SULFAGENIX BUSINESS OPPORTUNITY

Sulfagenix Inc. (www.sulfagenix.com), a clinical-stage private pharmaceutical company, is keenly interested in partnering to fully exploit the outstanding drug potential of orally-active SG1002.

SG1002 has successfully undergone Phase I and Phase II clinical trials demonstrating safety (800 mg twice a day - BID); it has also been demonstrated to be safe in mice & swine, and it is GRAS via self-affirmation.

SG1002 is a proprietary hydrogen sulfide prodrug. Upon reaching the intestine, SG1002 is metabolized at a slow and bioregulated rate by the intestinal microbiota and epithelial cells, and efficiently converted into hydrogen sulfide (H_2S) which is readily absorbed and stored as sulfane sulfur.

SG1002 is the only hydrogen sulfide prodrug that converts 100% into H_2S making SG1002 the most efficient H_2S-generating therapeutic agent available in clinical development.

Sulfagenix's intellectual property around SG1002 is exceptionally strong and broadly protected by 3 issued United States patents covering synthesis, composition of matter and method of use, as well as patents issued in Japan, Australia, China, Mexico and Europe, including additional filed patent applications (Brazil, Canada).

While the initially pursued indication is heart failure, rapidly accumulating evidence (obtained by us and many others independently of Sulfagenix) strongly supports carrying out clinical trials in the following indications: ischemia-reperfusion injury (heart, brain, liver, kidneys, etc.), atherosclerosis, peripheral artery disease (PAD), hypertension, dyslipidemia, HIV-AIDS, neurogenerative diseases (Alzheimer, Parkinson, multiple sclerosis), hyperproliferative diseases (cancer, psoriasis, etc.), preeclampsia, autoimmune diseases (Sjögren's syndrome, lupus, etc.), allergic disorders, fibrotic diseases, arthritis, asthma, osteoporosis, sarcopenia, diabetes, fatty liver, chronic kidney disease, refractory wounds/ulcers, organ transplantation, plastic surgery, male infertility, hearing loss, lens opacification, erectile dysfunction, and Duchenne muscular dystrophy (DMD).

The plurality of H_2S therapeutic targets goes hand in hand with its pleiotropic effects on multiple molecular pathways. It is now realized, on the basis of the large number of failed single-targeted drug agents in clinical trials/development , that molecularly targeted therapies are far from being ideally suited for treating effectively highly complex disease states such as cancer, HIV-AIDS and diabetes, since they require modifying integrated biological outcomes rather than targeting single pathways. In the case of diabetes, for instance, it is necessary to develop therapies aimed at simultaneously improving energy metabolism, insulin resistance, vascular function, blood pressure, and inflammatory/procoagulant status: The pleiotropic biological profile of H2S, which includes potent antioxidant, antiapoptotic, anti-inflammatory, vasoactive and cytoprotective effects on normal (non-transformed) cells can be harnessed to successfully treat such complex biological conditions. For an account of this new paradigm, please refer to Sestito S et al., "Hydrogen Sulfide: A Worthwhile Tool in the Design of New Multitargeted Drugs," Frontiers in Chemistry, 27 September 2017, Vol 5, Article 72.

Thus, protein S-sulfhydration (persulfidation) probably mediates: 1) the promotion of glucose uptake by cells via enhancement of insulin receptor sensitivity, 2) blood pressure lowering via activation of K_{ATP} channels, 3) inhibition of platelet aggregation, 4) atherogenesis inhibition via

downregulation of Hu R factor and MMP-9 expression, 5) inhibition of the activation of nuclear transcription factor NF-$_k$B via nuclear translocation, and 6) upregulation of endothelial NO synthase.

Preservation of mitochondrial function through H_2S direct and mainly indirect (via Nrf2 activation) antioxidant effects is at the root of H_2S-mediated cytoprotection during myocardial infarction; as such, it is important to point out that nuclear transcription factor Nrf2 is the master regulator of the expression of antioxidant proteins. Inhibition of inflammatory cytokines and reversible inhibition of cytochrome c oxidation seem to further contribute to cytoprotection. In fact, preservation of mitochondrial function is an effective strategy for treating other mitochondrial-driven diseases such as neurodegeneration and aging.

