



Executive Summary

Company: Novo Biosciences, Inc. is a pre-clinical stage **regenerative medicine** company developing first-in-class small molecules therapies to stimulate tissue repair and regeneration.

Overview: Regenerative medicine is the field of medical research that focuses on replacing, engineering or regenerating human cells, tissues or organs to restore function. The U.S. Department of Health and Human Services has called regenerative medicine the “vanguard of 21st-century healthcare”. The global market for regenerative medicine therapies is expected to exceed \$68 billion by 2020.

Our lead small molecule, ZF143: ZF143 is a readily synthesized natural small molecule that stimulates regeneration of heart, skeletal muscle, skin, bone, nerve, connective and vascular tissue in lower vertebrates and mice. Administration of ZF143 to mice 24 hours after myocardial infarction (MI) greatly increases survival, stimulates cardiomyocyte proliferation in the infarct border by 3-fold, improves heart function 2-fold, reduces ventricular wall thinning and reduces infarct size 55% 4 weeks post-MI.

ZF143 has previously been tested in human Phase 1 and 1b trials for the treatment of obesity and has been shown to be safe. The stimulatory effects of ZF143 on tissue regeneration occur at doses 50-times lower than the maximum safe human dose.

The protein target of ZF143 is well studied and functions normally to inactivate multiple signaling pathways that stimulate tissue repair and regeneration after injury. ZF143 inhibits its target with high specificity allowing these pro-regeneration and repair pathways to remain active. Genetic knockout of the ZF143 target in lower vertebrates and mice stimulates tissue repair and regeneration and slows aging-induced tissue degeneration, but does not alter sensitive developmental processes or induce tumor formation.

Therapeutic indications: Heart disease is the leading cause of death throughout the world. Coronary heart disease (CHD) is the most common type of heart disease and is responsible for ~7.4 million annual deaths worldwide. Current healthcare costs for CHD in the U.S. alone are \$126.2 billion and are expected to rise to \$177.5 billion by 2040.

The human heart has very limited ability to repair or regenerate muscle cells killed or damaged by a heart attack. Instead, dead cells are replaced by nonfunctional scar tissue that weakens the heart and can ultimately lead to complete heart failure and death. Our studies in lower vertebrates and mice demonstrate that ZF143 stimulates heart muscle regeneration and protects it from further injury following a heart attack.

Novo Biosciences' extensive studies in lower vertebrate and mouse models have demonstrated that ZF143 has multiple other potential therapeutic uses. For example, ZF143 dramatically stimulates mouse skeletal muscle stem cell activation 2-fold after injury. Ongoing pre-clinical research focuses on development of ZF143 for treatment of skeletal muscle damage including damage caused by *orphan* diseases such as *pediatric muscular dystrophies*.

Novo's immediate goal is to advance ZF143 into clinical trials for stimulating repair and regeneration of heart muscle following acute heart attack and to reverse skeletal muscle damage caused by muscular dystrophy.

Competition: Regenerative medicine R&D efforts for heart disease have focused extensively on development of stem cell-based therapies. These efforts have been reviewed in the scientific literature and in a recent news article entitled "*The elusive heart fix*" published in *Science* in 2014. Despite over 14 years of stem cell research to treat heart disease, positive effects seen to date are modest and are not reproducible from one research study to another. Stem cell treatments for skeletal muscle injury have also shown limited promise to date.

The development of small molecules to stimulate and activate innate tissue repair and regeneration processes represents the leading edge of regenerative medicine R&D. Small molecule therapies have considerable advantages over stem cell, gene therapy and tissue engineering therapies including much lower costs, ease of administration and ready reversibility.

Intellectual property: Novo Biosciences holds an exclusive license and pending U.S. and foreign utility patents for using ZF143 to stimulate and activate tissue repair and regeneration processes. Early U.S. patent application prosecution has revealed no prior art. Low dose efficacy suggests novel and patentable formulation strategies.

Additional lead molecules: Two additional lead molecules, ZF198 and ZF760, are in development for reversing peripheral neuropathy induced by cancer chemotherapy and possibly diseases like diabetes.

