Bessor Pharma

Building Value by Uniquely Translating University Assets into Promising Therapeutics

Bessor Pharma is utilizing an innovative technology/business model for new drug development and value creation, with a focus on translating opportunities from university laboratories into proof-of-concept or clinical-ready packages for the pharma/biotech industry. The Company, which has unique skills, connectivity and capital markets sophistication, is forging an ecosystem of academic and industry partners as key stakeholders facilitating translational R&D. Bessor is differentiated by its: aligned team with an unparalleled track record in drug development; operational progress; and unique collaborative partnerships with universities and investigators, fueling an innovative pipeline of highly needed drugs.

Bessor has made great progress in operationalizing its model. Key achievements in the last 24 months include:

- *From major in-licensed platforms, launched and advanced five novel projects across multiple indications in the areas of inflammation and cancer, each approximately 18 months from IND*
- *Established a growing set of relationships with major universities, such as Yale University and pending relationships with multiple other US institutions.*
- *Building a pipeline of in-licensing ready additional projects with R&D leaders.*
- *Created a set of standardized licensing and revenue sharing documents to streamline the partnership process with academic institutions and align incentives among all the parties.*
- *Awarded three government grants and sponsoring research at two academic medical centers.*
- *Established a fully integrated pharmaceutical network (FIPNET) including a growing network of more than 20 key advisors and companies.*

The Company is capitalizing on changing industry dynamics to access and advance promising opportunities from academia that have been generated through $30 billion annual NIH and other grant-funded research. In the current environment, many of these promising assets are increasingly untapped. We have developed a flexible, semi-virtual, project-oriented, capital-efficient approach that attacks and solves key translational, drug development and financing challenges.

With its efficient, proven and outstanding network of world class, research, clinical and drug development experts, Bessor rapidly advances projects to a significant value point – IND ready or predictive proof-of-concept (preclinical or clinical) with the objective of a strategic transaction or sale to pharmaceutical, large biotechnology or diagnostic companies in 18-30 months. At the same time our approach matches well with the deal dynamics and investment strategy big Pharma and big Biotech are increasingly emphasizing. The transactions, along with a project-based structure using individual project LLCs, are designed to generate a flow of investor/stakeholder returns from upfront payments, milestones, M&A events and royalties. Returns in our approach do not rely on a single project or the hope for a single liquidity event but are based on a portfolio of attractive innovative projects, providing "multiple shots on goal," serial liquidity and enhanced probabilities for success.

Bessor has assembled a top team of pharmaceutical R&D and business experts to select and advance our products. Collectively, the team members have played central roles in developing nearly 20 successful therapeutics, including Corlopam®, Tykerb®, Topotecan®, Gemzar®, and Coreg®. The team, along with complementary outside expertise, provides a fully integrated pharmaceutical development network. The operational team is led by Dr. Barry A. Berkowitz who has launched, grown, and created significant teams,

assets and value at both major pharmaceutical (Roche/GSK) and biotechnology companies, including Myco/Chemgenics (acquired by Millennium Pharmaceuticals), Fibrogen (IPO 2014) and New Chemical Entities, Inc. (acquired by AMRI).

Clear Need for Better Business Models and Improved R&D Process

The clinical need and commercial opportunity for innovative drugs remains enormous, yet at the same time it is apparent that traditional development and investment models are insufficient. Major pharmaceutical and biotechnology companies, facing increasing R&D costs, urgent needs for both increased R&D productivity and new, effective and innovative products, increasingly are turning to acquisitions and outsourcing.

Academic institutions continue to develop promising early stage research assets, driven in large part by top scientists and science fueled by NIH funding. Today, however, venture capital investment in USA, which has traditionally fueled company formation to advance technology from academia, has not increased or shifted to later stages of development as emerging company business models have proven neither cost effective nor generated attractive enough returns for most venture capital return-on-investment goals. Resources and goals at venture-backed companies can often become misaligned as projects evolve, increasing costs, slowing progress and limiting survival options. The established paths to liquidity – capital gains through IPOs or M&A – have become problematic. The IPO market is very cyclical and no longer a sufficiently reliable value generating option and high value acquisitions of entire biotech companies are rare.