H_2S therapeutic effects, including those related to inflammation, also depend to a great extent on its capacity to regulate the homeostasis of the cellular immune system, both directly and indirectly, via the H_2S-Cysteine-Glutathione connection (see Predmore-Lefer-Gojon, Open Access- "Hydrogen Sulfide in Biochemistry and Medicine," Antioxidants & Redox Signaling, 2012 , pp 119–140).

For further information regarding the mechanism of action of H_2S, please visit www.sulfagenix.com

CANCER: Regarding H_2S anti-cancer effects, please refer to Table 1 in Predmore-Lefer-Gojon, Open Access – "Hydrogen Sulfide in Biochemistry and Medicine," Antioxidants & Redox Signaling, 2012, pp 119–140, and see below.

SG1002 Profile

SG1002 physicochemical and therapeutic profiles match very closely those of the IDEAL H_2S PRODRUG, since it is:

- Safe, with a very high therapeutic index and very mild gastrointestinal side effects.
- Orally active and slow H_2S-releasing.
- Odorless and tasteless (it may be sprinkled on food if patient has trouble swallowing a capsule or tablet).
- Highly potent .
- Effective independently of H_2S-generating enzyme levels.
- Able to release H_2S at a slow, sustained and bioregulated rate and to increase sulfane sulfur levels in blood AND TISSUES OF ALL VITAL ORGANS.
- Indefinitely stable (shelf life greater than 2 years).
- Versatile (highly effective in prevention and/or treatment of multiple pathologies related to inflammation, immune dysregulation, oxidative stress, electrophilic stress and ER stress).
- Gastroprotective, enteroprotective, hepatoprotective, cardioprotective, renoprotective, neuroprotective, otoprotective, eye protective, chondroprotective, osteoprotective, pancreoprotective, and antifibrotic.

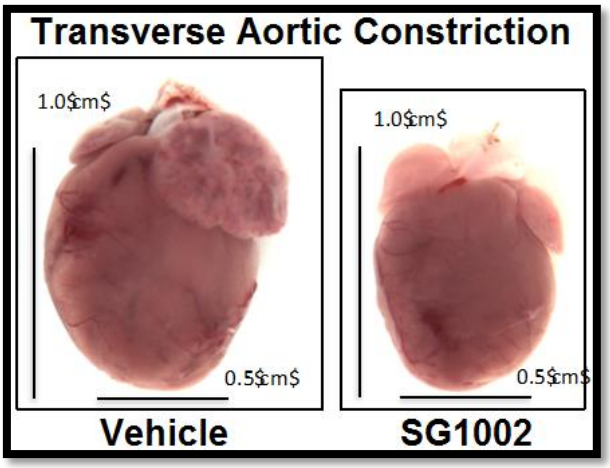
Capitalization of words in the following paragraph is ours:

According to highly regarded experts (John L Wallace et al., 2018, Antioxidants & Redox Signaling, vol. 28(16):1533-1540 and Cao Xu et al., 2019, Antioxidants & Redox Signaling, 31(1):22-36, "SG1002 for cardiovascular disorders and ATB-346 for arthritis have progressed into clinical trials and HAVE SHOWN CONSIDERABLE PROMISE… SG1002 produces more sustained and consistent levels of hydrogen sulfide in plasma… SULFAGENIX HAS DEMONSTRATED THAT ADMINISTRATION OF SG1002 CAN RESTORE TO NORMAL THE PLASMA H2S AND NO LEVELS IN CHF PATIENTS, thereby reducing the severity of, or preventing, heart failure… Importantly, the levels of hydrogen sulfide in these subjects (i.e., the volunteers participating in the Phase I clinical trial), REMAINED BELOW CYTOTOXIC CONCENTRATIONS".

