Corporate Background

Alpha Cancer Technologies Inc., (ACT) is a private clinical stage biotechnology company with Immunotherapy, Immuno-Oncology and Theranostics platforms under development. The company's drug products use ACT's patented recombinant human alpha fetoprotein (rHuAFP or ACT-101).

In nature AFP is an immune regulatory protein involved in protecting the fetus from attack by the mother's immune system and also functions as a carrier protein transporting nutrients from the mother to the embryo via AFP receptors which are found on all fetal cells. AFP receptors are also uniquely found on most cancer cells (solid and liquid) as well as Myeloid Derived Suppressor Cells (MDSCs) but are absent on normal adult cells.

Immunotherapy – ACT-101 (rHuAFP) has numerous Immunoregulatory effects. All these interactions are highly beneficial in many IgG-mediated diseases including Myasthenia Gravis (MG), IBD (Crohn's and Colitis), MS and many other diseases. ACT-101 has the potential to be a novel, best-in class, therapy for many of these autoimmune diseases. As immunotherapy treatment, it is given subcutaneously, which provides for much greater patient convenience and has a better safety profile than many other IV biologics.

ACT-101 can be commercially manufactured and has an approved Drug Master File (DMF) with the FDA. It also has an excellent safety record and has been in clinic in over 300 patients – demonstrating no serious adverse events and no neutralizing antibodies. ACT is ready to proceed in phase II trials with ACT-101 in MG, a devastating neuromuscular disease. An adaptive clinical design has been developed. ACT-101 already has Orphan Drug Designation from the FDA in this indication.

ACT is also ready to proceed with Phase II clinical trial in Ulcerative Colitis and can extend trials to Multiple Sclerosis (MS) and 40+ other autoantibody-driven diseases. Timing to advance these programs are now based on sponsor funding, which is being sought.

Immuno-Oncology – ACT-903 (AFP+linker+maytansine) can deliver chemotherapy to over 80% of solid and liquid cancer cells, as well as MDSCs, on a targeted basis providing greater efficacy with significantly reduced or no toxicity – a safe and targeted immuno-oncology platform.

Theranostics - Cancer imaging and therapeutic development work is underway with 3D imaging, Charles River Laboratories, Centre for Probe Development and Commercialization - AtomVie for ^{89}Zr-ACT-101 (diagnostic) and later using ^{177}Lu -ACT-101 (therapeutic).

Bristol-Myers Squibb holds a 14% equity stake in ACT with no pre-emptive nor commercial rights. A total of ~$25 million in equity and non-dilutive funding 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 and Safety Profile

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.

Inflammatory Bowel Disease (IBD) – A completed clinical development plan has been designed by world leader in IBD clinical studies – Alimentiv. Previously, in a randomized placebo controlled clinical study in patients with inflammatory bowel disease (IBD – Crohn's/Colitis), AFP extracted from human fetal tissue ("wild type") 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 half or more and 7% went off steroids completely
- No significant changes were observed in placebo patients during the study period

Pre-clinical 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, France, to corroborate these findings and data were presented at the World Congress of Gastroenterology. 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.

Myasthenia Gravis (MG) – In a study conducted at George Washington University using experimental model of chronic MG (EAMG model), treatment with ACT-101 given 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 immunoglobulin G2 (IgG2) level, a fraction of IgGs containing pathogenic MG antibodies while overall IgG levels were little changed. 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 with a significantly decreased membrane attack complex (MAC) deposition compared to the control group. There was no evidence that ACT-101 had a general immunosuppressive effect.

Potential Game Changer in Oncology

Targeted Immuno-Oncology Platform – AFP receptors disappear in humans after birth but show up again on almost all solid and liquid cancer cells as well as on Myeloid Derived Suppressor Cells (MDSCs). The company uses its proprietary recombinant human AFP, (ACT-101), 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 remission is achieved. Earlier candidate assets included non-covalently bound chemotherapy using taxol (ACT-901) and thapsigargin (ACT-902) and demonstrated superior efficacy and safety compared to chemotherapy alone. The company's lead immuno- oncology product, ACT-903, (AFP+linker+maytansine) is

chemically linked using a proprietary linker and carries a proprietary form of chemotherapy called maytansine. On its own, ACT-101 (AFP), has been proven safe in over 300 patients in Phase I and II clinical trials. ACT has completed numerous preclinical studies examining the activity, safety and efficacy of this molecule.