Bessor's Differentiated Development and Financing Model

The Company has a unique, flexible structure focused on projects that functions as a FIPNET to acquire, develop and sell a portfolio of carefully selected projects, primarily from universities, with the goal of creating a diverse flow of investor/stakeholder returns. The model is also designed to accommodate selected diagnostics; particularly those coupled to a follow on therapeutics, and we have already begun pre-IND work on such a project. The key elements and value of the model are:

Capital Efficiency – Bessor is a semi-virtual organization that leverages a world class team of research, drug development and clinical experts across its project portfolio on a just-in-time basis and integrates with partners to provide comprehensive, global development capabilities. The team, whose members have been integral to the development of multiple successful drugs, also plays key roles in the Company's project selection process. Each team is selected and designed to optimize the development of a specific project.

Focus on Value-Building Translational Projects –This approach is designed to integrate clinical and commercial expertise early in the process, along with predictive metrics such as biomarkers, to identify candidates with a high potential for success and to drop unsuccessful ones which fail rapidly.

The result is a more promising product portfolio for further development. Our focus is primarily mid-to-late stage research through clinic ready development, while we also bring capabilities to develop carefully chosen candidates through compelling proof-of-concept.

Scalable Model/Flexible Returns – Our model is differentiated as it is operational and efficiently enables multiple, carefully selected projects to be developed in parallel, increasing the chances for success and mitigating risk. The Company is structured to create opportunities for a sustained flow of returns on investment to stakeholders from license fees, milestones and royalties, as well as capital gains, thereby aligning investor returns with the risk-sharing approach preferred by pharmaceutical partners. Our model is efficiently scalable and flexible and can accommodate selected additional interfaces, for example with disease foundations or partners for focused pipeline needs.

Aligned, Committed Top Team – Bessor is structured to better align the interests of all its stakeholders. The highly experienced team is committed to working collaboratively and has a shared passion for active engagement in developing innovative new drugs and diagnostics. A culture of and commitment to drug

discovery and development is broadly shared by Bessor's team. Unique alignment features include synergies among the key stakeholders and three strong drivers of progress: Top notch R&D/business team; university/medical center input and champions that collaborate closely with the Bessor team on translational projects; capital market and finance sophistication.

Streamlined project evaluation and licensing terms, strong collaborative partnerships with universities. Bessor offers universities attractive, standardized, straightforward, non-dilutive licensing terms co- designed by us and university technology transfer leaders. Each university receives the exclusive and full benefit of its own project successes because projects are developed on a standalone basis. Novel means for university partners to further share in exceptional success is built into the interactions. Moreover, our streamlined approach is designed to avoid the usual conflicts of interest and the almost endless and non-efficient haggling that usually precedes and slows such alliances. Through the evaluation process and project development, Bessor builds highly collaborative relationships with the university and investigators to synergize its projects.

Validated – The Company is operational and producing results, with three projects launched, an additional IND expected in approximately 18 months of the current financing, established university relationships, a growing IP portfolio and identified promising additional projects.

Bessor's Initial Projects

The company has launched a portfolio of innovative projects across multiple indications in the areas of inflammation and cancer.

Project Areas	Therapeutic Areas
Inflammation Renalase agonists TSG-6	 Acute Pancreatitis Acute Kidney Injury Ophthalmology (Dry eye, Corneal injury)
Cancer and Immuno-oncology Anti-renalase antibodies Renalase agonists	 Pancreatic cancer, melanoma Chemotherapy tissue damage reversal -Cisplatin kidney toxicity
Stem cell platform technology (mesynchymal stem cells, TSG-6, exosomes)	 Traumatic brain injury/concussion, periodontal disease, cardiovascular disease, Ophthalmology

Renalase Technology/ Inflammation

Renalase (RNLS) is a secreted flavoprotein, produced in the kidney, pancreas and other tissues, that was discovered by our collaborator, Dr. Gary Desir, Chairman of Medicine at Yale and colleagues. Independent of its initially identified activity in metabolizing catecholamines, Dr. Desir's group has shown that RNLS can function as a survival factor that acts through a pro-survival, anti-apoptotic signaling cascade (MAPK). They have also identified the RNLS receptor and the RNLS regions that interact with the receptor. They have established a strong therapeutic rationale for the short-term activation of the RNLS signaling pathway with RNLS peptide mimics to treat a number of acute conditions characterized by RNLS deficiency. We are on path for an initial IND submission in for a therapeutic antibody in about 18 months. In addition, they have shown that RNLS is a promising new target for pancreatic cancer, melanoma, and potentially other cancers. An anti-RNLS antibody is approximately 18 months from IND. RNLS levels' link to these conditions provides a potential new and useful biomarker for early diagnosis and monitoring of drug response.