SELECTED SG1002 DEVELOPMENT MILESTONES

Circa 2010 (Cancer): A pediatric cancer consecutive clinical study was conducted including 11 terminally ill children presenting with osteosarcoma, medulloblastoma, squamous cell carcinoma and acute lymphoblastic leukemia. These patients (all refractory to chemotherapy and/or radiotherapy) received up to 3600 mg of SG1002 DAILY. **Results:** In all cases the patients' condition improved, no adverse effects were reported, TUMORS SHRANK OR DISAPPEARED, and both mood and outlook also improved (US PATENT 8,771,755). Please note that the probability of "spontaneous remission" in a group of 11 terminal cancer patients is less than 1 in 10 to the 55th power.

February 2013 (Heart Failure): First report on SG1002 composition and outstanding results of preclinical study (murine model of heart failure) published in the journal CIRCULATION (Kondo K et al., 127:1116-1127). One of the remarkable *in vivo* results is illustrated in the picture below.



August 2014 (Alzheimer's disease): Paul Lombroso (Yale University School of Medicine) published a paper ("Inhibitor of the tyrosine phosphatase STEP reverses cognitive deficits in a mouse model of Alzheimer's disease", PLOS Biology, vol. 12(8): e1001923). **Results: Elemental sulfur potently inhibits the tyrosine phosphatase "STEP", thereby reversing cognitive deficits in a murine model of Alzheimer's disease.** Since SG1002 COMPRISES ZEROVALENT SULFUR, these results are highly relevant.

March 2015 (Phase 1/Heart Failure): Publication of the HIGHLY ENCOURAGING results of SG1002 PHASE I CLINICAL TRIAL in the journal Cardiovascular Therapeutics. This trial was sponsored by SULFAGENIX AUSTRALIA PTY LTD, and carried out in Australia; Dr Henry Krum, an internationally recognized heart failure researcher from Monash University, served as co-Principal Investigator. **Results:** Phase 1 trial demonstrated that SG1002 is SAFE, with an AMPLE THERAPEUTIC WINDOW and provided preliminary evidence supporting EFFICACY ("A Novel Hydrogen Sulfide Prodrug, SG1002, Promotes Hydrogen Sulfide and Nitric Oxide Bioavailability in Heart Failure Patients", Cardiovascular Therapeutics 2015, Vol. 33, 216–226).

June 2015 (Phase 2/Oligoasthenozoospermia): Article titled "A randomized clinical study assessing the effects of the antioxidants resveratrol and SG1002, a hydrogen sulfide prodrug, on idiopathic oligoasthenozoospermia" is published (Asian Pacific Journal of Reproduction, vol. 4:106-111). **Results:** Men presenting with oligoasthenozoospermia benefited from treatment with SG1002 (1500 mg per day) as their sperm count and motility increased, and their spermatozoa displayed less morphologic abnormalities vs patients that received placebo.

June 2017 (Ischemic Cardiomyopathy): Bharat Balan's MSc Thesis (Virginia Commonwealth University) is published. The thesis title is "Novel orally active hydrogen sulfide-releasing compound SG1002 improves left ventricular function and survival in a murine model of ischemic cardiomyopathy".

