On 28 June 2005, ChemGenex Pharmaceuticals Ltd completed a dual-listing on the NASDAQ exchange and announced the signing of a deal with the Swiss API manufacturer Stragen Pharma that would accelerate the development of Ceflatin, ChemGenex’s leading anticancer agent. The two announcements capped an outstanding year for the company, a year that had already seen the successful merger with a private US-based biotechnology company, the partnering of the company’s depression gene discovery and validation program with the leading European biopharmaceutical company Vernalis plc, and the commencement of two Phase 2 clinical trials for anticancer agents. This article provides an overview of the company as it moves to accelerate its clinical programs and move toward market.

ChemGenex is an Australian biotechnology company that commenced operations in 1996. Consistent with the dominant business models of the international biotechnology industry in the late 1990s, the human genomics company (then known as Autogen) exploited a “platform technology” that combined the use of proprietary animal models and human genetics to discover and validate novel gene and protein targets in the fields of diabetes, obesity, depression and anxiety. The company was, and remains a global leader in this field, and has established and maintained several industry partnerships that have been worth more than A$40 million (US$30.4 million) over eight years.
In mid-2002, ChemGenex appointed Dr. Greg Collier as CEO and managing director of the company and renamed itself AGT Biosciences. The appointment of Dr. Collier ushered in a new vision for the company, with a clearly articulated plan for growth via merger and acquisition and realization of shareholder value through dual-listing on the NASDAQ exchange in the US.

In an Australian biotech industry that has a large number of micro-cap companies, there is a growing recognition that non-organic growth is an attractive model to achieve scientific critical mass and higher market capitalization values. The first and largest acquisition made by an Australian company in the past year was the acquisition by AGT Biosciences of the California-based private company ChemGenex Therapeutics (a deal worth US$11.4 million). This strategic acquisition combined the genomics-driven target discovery platform of AGT Biosciences with the personalized medicine and drug development capabilities of ChemGenex Therapeutics to create an integrated biopharmaceutical company with a substantial research engine, a strong management team with extensive experience in product development and commercialization, a balanced product portfolio and two drugs in clinical trials. The merged company renamed itself ChemGenex Pharmaceuticals, and has enjoyed significant support from both Australian and US investors since its merger.

ChemGenex’s mission is to develop targeted medicines for the treatment of cancer, diabetes, obesity and depression. By focusing on validated targets in diseases with genetic components, ChemGenex seeks to bring targeted therapeutics to market that address chronic diseases with high unmet medical need. The company’s clinical pipeline of cancer drugs, coupled with its partnered discovery and development programs in diabetes and depression, provides it with a solid foundation to meet these objectives.
Product Candidates

ChemGenex's most advanced product candidate, Ceflatonin® (homoharringtonine or HHT), is an investigational small molecule agent in Phase 2 clinical trials to evaluate its safety and potential efficacy for the treatment of chronic myelogenous leukemia (CML) and myelodysplastic syndrome (MDS) at the M.D. Anderson Cancer Center in Houston, Texas. Ceflatonin® induces the death of cancerous cells through the process of apoptosis, or programmed cell death. This drug has demonstrated promising clinical activity in CML patients who have developed resistance to Gleevec® (imatinib mesylate). In June 2005, ChemGenex announced an alliance with the Swiss private company Stragen Pharma to accelerate the clinical development of Ceflatonin®. This alliance gives ChemGenex an exclusive global license to Stragen's patents for the purification of HHT as well as the rights to a suite of derivate analogs of HHT and establishes a joint venture to commercialize Ceflatonin® in Europe.

ChemGenex’s second product candidate, Quinamed® (amonafide dihydrochloride), is in a Phase 2 trial for the treatment of hormone refractory prostate cancer. In a Phase 1 study to determine the best dose based on a patient’s genotype, Quinamed® generated responses in patients with refractory prostate, ovarian and gastric tumors. In Phase 2, patients are genotyped prior to therapy to determine how quickly they metabolize the drug and are then assigned a specific dose based on their metabolic profile, or genotype. The goal is to maximize Quinamed®’s therapeutic potential while minimizing drug side-effects.

ChemGenex’s third product candidate, CXS-299 (DACH-Ac-Pt (IV)), is in late pre-clinical development for the treatment of solid tumors refractory to chemotherapy. CXS-299 targets the G1 phase of the cell cycle; its activity is significantly enhanced in chemotherapy-refractory solid tumor cell lines in the presence of wild type p53 genes. Refractory patients with wild type p53 status (approximately 50% of patient population) may represent a population most likely to respond to therapy.