Bessor has exclusive rights from Yale to patent applications covering RNLS, analogs, regulators and diagnostic assays. We have established an LLC, Personal Therapeutics to translate these discoveries into therapeutic candidates.

Renalase agonists

Pancreatitis. Inflammation, pain and cell death are universal hallmarks of pancreatitis, the most common gastro-intestinal cause of hospital admissions. There are no approved drugs for pancreatitis in the U.S. Our initial data show: Deletion of RNLS increases the severity of acute pancreatitis in mice; serum RNLS levels are decreased in mice and humans with acute pancreatitis and exogenous RNLS reduces injury in a model of acute pancreatitis. The project is also supported by an SBIR grant from the Natl. Institute of Diabetes and Digestive and Kidney Diseases.

> The Serum Protein Renalase Reduces Injury in Experimental Pancreatitis. Thomas R. Kolodecik, Anamika M Reed, Kimie Date, Christine Shugrue Vikhik Patel, Shang-Lin Chung, Gary V. Desir, Fred S Gorelick. Journal of Biological Chemical Chemistry, E-publication Oct. 17, 2017
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> Su1900 Renalase Deficiency Worsens Acute Pancreatitis in Mice**.** Anamika Reed, Thomas R. Kolodecik, Fred S. Gorelick, Gastroenterology Volume 146, Issue 5, Supplement 1, Page S-496 ay 2014

Acute Kidney Injury (AKI). AKI is commonly associated with sepsis, surgery, and certain drugs, affects up to 20% of hospitalized patients and can lead to in hospital or longer term mortality. There is no effective treatment other than supportive care. We have demonstrated that acute administration of RNLS or activation of the RNLS pathway with novel RNLS peptide analogs prevents or treats AKI.

> Renalase in hypertension and kidney disease. Desir GV, Peixoto AJ. Nephrol Dial Transplant. 2014 Jan;29(1)

Chemotherapy tissue damage reversal. We are developing renalase agonists to protect against acute kidney injury (AKI), including those caused by the commonly used chemotherapeutic cisplatin and potentially other chemotherapeutics, to allow longer use of effective anticancer therapies and prevent progression to chronic kidney disease. Too often otherwise effective chemotherapy must be stopped due to side effects; there are no effective drugs used to blunt such serious adverse effects. Cisplatin is among the most widely used chemotherapeutics. However, cisplatin's use is severely limited by kidney toxicity, with 25-35 percent of patients needing to reduce or stop otherwise effective therapy. We have shown that RNLS deficiency is associated with dramatically more severe cisplatin-mediated AKI, elevated plasma creatinine and chronic kidney injury. Acute RNLS administration ameliorates cisplatin-induced toxicity in in vivo clinical models without interfering with cisplatin's anti-tumor activity. The project has been supported by an STTR grant from the US Natl. Cancer Institute.

> Three-Dimensional Morphology by Multiphoton Microscopy with Clearing in a Model of Cisplatin-Induced CKD. Torres R, Velazquez H, Chang JJ, Levene MJ, Moeckel G, Desir GV, Safirstein R., J Am Soc Nephrol. 2016 Apr;27(4):1102-12.
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> Renalase protects against cisplatin acute kidney injury in mice. Gary V Desir, Ling Wang, Heino Velazquez, Gilbert Moeckel and Robert Safirstein. The FASEB Journal April 2013 vol. 27 No. 1 Supplement 910.7

Anti-Renalase Antibodies for Pancreatic Cancer, Melanoma, and other challenging cancers. Pancreatic ductal carcinoma is among the most lethal tumor types. It is the ninth most common tumor type, but ranks third in cancer deaths. Despite recent significant advances, such as immune checkpoint inhibitors, many patients are not cured and the projected death rate from melanoma in 2015 in the United States has risen by 30% to 9,940 from 7,600 in 2013. Renalase is expression is increased in these tumors and in tumor associated macrophages (TAMS), expression inversely correlates with survival, and signaling inhibition has anti-tumor activity. Preclinical *in vivo* proof-of-concept in vitro and in in vivo models has been

demonstrated with candidate therapeutic antibodies. The renalase antibody is active in vitro and in in vivo models in cancers resistant to current top therapies and demonstrates synergy with such agents.