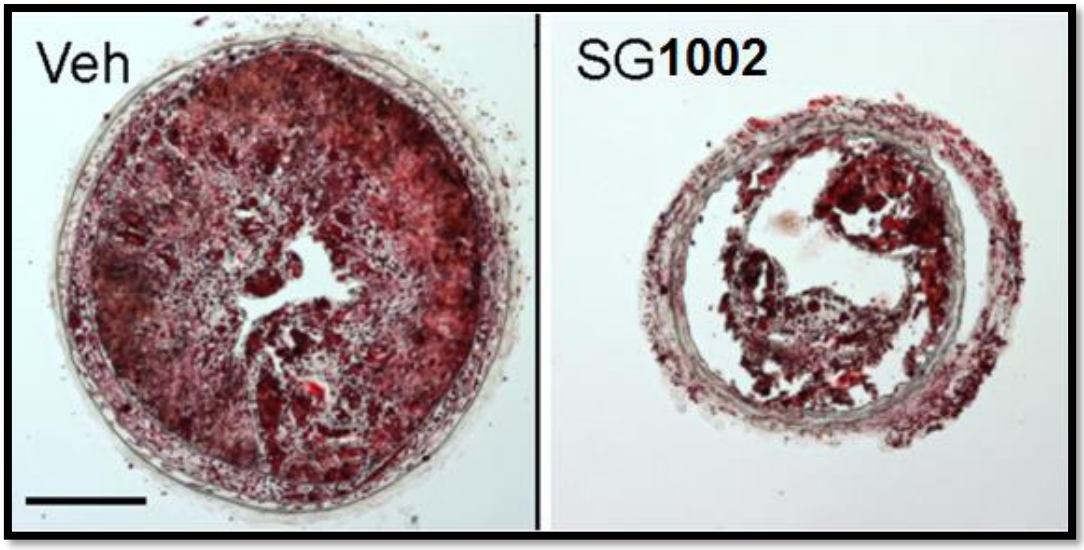
December 2017 (Global Impact): SG1002 had been mentioned in 100 scientific papers and conference/meeting abstracts AND ALWAYS IN THE CONTEXT OF HEALTH-PROMOTING PROPERTIES AND EFFECTS.

March 2018 (Heart Failure): The research group of Dr. John W. Calvert (Emory University School of Medicine) publishes a paper (J Mol Cell Cardiol, vol. 116: 29-40) reporting that "restoring H_2S levels with SG1002 in the setting of heart failure increased cardiac mitochondrial content, improved mitochondrial respiration, improved ATP production efficiency and improved cardiac function."

January 2, 2019 (Atherosclerosis): Ground-breaking study carried out in Europe and published in the journal CIRCULATION (vol. 139:101-114) by Sofia-Iris Bibli, Ingrid Fleming and co-workers. **Results:** Excellent results were obtained upon SG1002 treatment of atherosclerosis in a murine model. The authors point out that "oral supplementation with hydrogen sulfide donors (e.g., SG1002) may serve as a therapeutic approach to attenuate atherosclerosis development in humans." Importantly, BIBLI ET AL WERE ABLE TO INCREASE BLOOD H2S LEVELS BY 60%.

January 2, 2019 (Atherosclerosis): In the editorial of the January 2 issue of the journal CIRCULATION, two distinguished Swiss clinicians conclude that "provided that this drug (SG1002) is proven to be safe, clinical testing in patients with coronary atherosclerosis may be warranted."

January 14, 2019 (Atherosclerosis): On January 14, 2019, the highly prestigious journal Nature Medicine published a summary of the remarkable impact of SG1002 in protecting against clogged arteries providing irrefutable proof of the high impact and promise SG1002 offers as a therapeutic agent for atherosclerosis. See picture below.
(https://www.nature.com/articles/d41591-019-00001-0)



"The finding, published in the January issue of the journal Circulation, offers solid and direct evidence that hydrogen sulfide generated by cells lining the body's blood vessels can protect against atherosclerosis."

Ingrid Fleming (corresponding author) is quoted as saying that SG1002 may have the potential to help people with atherosclerosis. "We actually chose to use this compound because it completed Phase 1 clinical trials, and a Phase 2 trial is running to assess its safety in heart failure patients"; she also stated that "the effect of SG1002 exceeded our expectations".

February 2019 (Peripheral Artery Disease): Dr. David J Lefer et al. (LSU Health Sciences Center - New Orleans) publish a paper titled "Effects of a novel hydrogen sulfide prodrug in a porcine model of acute limb ischemia" (J VASC SURG). **Results:** Daily oral administration of SG1002 led to an increase in circulating hydrogen sulfide and nitric oxide, and that "SG1002 preserves the vascular architecture in ischemic limbs and exerts vascular protective effects in the coronary vasculature in a model of peripheral vascular disease".

