



## **Executive Summary**

**Non-Confidential**

**Licensor's Interest:  
Collaboration and License Agreement  
Dated April 19, 2001 Between  
MedImmune, Inc. and Genaera Corporation (the "License")**

*Monoclonal Antibody to Interleukin-9 as Therapy  
for Moderate to Severe Persistent Asthma*

The Genaera Liquidating Trust  
610 Second Street Pike  
Southampton, PA 18966  
Phone: 267-988-4075  
Fax: 267-988-4082

Prepared by  
**Argyce LLC**  
Trustee  
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AstraZeneca, through its MedImmune subsidiary, is actively developing MEDI 528, a fully humanized monoclonal antibody to interleukin-9 (“IL-9”), as therapy for moderate to severe persistent asthma (collectively “the IL-9 program). The Genaera Liquidating Trust (the “Trust”) holds the licensor’s interest formerly held by Genaera Corporation in the IL-9 program and wishes to divest or otherwise monetize its interest in the License.

That Trust believes that Astra Zeneca’s active development of MEDI 528 implies sales potential in excess of a billion dollars per year. Comparisons and calculations shown in this document indicate minimum peak year sales of \$1.5 Billion. Proprietary estimates from independently sourced market data support projected peak year sales of \$3 to \$4 Billion on conservative assumptions and penetration rates.

The licensor interest provides royalties and milestones from a product whose attributes include:

- Actively developed by the world’s premier marketer of respiratory products;
- Market potential significantly larger than Xolair;
- Expected to have an excellent safety profile;
- Targeted to patients for whom product cost and administration is readily justified against hospitalization and other treatment costs for inadequately controlled persistent asthma; and
- Potential for faster action and better efficacy than other therapy – based on inhibition of IL-9 which plays a fundamental role in the asthma inflammatory cascade.

In 2007 and early 2008, Wall Street research analysts looking at the scientific underpinnings and the market potential for this program valued Genaera Corporation’s licensor interest at \$33 to \$43 million based on launch dates Genaera estimated as 2011/2012. With MedImmune’s commencement of a new 320 subject Phase 2b study in October 2009, the potential launch date is farther away but more credibly estimated. The Trust believes the probability adjusted net present value of the licensor’s interest is now a substantial fraction of the earlier valuations – meaningful to the Trust’s unit holders, but right sized for life sciences investors with outsized return potential relative to the risk.

### **Asset and Licensor Background**

Genaera Corporation (“Genaera”) was a NASDAQ traded biopharmaceutical company that operated for nearly two decades. IL-9 antibody therapy for asthma was conceived and developed at Genaera in the mid-90s from its research and intellectual property with technology and materials licensed from the Ludwig Institute of Cancer Research (“LICR”). Scientific studies and independent peer-reviewed publications indicate that IL-9 controls other well-known factors involved in promoting lung inflammation in asthma, including a group of proteins that modulate the growth and functional activities of immune cells.

In 2001, Genaera’s IL-9 development program was licensed to MedImmune, Inc., which assumed responsibility for development and commercialization efforts on the IL-9 program. Using the licensed materials and technology, MedImmune developed a humanized antibody to IL-9 now known as MEDI-528. MedImmune and subsequently AstraZeneca have followed a highly systematic preclinical and clinical development plan and have committed substantial resources to the continuing development of MEDI-528. The compound has been tested in multiple phase 1 and phase 2 clinical studies and a 320 subject phase 2b study is scheduled to begin enrollment imminently.

Under the License, Genaera and LICR transferred materials and technology to MedImmune and MedImmune licensed and sublicensed, respectively, Genaera and LICR intellectual property. The License provides for royalties on sales for a minimum of ten years following commercial launch and up to \$55 million in regulatory and sales milestones. Genaera received the first \$1.0 million for Phase 1 & 2 milestones. Royalties are tiered according to sales levels and the License provides for a minimum royalty for sales in any country in which there is no longer a licensor patent in force. The link to the redacted License on EDGAR is <http://www.sec.gov/Archives/edgar/data/880431/000103605001500576/dex104.txt>.

On June 12, 2009, Genaera filed a Certificate of Dissolution with the Delaware Secretary of State and transferred all its assets, liabilities and contracts to the Trust pursuant to a Liquidating Trust Agreement. While the Trust can operate for three years or more if necessary, its purpose is to satisfy or otherwise resolve all Genaera's legitimate obligations, to monetize assets and to distribute funds remaining after liabilities and expenses to former Genaera stockholders.

### **The Technology**

Interleukin-9 (IL-9) is a Th2 cytokine with a role in multiple activities that are important in the pathogenesis of asthma. IL-9 was originally recognized as T-cell growth factor and for its induction of mast cell recruitment and differentiation in the lungs. It also increased the number of high-affinity IgE receptors on mast cells and enhanced production of IgE by IL-4 stimulated B cells, i.e. both increasing the ligand and receptor on the mast cell that leads to release of histamine, leukotrienes, and proteases<sup>1-4</sup>.