Inhibition of renalase expression and signaling has antitumor activity in pancreatic cancer. Guo X, Hollander L, MacPherson D, Wang L, Velazquez H, Chang J, Safirstein R, Cha C, Gorelick F, Desir GV. Sci Rep. 2016 Mar 14;6:22996.

Renalase expression by melanoma and tumor associated-macrophages promotes tumor growth through a STAT3-mediated mechanism. Hollander L, Guo X, Velazquez H, Chang J, Safirstein R, Kluger HM, Cha C, Desir G. Cancer Res. 2016 May 9. pii: canres.1524.2015.

Stem Cell and Stem Cell Signaling Platform

We are advancing a platform for developing novel therapeutics for tissue repair and inflammatory diseases based on mesenchymal stem cells (MSCs), stem cell signaling molecules, and exosomes. The initial technology is built around discoveries by Dr. Darwin Prockop and colleagues that the beneficial effects of mesynchymal stem cells (MSCs) in models of several disorders, including ophthalmic inflammatory disorders, traumatic brain injury, stroke, result primarily from MSC expression of TSG-6. TSG-6 uniquely functions at an early stage of the inflammatory process, decreasing the TLR/NF-ķB responses of resident macrophages.

Production of TSG-6 has been rate limiting to its therapeutic development. Prockop and colleagues have developed a scalable manufacturing process to enable supply for subsequent research and that has potential to be optimized for producing clinical material. We have formed an LLC, Temple Therapeutics, to focus on and accelerate product development. The initial project being advanced is TSG-6 for the treatment of ocular inflammatory disorders. We have licensed exclusive patent rights from Texas A&M to technology related to the platform including an issued US Patent (8,785,395) covering use of adult stem cells/progenitor cells and stem cell proteins for treatment of eye injuries and diseases.

TSG-6 for ocular inflammation.

Inflammation is a critical driver of tissue damage in corneal injury and dry eye syndrome. There are no effective treatments for corneal injury due to chemical or mechanical injury. The leading current treatment for dry eye, cyclosporine, is not effective in many patients and is poorly tolerated; long term-steroid use carries cataract and glaucoma risks. We and our collaborators have demonstrated preclinical proof of concept with TSG-6 in models of corneal injury and dry eye disease. Early studies suggest TSG-6, unlike steroids, does not damage corneal epithelium.

We expect to submit an IND in approximately 18 months. The technology has also been shown to have important potential in the treatment of other ophthalmic conditions, including retinal disorders and uveitis.

Comparison of Topical Application of TSG-6, Cyclosporine and Prednisolone for Treating Dry Eye. Yu Jeong Kim, MD, Jin Suk Ryu, MS, Se Yeon Park, DS, Hyun Ju Lee, DS, Jung Hwa Ko, MS, Mee Kum Kim, MD, PhD, Won Ryang Wee, MD, PhD, and Joo Youn Oh, MD, PhD. Cornea. 2016 Apr;35(4):536-42.

Chromatographically isolated CD63+CD81+ extracellular vesicles from mesenchymal stromal cells rescue cognitive impairments after TBI Dong-ki Kim , Hidetaka Nishida , Su Yeon An, Ashok K. Shetty, Thomas J. Bartosh, and Darwin J. Prockop. Proc Natl Acad of Sci USA 2016 Jan 5, 170-175

Topical TSG-6 administration protects the ocular surface in two mouse models of inflammation-related dry eye. Lee MJ, Kim DH, Ryu JS, et al. Invest Ophthalmol Vis Sci. 2015;56:5175–5181.

TSG-6 as a biomarker to predict efficacy of human mesenchymal stem/progenitor cells (hMSCs) in modulating sterile inflammation in vivo. Lee RH, Yu JM, Foskett AM, Peltier G, Reneau JC,

Bazhanov N, Oh JY, Prockop DJ. Proc Natl Acad Sci U S A. 2014 Nov 25;111(47), 16766-71

Phase-directed therapy: TSG-6 targeted to early inflammation improves bleomycin-injured lungs., Foskett AM, Bazhanov N, Ti X, Tiblow A, Bartosh TJ, Prockop DJ. Am J Physiol Lung Cell Mol Physiol. 2014 Jan;306(2):L120-3

Anti-Inflammatory Protein TSG-6 Promotes Early Gingival Wound Healing: An In Vivo Study. Beltran SR, Svoboda K, Kerns DG, Sheth A, Prockop DJ. J Periodontol. 2014 Sep 30:1-17

Administration of TSG-6 improves memory after traumatic brain injury in mice.Watanabe J, Shetty AK, Hattiangady B, Kim DK, Foraker JE, Nishida H, Prockop DJ. Neurobiol Dis. 2013 Nov;59:86-99.