April 2019 (Duchenne Cardiomyopathy): Chad Cain et al. publish in The FASEB Journal (vol. 33, in press) a paper titled "Prevention and Treatment of Duchenne Cardiomyopathy with Hydrogen Sulfide-Donor Therapy". **Results:** In a 'humanized' mouse model of Duchenne muscular dystrophy (DMD), early treatment with SG1002 preserved cardiac function (ejection fraction; EF) throughout study duration and strongly supports a daily H_2S therapy for preservation of cardiac function, attenuation of skeletal muscle fibrosis and cardiac NLRP3 expression.

April 2019 (Duchenne Muscular Dystrophy): Gurpreet Randhawa et al. publish in The FASEB Journal (vol. 33, in press) a paper titled "Hydrogen Sulfide Improves Aberrant Gastric Smooth Muscle Function in Duchenne Muscular Dystrophy Mice". **Results:** Orally active and slow H_2S-releasing SG1002 restores gastric smooth muscle function and contractile protein expression suggesting a therapeutic potential for SG1002 to treat motility disorders in Duchenne muscular dystrophy (DMD).

April 2019 (Duchenne Muscular Dystrophy): Kulpreet Singh et al. publish in The FASEB Journal (vol. 33, in press) a paper titled "Restoration of Contractile Protein Expression and Colonic Smooth Muscle Function by H_2S in Duchenne Muscular Dystrophy Mice". **Results:** Acetylcholine-induced contractions in mice were decreased and partly reversed by SG1002

treatment. Similarly, expression of contractile proteins was also decreased and reversed by SG1002. The results support the therapeutic potential of SG1002 for the control of DMD-induced gastrointestinal motility disorders.

May 2019 (Diabetic Hyperhomocysteinemia/Cardiac Remodeling): Kar S. et al. publish an article in the journal Frontiers in Physiology titled "Hydrogen sulfide ameliorates homocysteine-induced cardiac remodeling and dysfunction" (10:598). **Results:** SG1002 treatment alleviates cardiac remodeling and dysfunction in hyperhomocysteinemic mice. These results are relevant in the setting of diabetes therapies, since diabetic patients show elevated levels of homocysteine, which is strongly associated with the development of cardiovascular disease.

HEART FAILURE MARKET OPPORTUNITY

From Novartis 2018 10K annual report: Entresto® was approved in the US and in the EU in 2015. It is now approved in more than 100 countries and launched in more than 90 countries. Both European Society of Cardiology heart failure guidelines and US heart failure guidelines have given a Class I recommendation, the strongest class of recommendation, for the use of sacubitril/valsartan in patients with HFrEF (chronic heart failure with reduced ejection fraction).

The **strong sales growth** was driven by volume growth of 9 percentage points (cc), mainly driven by Cosentyx, AAA and four additional **drugs reaching blockbuster status** (Promacta/Revolade, Tafinlar + Mekinist, **Entresto®** and Xolair).

The Pharmaceuticals Business Unit grew 7% (cc), driven by Cosentyx reaching USD 2.8 billion and **Entresto®** reaching **USD 1.0 billion**.

Regionally, in the US (USD 11.9 billion, +9%), the strong performance was driven by Cosentyx, **Entresto®**, Promacta/Revolade and Lutathera. **Europe** sales (USD 12.3 billion, +8% cc) were driven by Cosentyx, **Entresto®** and Jakavi.

The following table provides the top 20 Innovative Medicines Division product net sales – 2018

			US		Rest of world			Total		
Brands	Business franchise	Indication	USD m	% change USD/cc[2]	USD m	% change USD	% change cc[2]	USD m	% change USD	% change cc[2]
Entresto	Cardio-Metabolic	Chronic heart failure	556	87	472	125	124	**1 028**	**103**	**102**

[2] Constant currencies (cc) is a non-IFRS measure. For an explanation of non-IFRS measures, see " —Item 5.A Operating results—Non-IFRS measures as defined by Novartis."

