmed improvement in the intestinal mucosa with reduction of the number of ulcerative lesions
- 30% of Crohn's patients were able to reduce steroid dose to half and 20% went off steroids completely. 32% of colitis patients were able to reduce steroid dose by 2-3 fold and 7% went off steroids completely
- No significant changes were observed in placebo patients

Studies using the TNBS model of IBD were carried out by Intestinal Biotech Development a Clinical Research Organization (CRO) at the Lille School of Medicine to corroborate these findings and data were presented at the World Congress of the American College of Gastroenterology Meeting. The studies showed that ACT-101 was as good as or better than Anti-TNF α (Humira/Remicade) with a better safety profile. These results showed a 53% reduction in Ameho scores (inflammatory score) for ACT-101 versus a 45% reduction for anti-TNF α .

Targeted Immuno-Oncology Platform – AFP receptors disappear following fetal stage but show up again on almost all solid and liquid cancer cells. The company uses its proprietary recombinant human AFP to deliver a chemotherapy payload to selectively kill cancer cells. Lower toxicity of this targeted approach offers the ability to treat the patient more frequently until the patient is cancer free.

ACT has several lead products that include non-covalently bound chemotherapy (paclitaxel, thapsigargin) and chemically linked chemotherapy (maytansine). In addition to proven efficacy and known safety profile of generic chemotherapy drugs, AFP itself has been proven safe in over 300 patients in Phase I and II clinical trials. ACT’s products are being developed as a treatment for multiple cancer indications as almost all cancer cells (solid and liquid) express AFP receptors and healthy cells do not.

As reported in the journal “**Cancer Immunology, Immunotherapy**” in January, 2018 – AFP conjugated with chemotherapy will kill Myeloid Derived Suppressor Cells (MDSCs) as these cells also express AFP receptors. MDSCs are the cells that block a patient’s immune system from recognizing and attacking the cancer. Eliminating MDSCs allows the patient’s immune system to recognize and attack the cancer. Our preclinical studies as well as data published by others, have demonstrated that we can directly target cancer cells expressing AFP receptors and eliminate MDSCs. We look to demonstrate this one-two punch to cancer in upcoming clinical trials showcasing our safe targeted immuno- oncology approach.

THERAPY	INDICATION	PARTNERS	DISCOVERY	PRE-CLINICAL	PHASE I	PHASE II
ACT-101 (AFP)	IMMUNOTHERAPY a) Myasthenia Gravis (muscle weakness) b) Inflammatory Bowel Disease (Crohn’s/Colitis) c) Hashimoto Disease d) Multiple Sclerosis, others					
ACT-901 AFP + paclitaxel	Targeted Immuno-Oncology Solid and liquid tumors	Collaboration University Health Network				
ACT-902 AFP + thapsigargin	Targeted Immuno-Oncology Solid and liquid tumors	Collaboration University Health Network, Princess Margaret Cancer Center				
ACT-903 AFP + Linker + maytansine	Targeted Immuno-Oncology Solid and liquid tumors	Collaboration (Abzena) U.K.				

Preclinical Studies

In collaboration with researchers at the Princess Margaret Cancer Centre in Toronto, ACT has completed preclinical studies examining the activity, safety and efficacy of ACT-901 and ACT-902. In vitro and in vivo results have shown that ACT-901 (AFP+ paclitaxel) and ACT-902 (AFP+thapsigargin) can successfully target and kill cancer cells with little to no toxicity and without the “off-target” damage to healthy cells. Similarly, we obtained highly encouraging results with ACT-903 (AFP+linker+maytansine).

A targeted delivery platform technology, transporting a well-established chemotherapeutic drug directly to cancer cells, will enable uptake and use of ACT’s platform in multiple forms of cancer; starting with ovarian and testicular germ cell cancers, rare disease indications, providing ACT-901 a valuable orphan drug designation in the US and Europe, and early commercial approval followed by expanded usage to other solid and liquid cancers. Dr. Daniel Von Hoff, a key oncology opinion leader, is advising the company on the upcoming clinical trials.

Additional Potential Benefits of ACT's Approach

Immuno-Oncology is currently one of the most active areas of research with almost every major pharmaceutical company developing such products. However, almost all the approaches being explored aim at unblocking a specific immune check-point in the very complex universe of immune system interactions and carry risk of serious side-effects and limited efficacy in most tumors. ACT-903 biodistribution study demonstrated that this compound was stable in blood and released the toxin once it entered the tumor while bone marrow toxin levels were below detection level.

ACT’s delivery technology targets unique receptors found on almost all cancer cells and MDSCs. Watch animation at alpha-cancer.com