IL-9 levels have been demonstrated to be elevated in asthmatic airways in humans<sup>5</sup>. In fact the link between the IL-9 cytokine and asthma has been established in a number of studies. IL-9 has been shown to cause airway inflammation through induction of IL-13 expression<sup>6</sup>. IL-13 is an important inflammatory cytokine secreted by Th2 cells, which have in turn been shown to stimulate airway hyper-responsiveness, secretion of mucus and attraction of inflammation effector cells to the lung tissue. In addition, IL-9 has been shown to stimulate mucus production through pathways both dependent<sup>6</sup> and independent<sup>7</sup> of IL-13. Because of its action upstream of IL-4, IL-5, and IL-13 and its ability to influence mast cells, B-cells, T-cells, eosinophils, and airway epithelium, IL-9 is considered a major early inducer of airway hyper-responsiveness and a key in the asthmatic response including mucus production, lung eosinophil and mast cell recruitment, proliferation and activation, IgE production, and subsequent release of inflammatory mediators<sup>1-4</sup>. Studies in animal models have also demonstrated that this cytokine is a determining factor in the pathogenesis of bronchial hyper-responsiveness<sup>1,2,3</sup>.

Because IL-9 plays a fundamental role in the asthma inflammatory cascade, strategies to inhibit IL-9 could prevent the production of immunoglobulin E under the specific conditions that lead to asthmatic lung inflammation. Importantly, host defense systems are not compromised when IL-9 is blocked or knocked-out<sup>1</sup>. Thus an IL-9 targeting therapy has the potential for a faster onset of action, better efficacy and greater safety than molecules targeting IgE once it has already been generated.

Generally, asthma is broadly classified on the basis of the nature of the principal stimuli that are associated with or incite acute exacerbations into two categories: allergic and idiosyncratic<sup>7</sup>. Allergic asthma is often associated with family history and elevated IgE levels and is the predominant form of asthma, variously estimated as 90% of children with asthma<sup>8</sup>, 50% of adults with asthma<sup>8</sup> and 60% of all asthmatics<sup>9</sup>. Idiosyncratic patients cannot be described on immunological mechanisms like increased IgE. In its most typical form, asthma is an episodic disease. Asthma morbidity and mortality is hypothesized to be due to persistent airway inflammation<sup>10,11</sup>. The most typical finding is a generalized

increase in the number of various types of inflammatory cells and number of capillaries in the walls of the airways. The physiological and clinical features of asthma derive from an interaction among resident and infiltrating inflammatory cells, inflammatory mediators, and cytokines in the airway lining. Mast cells, eosinophils, B-cells and T lymphocytes all appear to be important in the inflammatory response<sup>11</sup>.

### Market Potential

It is estimated that asthma affects about 300 million people worldwide<sup>12</sup>, approximately 23 million of whom are Americans<sup>13</sup>. The number of people with moderate to severe persistent asthma is variously estimated as 40-50% of all asthmatics<sup>14</sup>. Less than 10% of all asthmatics suffer severe persistent asthma but these patients account for a disproportionate share of costs and morbidity associated with asthma<sup>15</sup>.

MEDI-528's closest comparator is Xolair which was launched in the US in 2003 and is co-marketed by Genentech and Novartis. It is approved for the treatment of moderate-to-severe persistent asthma in adults and adolescents older than 12 in the United States, Europe and Japan as well as children under the age of 12 in Europe. Xolair is a humanized antibody targeting IgE. Notably, Xolair is only prescribed for patients with allergic asthma (about 50% of adult asthmatics)<sup>8</sup>. MEDI-528 is expected to be targeted to patients with either allergic or idiosyncratic moderate to severe persistent asthma.

Details of the Trust's comparison of MEDI 528 to Xolair are shown below.

<u>Xolair – Suited for Patients Who<sup>16</sup>:</u>	<u>MEDI 528 – Targeted to Patients Who:</u>
• Are 12 years of age and above;	• Are 12 years of age and above;
• Have moderate to severe persistent asthma;	• Have moderate to severe persistent asthma; AND
• Continue to have asthma symptoms even though taking inhaled steroids; AND	• Continue to have asthma symptoms even though taking inhaled steroids.
• Have asthma triggered by year-round allergens in the air (skin or blood test to confirm). <i>“XOLAIR captures most of the IgE related to allergic asthma.”</i>	<i>Not limited to allergen triggered asthma, IL9 is fundamental in the asthma inflammatory cascade, upstream of IL13, and based on influence on mast cells is considered early inducer of BHR, Anti-IL9 therapy is expected to prevent IgE production as opposed to capturing it.</i>
<b>PLUS:</b> Black Box Label for Anaphylaxis	N/A

To estimate minimum sales potential of MEDI-528 we start with projected Xolair sales:

