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 ACT's patented 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 on all fetal cells. AFP receptors are also found on most cancer cells and immune system suppressor cells but are absent on normal cells.

Immunotherapy – ACT-101 is one of the 3 natural ligands of the FcRn receptor - the key regulator of IgG levels. AFP binding to FcRn results in decreased blood IgG levels with positive effects in many IgG-mediated diseases including myasthenia gravis, IBD, Hashimoto, ITP and many others. ACT-101 has the potential to be first-in class, best-in class, high value neonatal receptor modulator (FcRn). It is given subcutaneously (like insulin) which provides for much greater patient convenience and has a better safety profile. It is ready for commercial manufacture and has an approved Drug Master File (DMF) with the FDA. It also has an excellent safety record and has been used in over 300 patients (three times as many as the closest competitor).

In recent regulatory communications, FDA commented that if ACT adequately powers the planned trial of ACT-101 in myasthenia gravis (MG), a devastating neuromuscular disease, the data can be used to apply for registration. ACT-101 already has Orphan Drug Designation from the FDA for MG. The MG study will be followed by Phase II clinical trial in Ulcerative Colitis with extensions to Hashimoto Disease, Multiple Sclerosis (MS) and 40+ other autoantibody-driven diseases.

Immuno-Oncology - AFP can deliver chemotherapy to over 80% of solid and liquid cancer cells as well as Myeloid Derived Suppressor Cells (MDSCs) on a targeted basis providing greater efficacy with significantly reduced or no toxicity – a safe and targeted immuno-oncology platform.

Celgene (merger with Bristol-Myers Squibb to close Q4 2019) has invested US$10.5 million and owns a 15% equity stake in ACT with no other commercial rights. A total of US$20 million has been raised to date.

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 complement activating immunoglobulin G2 (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 pre-IND submission to the FDA to discuss the clinical development plan developed by leaders in IBD clinical studies – Robarts Clinical Trials. Previously, in a randomized placebo controlled clinical study in patients with inflammatory bowel disease (IBD – Crohn's/Colitis) AFP extracted from human fetal tissue 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 AFP daily (10 Crohn's and 28 colitis) 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 during the study period

Studies using the pre-clinical gold standard 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 Gastroenterology Meeting. The studies showed that ACT-101 was as good as or better than Anti-TNFα (Humira®/Remicade®) in decreasing inflammation in this model. These results showed a 53% reduction in inflammatory scores for ACT-101 versus a 45% reduction for anti-TNFα.

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**" AFP conjugated with chemotherapy also kills Myeloid Derived Suppressor Cells (MDSCs) as these are the only normal cells also expressing 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 as well as 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, MS, 40+ other autoantibody diseases					
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				

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) conducted by Southern Research Institute. ACT-903 biodistribution study demonstrated that ACT-903 was stable in blood and released the toxin once it entered the tumor while bone marrow toxin levels were below detection levels. This compares favorably to Kadcyla® (HER2+linker+Maytansine) where bone marrow toxicity is dose limiting.

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 checkpoint in the very complex universe of immune system interactions and carry risk of serious side-effects and limited efficacy for most patients. ACT's immuno-oncology platform overcomes most of the limitations of the current approaches and offers an opportunity to provide a safe and effective therapy to most cancer patients.

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