As reported at the **European Society of Medical Oncology** (ESMO) in September 2021, in vitro and in vivo studies conducted by Southern Research Institute have shown that ACT-903 can successfully target and kill cancer cells with little to no toxicity. In a Colo-205 xenograft study, ACT-903 demonstrated significant positive effects on tumor regression and survival. All control animals were dead at day 38 (50% at day 24) and all animals in the treatment group were alive at the end of the study on day 60. ACT-903 targets the AFP receptors expressed on tumor cells and preferentially delivers toxin to tumors with minimal off-target distribution. ACT-903 biodistribution study demonstrated that ACT-903 was stable in blood and released the toxin only once it entered the tumor, with bone marrow toxicity below detection levels. This compares favorably to Kadcyla® (HER2+linker+maytansine) where bone marrow toxicity is dose limiting.

As reported at the **American Association of Clinical Oncology** (ASCO) in May/June 2022, Kaplan-Meier Survival – following 1 and 2 doses for Group 1 and 2 - 90% of treated animals at 40mg/kg were alive at Day 60. **CONCLUSIONS** - Significant anti-tumor efficacy and prolonged survival was observed in mice bearing COLO-205 colon tumors who received two IV doses of either 40 or 50 mg/kg, administered 15 days apart, with the first dose administered when tumor volumes were approximately 150 mm^3. During the study, animals were monitored for both ocular toxicity and tail scarring. No such adverse events, or any other gross pathology, were observed in any dosing group. This supports a dose regimen for ACT-903 in clinic of either once a week or once every other week for future studies. The 40 mg/kg dose demonstrated equivalent or better efficacy (tumor growth, survival) than 50 mg/kg supporting its use as the highest single dose in future studies. The very low percentage of free maytansine detected in serum supports the stability of the conjugate during transit through the bloodstream to the tumor. Gross pathology examination at necropsy found no lesions on any of the livers in any of the control or treated animals.

Additional data has recently been generated in an ovarian xenograft model by Southern Research Institute – these data have been submitted for publication with the **American Association of Cancer Research** (AACR). Treatment with ACT-903 Induced 100% (complete) reduction in tumor volume in A2780 – primary patient-derived ovarian cancer xenograft. No tumor regrowth was seen by day 62 – study end. These superior results do not demonstrate the power of ACT-903 also taking down the MDSC shield allowing the immune system to simultaneously attack the tumor, as this xenograft model use immune-deficient mice. This additional effect is expected to be demonstrated in clinical studies.

We have shown that receptors for AFP are also found on MDSCs. MDSCs are the cells that block the patient's immune system from recognizing and attacking the cancer. By reducing or eliminating MDSCs ACT-903 unleashes the patient's immune system to target the cancer directly. Our preclinical studies, as well as data published by others, have demonstrated that we can directly target MDSCs at the same time as tumors with the ACT-903. We look forward to demonstrating this **one-two punch** to cancer in upcoming clinical trials showcasing this safe, targeted immuno-oncology approach.

THERAPY	INDICATION	PARTNERS/KOLS	DISCOVERY	PRE-CLINICAL	PHASE I	PHASE II
ACT-101 (AFP)	**IMMUNOTHERAPY** a) Myasthenia Gravis (muscle weakness) Orphan Drug Designation b) Inflammatory Bowel Disease (Crohn's/Colitis) c) MS, 40+ other diseases (Portfolio in a product)	George Washington University, Hadassah IBD - Lille Medical School, Alimentiv Hadassah Brain Labs, Women's and Brigham (Harvard)				
^{89}Zr-ACT-101 and ^{177}Lu-ACT-101	**Companion Dx and Tx** Solid and liquid tumors	CPDC, 3D Imaging, Charles River				
ACT-903 (lead) AFP + Linker + maytansine	**Targeted Immuno-Oncology** Solid and liquid tumors	Abzena, University Health Network, Princess Margaret Cancer Center, Sunnybrook, Ohio State				

Studies Underway

Southern Research Institute, Charles River Laboratories, Ohio State University, and Sunnybrook Research Institute are currently running additional MDSC, xenograft and organoid studies, including some with active comparators. GMP manufacturing of the conjugate is underway to prepare for clinical studies. In addition, ACT is developing conjugates of ACT-101 linked to positron and gamma emitting radionuclides as companion diagnostic (and therapy) for use as an imaging agent to monitor response to therapy.

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, both rare disease indications, providing ACT-903 a valuable orphan drug designation in the US and Europe, and could lead to early commercial approval followed by expanded usage to other solid and liquid cancers.

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, as well as having 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 the majority of cancer patients.

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