Historical and Estimated Xolair Sales<sup>17,18</sup> in Billions of Dollars

	<b>Actual</b>			<b>Estimated</b>									
	<u>2006</u>	<u>2007</u>	<u>2008</u>	<u>2009</u>	<u>2010</u>	<u>2011</u>	<u>2012</u>	<u>2013</u>	<u>2014</u>	<u>2015</u>	<u>2016</u>	<u>2017</u>	<u>2018</u>
US Sales	\$0.43	\$0.47	\$0.52	\$0.57	\$0.61	\$0.64	\$0.67	\$0.71	\$0.74	\$0.78	\$0.82	\$0.86	\$0.90
Ex US	\$0.10	\$0.14	\$0.21	\$0.30	\$0.33	\$0.36	\$0.40	\$0.43	\$0.45	\$0.48	\$0.50	\$0.52	\$0.55
Total	\$0.53	\$0.61	\$0.73	\$0.87	\$0.94	\$1.00	\$1.07	\$1.13	\$1.19	\$1.25	\$1.32	\$1.38	\$1.45

On this basis, MEDI 528 peak year sales worldwide should surpass \$1.5 Billion and could be twice that.

90 to 95% of asthma cases can be controlled with medication but the remaining 5-10% are severe asthmatics who do not respond well to treatment, are likely to have more attacks and are at greater risk of a fatal attack<sup>19</sup>. In confidential diligence, the Trust can provide projections based on reasonable market penetration among the aforesaid 5-10% of asthmatics that credibly project peak year sales in the \$3 to \$4 Billion range for MEDI-528 from proprietary, independent market data acquired by the Trust.

### Clinical Development

Currently, three dose levels of MEDI-528 are being tested in a Phase 2b study for safety and efficacy with a placebo control with an anticipated enrollment of 320 subjects. The AstraZeneca/MedImmune clinical development program to date for MEDI-528 is summarized below:

#### MEDI-528 Clinical Study Summary

[www.clinicaltrials.gov](http://www.clinicaltrials.gov)

Study	Phase	Condition	Interventions	Study Population	Study Design	Start Date	Completion Date	Status
A Study to Evaluate the Effectiveness and Safety of MEDI-528 in Adults	II	Asthma	Biological: MEDI-528 Other: Placebo	320	<b>Safety/Efficacy Study</b> Treatment Randomized Open Label Placebo Control	October-09	March-12	Recruiting Expected to Start Imminently
A Phase 2A Study to Evaluate the Safety and Effect on Exercise Challenge Testing of MEDI-528 in Adults with Asthma	II	Asthma	Biological: MEDI-528 Other: Placebo	54	<b>Safety Study</b> Treatment Randomized Double-Blind (Subject, Investigator) Placebo Control	March-08	June-09	Suspended
A Study to Evaluate the Safety and Tolerability of the Administration of MEDI-528 When Administered in Multiple Doses to Adults With Mild Persistent Asthma	II	Asthma	Biological: MEDI-528 Other: Placebo	35	<b>Safety Study</b> Treatment Randomized Double-Blind (Subject, Investigator) Placebo Control	July-07	August-08	Completed
A Study to Evaluate the Effect of a Single-Dose Intravenous Administration of MEDI-528	II	Asthma	Biological: MEDI-528 Other: Placebo	30	Treatment Randomized Double Blind (Subject, Investigator) Placebo Control	July-07	March-09	Suspended
A Study to Evaluate the Efficacy of MEDI-528 in Late Asthmatic Response With Atopic Asthma	II	Asthma	Biological: MEDI-528 Other: Placebo	30	<b>Efficacy Study</b> Treatment Randomized Double-Blind (Subject, Investigator) Placebo Control	November-06	December-07	Completed
Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Immunogenicity of Single-Dose Subcutaneous Administration of MEDI-528	I	Healthy	Biological: MEDI-528	24	<b>Safety Study</b> Treatment Non-Randomized Open Label Dose Comparison	June-05	March-07	Completed
Study to Evaluate the Safety, Tolerability, Immunogenicity, and Pharmacokinetics of MEDI-528 in Healthy Adult Volunteers	I	Asthma	Biological: MEDI-528	24	<b>Safety/Efficacy Study</b> Treatment Non-Randomized Open Label Dose Comparison	August-04	March-05	Completed

From the recently posted Phase 2b study, one can safely infer that the suspension of earlier studies, so called “clinical hold”, was not related to the study drug. The Trust believes that the new study underscores the implied safety of MEDI-528.

### **Additional Information**

AstraZeneca/MedImmune is contractually entitled to keep the redacted terms of the License as well as development plans and other details of the IL-9 program confidential indefinitely. Given AstraZeneca’s size, many details of clinical studies, outcomes and regulatory interactions may never appear in FORM 8-Ks or press releases. The Trust can only provide information it has received confidentially to parties who execute a Confidentiality Agreement. Interested institutional investors should contact the Trustee:

Argyce LLC  
Trustee of the Genaera Liquidating Trust  
Attn: John Skolas  
[jskolas@argyce.com](mailto:jskolas@argyce.com)  
Office 267 988 4075  
Mobile 267 303 0834

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#### **End Notes**

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12. Global Initiative for Asthma. Global Burden of Asthma. <http://www.ginasthma.com/BackgroundersItem.asp?intId=19>
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16. From the Xolair.com website, <http://www.xolair.com/about.html>, Retrieved October 29, 2009.
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