Capabilities and Technologies

Animal model

ChemGenex has exclusive access to Deakin University’s out-bred colony of Psammomys obesus for the discovery and validation of novel targets for metabolic diseases. P. obesus is a unique rodent model of the Metabolic Syndrome. Its natural habitat is the desert regions of the Middle East, where it subsists on a diet of saltbush and remains lean and normoglycemic. However, when housed in laboratory conditions and fed ad libitum chow, a diet on which many other rodent species remain healthy, a range of metabolic responses have been observed.

P. obesus is not a standard diet-induced obesity (DIO) model. Firstly, the diet is a standard rodent diet, not a high-fat diet (crude fat content 6% w/w). Other rodents fed on this diet show no signs of obesity. Importantly, due to the outbred, polygenic nature of the P. obesus colony, only a proportion of the animals fed this diet show evidence of metabolic disturbances, strongly suggesting that P. obesus has a genetic predisposition to these common metabolic diseases. Therefore, outbred P. obesus provides a unique animal model for pre-clinical testing of novel therapeutic agents for obesity and Type 2 diabetes.
Human genomics for discovery
ChemGenex Pharmaceuticals has a robust human genomics program that it uses for in-house discovery and offers to its industry partners. The program integrates two unique resources, the human populations repository of over 50,000 samples and a world leading statistical genetics analysis software development and computing facility. The program serves ChemGenex's own internal target discovery and validation needs and in parallel has the capacity to augment and enhance the discovery and validation programs of ChemGenex’s alliance partners. Supported by a suite of core technologies the program has a proven capability to discover novel mechanistic and physiological relationships to identify drug targets and can also be used to identify key biomarkers relevant to a pathway or disease of interest for development as predictive diagnostics and personalized medicine regimens.

Lead Targets
CXS829 is an ion channel involved in the signaling of satiation via the stomach-brain axis. The ion channel was discovered using an animal model and genotyping of human samples confirms that it is significantly associated with human obesity. CXS829 is located at a chromosomal region strongly linked with obesity phenotypes in several population groups and ChemGenex has discovered a SNP that corresponds to an amino acid substitution that shows strong association with BMI ($p = 0.0018$). Preliminary chemistry indicates that the target is druggable and ChemGenex believes that CXS829 offers significant potential in both the Rx and OTC markets.

Selenoprotein S (SelS) was discovered by ChemGenex following the observation of increased hepatic gene expression in diabetic *Psammomys obesus*. The company has since determined the gene's sequence and location on the human chromosome and the characteristics of the gene's protein product. Evidence indicates that SelS represents an important target not only in diabetes but potentially in other diseases, such as inflammation. The role of the SelS protein in cellular metabolism has been determined, and analysis of the SelS gene in more than 600 human samples has shown several SNP variants that are highly associated with markers of inflammation.

PSARL was discovered by ChemGenex and is a novel mitochondrial protein associated with insulin resistance. Genetic variation in PSARL is strongly associated with insulin resistance in human populations, and ChemGenex believes that the gene is a promising target for intervention in the treatment of diabetes and insulin resistance.

SGIP1 is a novel protein found exclusively in the brain, and is specifically located in the regions of the brain known to regulate appetite. Blocking SGIP1 in rats profoundly reduced food intake, and led to substantial loss of body weight within days of commencing treatment. Genetic variation in the human SGIP1 gene is associated with both body weight and the amount of body fat. SGIP1 is an exciting new target for the regulation of food intake and body weight.
Partnerships

ChemGenex has a strong track record of establishing and maintaining value-creating commercial partnerships with both pharmaceutical and biotechnology companies. The company has commercial relationships with companies including Merck KGaA, Vernalis, Sequenom, Stragen Pharma, Kyokuto Pharmaceutical, Starpharma, and the Institutes of Pharmaceutical Discovery.

In addition to its commercial partnerships, ChemGenex has established research partnerships with leading international groups in diabetes, obesity, depression and cancer research. The company has research relationships with Stanford University in Palo Alto, the University of Virginia at Charlottesville, the M. D. Anderson Cancer Center in Houston, the Sarah Cannon Cancer Center in Nashville, the Southwest Foundation for Biomedical research in San Antonio, the Medical College of Wisconsin, Deakin University in Geelong, The Garvan Institute in Sydney and the International Diabetes Institute, The University of Melbourne and RMIT University in Melbourne.

In summary, it is clear that there are significant opportunities for Australian biotechnology companies to pursue value-creating merger and acquisition strategies in the US and other markets. ChemGenex has shown that if these mergers are based on scientific synergies and are well planned and executed then tangible benefits can be realized. As ChemGenex looks forward to the commencement of registration-directed trials for Ceflatonin® within the next year, it is well positioned to benefit from its NASDAQ listing and to realize significant up-side from its well-executed growth strategy.

Contact Details:
ChemGenex Pharmaceuticals
Address: PO Box 1069, Grovedale, Victoria, 3216, Australia
Tel: +61 3 5227 2752
Fax: +61 3 5227 1322
URL: www.chemgenex.com