Management team: The Novo Biosciences management team comprises a multidisciplinary blend of scientific, academic, clinical and business expertise and experience in regenerative biology and medicine, management, drug development, startup companies, investment, intellectual property, and regulatory affairs.

Kevin Strange, Ph.D., Co-founder and CEO: Dr. Strange is co-inventor of the ZF143 technology and president of the MDI Biological Laboratory. Prior to becoming president in July 2009, Dr. Strange was associate professor at Harvard Medical School and the John Parker Professor at Vanderbilt School of Medicine. He has been funded by the NIH since 1986 and has raised over \$40 million in competitive federal and private research funding throughout the course of his career. Dr. Strange focused the MDI Biological Laboratory's R&D efforts on regenerative medicine. Three years after establishing this new research focus, the Institution was recognized by the NIH as a Center of Biomedical Research Excellence in this field. Novo Biosciences has been highlighted as a success story of this program in the 2017 budget request presented to Congress by the National Institute of General Medical Sciences.

Voot Yin, Ph.D., Co-founder and CSO: Dr. Yin is co-inventor of the ZF143 technology, and assistant professor at the MDI Biological Laboratory. He developed the screening platform that

led to the discovery of ZF143. Dr. Yin is a recipient of NIH and Department of Defense funding and is a Young Investigator of the American Heart Association. He has extensive expertise in heart, muscle and limb tissue regenerative biology.

Michael Zasloff, M.D., Ph.D., Senior Research Scientist: Dr. Zasloff discovered ZF143 and has extensive expertise in its biological properties and chemistry. He is co-inventor of the ZF143 regeneration application and founder of Magainin Pharmaceuticals. Dr. Zasloff has been awarded 55 U.S. and international patents and through his clinical work and commercial ventures has gained extensive experience with clinical trials, the FDA approval process and investment fundraising.

Business, scientific and legal advisors:

Denise Barbut, M.D., MRCP, Business Advisory Board: Dr. Barbut is former Professor of Neurology, Chief of the Neurovascular Division and head of the stroke research program at Cornell University. Dr. Barbut is a serial entrepreneur. She has launched several biotech companies and has been awarded over 200 patents.

David Huizenga, Ph.D., J.D., Business Advisory Board: Dr. Huizenga is co-founder and Chief Executive Officer of Tao Life Sciences. He has extensive expertise in biomedical commercialization routes and strategies and has worked for over 15 years with early stage technologies at numerous universities around the country.

Dr. Sara Yin, Ph.D., MBA, Business Advisory Board: Senior Manager for Global Market Access at Biogen Idec, Cambridge, Massachusetts. Dr. Yin received her Ph.D. in pharmacology from Vanderbilt University and her MBA from the MIT Sloan School of Management. She has broad commercial experience in the life sciences sector with a focus in cardiovascular and neuromuscular diseases.

Dr. Peter Kowey, M.D., Scientific Advisory Board: Professor at the Lankenau Institute for Medical Research, the William Wikoff Smith Chair in Cardiovascular Research and Chief of the Division of Cardiovascular Diseases, Main Line Health System. Dr. Kowey was named one of America's top cardiologists in 2006, 2008, 2009, 2012 and 2013 and has served as an ad hoc consultant to over 160 pharmaceutical and biotech companies.

Dr. Judith Swain, M.D., Scientific Advisory Board: Executive Director of the Singapore Institute for Clinical Sciences, former Professor of Medicine and Chair of Medicine at Stanford University School of Medicine and former Director of Cardiovascular Medicine at the University of Pennsylvania. Dr. Swain has published extensively in the field of cardiology and holds several patents, including two patents for methods of increasing the energy metabolism of heart and skeletal muscle, and one for a method of identifying patients at risk for heart failure.

Dr. Phil Newmark, Ph.D., Scientific Advisory Board: Howard Hughes Medical Institute investigator and Professor of Cell and Developmental Biology at the University of Illinois. Dr. Newmark's research focuses on the role of stem cells in tissue regeneration and maintenance.

Preti Flaherty, Boston, MA; Wyche, Columbia, S.C.: Patent, legal and business counsel.

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