Anti-inflammatory protein TSG-6 secreted by activated MSCs attenuates zymosan-induced mouse peritonitis by decreasing TLR2/NF-κB signaling in resident macrophages. Choi H[1], Lee RH, Bazhanov N, Oh JY, Prockop DJ. Blood. 2011 Jul 14;118(2):330-8.

Intravenous mesenchymal stem cells prevented rejection of allogeneic corneal transplants by aborting the early inflammatory response. Oh JY, Lee RH, Yu JM, Ko JH, Lee HJ, Ko AY, Roddy GW, Prockop DJ. Mol Ther. 2012 Nov;20(11):2143-52

Intravenous hMSCs improve myocardial infarction in mice because cells embolized in lung are activated to secrete the anti-inflammatory protein TSG-6., Lee RH, Pulin AA, Seo MJ, Kota DJ, Ylostalo J, Larson BL, Semprun-Prieto L, Delafontaine P, **Prockop DJ**., Cell Stem Cell. 2009 Jul 2;5(1):54-63

Management Team

Barry A. Berkowitz, PhD *Chairman of Board of Directors & CEO* Drug R&D Executive and Entrepreneur	Former: Co-founder and/or CEO, Myco/ Chemgenics, Fibrogen, New Chemical Entities; Senior positions at Roche, SmithKline; Corlopam®
Wallace Dairman, PhD *VP Toxicology and Drug Development*	Former Roche; senior leader Toxicology
Martin Hynes, PhD *VP Project Management & Quality Assurance*	Former Lilly, Director, Project Management and Quality Assurance, Neuroscience
Satish Menon PhD *VP Biotechnology R&D (Biopharm R&D)*	Former Schering-Plough; Director, Process Development, Allergan
Eliot Ohlstein, PhD *VP Pharmacologic R&D including CV/Renal*	Former VP GSK (Coreg®); Head Center of Excellence
Mark Roffman, PhD *VP Drug Devel and Reg Affairs (Neuroscience)*	Former GSK; more than 30 years, drug dev. clinical research, regulatory affairs, orphan drug experience
Allan M. Cohen, Esq., CPA *General Counsel, Licensing, IP and Bus. dev.*	Former: Auven Therapeutics; Celtic Pharma; McDermott, Will & Emery; Arthur Andersen & Co.
Robert Morgan, *CFO*	Former: PriceWaterhouse; Co-Founder, Chemgenics New Chemical Entities; NewCoGen (Flagship VC fund)

Board of Directors

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George Demetri, MD *Scientific Advisory Board*	Director, Center for Sarcoma and Bone Oncology, SVP for Experimental Therapeutics, Institute Physician, Dana-Farber Cancer Institute (Gleevec®)
Gary V. Desir, MD *Scientific Advisory Board Bessor Pharma and Scientific Advisory Board, Chair, Personal Therapeutics*	Chairman of Medicine, Yale Co-founder Personal Therapeutics
John E Edwards MD *Scientific Advisory Board*	Emeritus, Chief Infectious Disease, Harbor-UCLA Medical Center
Homer Pearce, PhD *Scientific Advisory Board* Medicinal chemistry and R&D expert	Former VP, Lilly; Gemzar® (gemcitabine), ALIMTA® (pemetrexed)
Neil Spector, MD *Scientific Advisory Board* Drug development and biomarker expert	Dir., Translational Res, Oncology and Co- Director of the Experimental Therap. Program Duke Cancer Center; Tykerb® (lapatinib), Arranon® (nelarabine);
Key Consultants/Advisors include: **Richard L Sherman** (ex- Dep. Gen. Counsel, SmithKline Beckman); **Armand Keating**, MD, Chair Cell Therapy and Transplantation, U. of Toronto; **Darwin J Prockop, MD, PhD** (Dir Inst Regen Med Texas A&M); **Anthony J Day,** DPhil (Univ of Manchester)	Stem cells and cell therapeutics, inflammation and immune modulation, drug development and strategic alliances

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