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CARDIOVASCULAR OPPORTUNITY

The global cardiovascular drugs market was valued at US$ 80.0 billion in 2016 and it is projected to register a CAGR of over 1.0% from 2017 to 2025 collecting US$ 95 billion. Main markets include North America and Western Europe.

Cardiovascular disease (CVD) is a key cause of deaths globally. These diseases are mainly related to heart and blood vessel disorders including dyslipidemia, ischemic heart disease, stroke, thrombosis, coronary artery diseases, atherosclerosis, and peripheral artery disease. These diseases and disorders are mainly caused by high cholesterol, obesity, excess alcohol, smoking, and poor or sedentary lifestyle.

According to the World Health Organization (WHO), roughly **15 million deaths** are caused by CVD **each year** globally. **This surge in incidences is boosting the need for CVD drugs globally which in turn is driving growth of the global CVD drug market.**

Additionally, **the CVD drug market is expected to benefit from increasing incidences of obesity and diabetes among patients.** Poor life style and rising geriatric population are some of the key factor driving growth of the global CVD drug market.

ATHEROSCLEROSIS OPPORTUNITY

Arteriosclerosis is a common disease in our days, which consists of the hardening of the walls of arteries. Growing incidence of heart attacks due to atherosclerosis or coronary heart disease is expected to increase demand for atherosclerosis treatment products. The rise in the aging population is expected to propel demand over the forecast period. As per CDC (Centers for Disease Control and Prevention), **coronary illness accounts for around 610,000 deaths per year in the United States** - roughly being **responsible for 1 of every 4 deaths** reported. Coronary illness is the most widely recognized kind of cardiovascular disease, killing more than 370,000 individuals every year. This **increase in the baby boomer population is expected to add to the patient pool of atherosclerosis** and thus in turn increase demand for treatment over the forecast period.

In the United States, approximately **1.5 million myocardial infarctions occur annually**, and **more than 11 million Americans have chronic coronary artery disease**. Of persons older than 50 years, 30% have some evidence of carotid artery disease, and cerebrovascular disease is responsible for over 200,000 deaths per year in the United States.

North America and Western Europe are expected to be the leading markets in the global atherosclerosis market. Japan, Eastern Europe and Latin America markets are also expected to witness above average growth over the forecast period. The overall market is expected to reach US$15.4 billion in 2018.

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SULFAGENIX BUSINESS OPPORTUNITY SUMMARY

Joint clinical development of SG1002 for Heart Failure, Atherosclerosis, Peripheral Artery Disease, Ischemic Cardiomyopathy and Duchenne Cardiomyopathy. Orally-active SG1002 enables achievement of high H_2S and sulfane sulfur blood and tissue levels, is cytoprotective and has demonstrated safety in Phase 1 and Phase 2 clinical trials, displays a broad therapeutic window with 100% SG1002-to-H_2S conversion efficiency. Strong and broad intellectual property protection (granted patents). Demonstrated safety in Phase 1 and Phase 2 clinical trials opens opportunity for direct Phase 2 development of SG1002 in several diseases.

Heart Failure Opportunity: The heart failure market is set to rise from around US$ 3.2 billion in 2015 to US$ 11.8 billion by 2025, representing a compound annual growth rate of 13.7%. The seven major markets are the US, France, Germany, Italy, Spain, the UK, and Japan.

Cardiovascular Opportunity: The global cardiovascular drugs market was valued at US$ 80 billion in 2016 is projected to register a CAGR of over 1.0% from 2017 to 2025 collecting US$ 95 billion. Main markets include North America and Western Europe.

Atherosclerosis Opportunity: The overall market is expected to reach US$ 15.4 billion in 2018. The U.S. incidence/prevalence in 2018 was 18,749,358 people and it is projected to increase to 20,424,482 people by 2025.

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