



## Company Profile

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ProNAi Therapeutics, Inc. is a biopharmaceutical drug development company pioneering a new class of nucleic-acid drugs based on DNA interference (DNAi®), which employs single strands of DNA to target and treat non-transcribed regions of genomes responsible for complex genetic diseases.

ProNAi is currently developing multiple DNAi®-based drug candidates with the potential to treat multiple cancers, including non-Hodgkin's lymphoma, prostate, breast, and colon cancers. The company's lead drug candidate, PNT2258, which has demonstrated *in vivo* efficacy in several human tumor xenograft models, is currently in preclinical development. ProNAi is also exploring the potential of DNAi®-based therapies for indications such as diabetes, Alzheimer's and inflammatory disease.

To date, the company has successfully recruited a seasoned Senior Management team and a Board of Directors with a proven track record in discovery research, research operations, product development, and business development. ProNAi's Scientific Advisory Board has significant experience in nucleic acid research, and clinical trial design and development.

ProNAi has raised Angel and Series A funding, and has successfully completed its Bridge financing round, prior to raising Series B investment.

ProNAi intends to file an IND in 2008 for PNT2258.

## Company Facts

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**Founded:** 2004

**Number of Employees:** 9

**Ownership:** Privately-held

**Funding to Date:** \$13 million

**Investors:** Grand Angels (Grand Rapids, MI), Biosciences Research Commercialization Center (Kalamazoo, MI), Apjohn Ventures (Kalamazoo, MI), Michigan Technology Tri-Corridor (Lansing, MI) Michigan Economic Development Corporation (Lansing, MI), Amherst Fund (Ann Arbor, MI), Sigvion Capital (Chicago, IL)

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## DNAi®

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ProNAi is one of the few - and the most advanced - companies targeting DNA-related therapies. In the past, other companies and researchers have investigated DNA therapies to treat diseases. However, due to the lack of specificity and potency as well as high manufacturing costs and drug delivery issues, these efforts have failed, are languishing, or have been abandoned.

ProNAi has successfully overcome these commercialization obstacles.

Other recent efforts in nucleic acid cancer research and development have focused on RNA rather than DNA. Current RNAi and antisense treatment approaches concentrate on binding to messenger RNA (mRNA) to slow or stop disease progression. However, because mRNA molecules are continually synthesized from a disease gene, the need for inhibition of the molecules must be continuous for the therapy to remain effective.

By acting at the DNA level, where only one or two copies of the gene exist per cell, treatment can be targeted more efficiently. With fewer targets, the activity of a DNAi® drug is expected to be more efficacious, persist at lower doses, and reduce some of the toxicity and safety issues prevalent with other marketed therapies. Additionally, DNA-related therapies will be more cost effective to produce.

All of ProNAi's product candidates originate from its proprietary nucleic acid interfering technology (DNAi®) that targets DNA directly using sequence-specific therapeutic agents. The company's proprietary DNAi®-HiT technology screens DNAi®'s that target known oncogenes as well as specific genes involved in other diseases. The overall impact is similar to that of antisense and RNAi products in development, but because it works at the level of DNA, the product candidates developed by ProNAi have significant advantages.

ProNAi is also using its DNAi® technology as a drug design engine. The technology has displayed a number of benefits in the development of novel therapies. These include:

- ProNAi is able to pursue disease targets that were previously thought untreatable. While targets for some diseases are inaccessible to small molecules, they can be targeted and potentially controlled at the level of DNA.
- DNAi® technology should lead to the discovery and validation of therapies in a number of disease categories beyond ProNAi's current oncology focus.
- The resulting DNA-related product candidates exhibit specificity and selectivity, and can anneal directly to a diseased gene. This can reduce side effects and toxicity issues.
- By targeting DNA, ProNAi has shortened the lead identification time for new drug candidates. Leveraging information secured through the Human Genome Project, ProNAi more effectively designs targeted therapies. This eliminates the need to screen a large chemical library to identify a few compounds that "hit" a particular target, as is the case in the identification of small molecule therapies.

## Executive and Drug Development Leadership

- **Donald Parfet, MBA, Chairman of the Board** - Mr. Parfet chairs the Board. He is also the Managing Director of the Apjohn Group. Prior to founding the Apjohn Group, Don was a Senior Vice President at Pharmacia. At Pharmacia, Don's responsibilities included all of the associated businesses including Animal Health, Diagnostics, Pharmaceutical Commercial Services and Plasma Products. Additionally, Don oversaw the company's investments in Amersham Pharmacia Biotech and Biacore International AB. He still serves on the Board of Biacore. Don received his BA degree in economics from the University of Arizona in 1975 and his M.B.A. degree in finance from the University of Michigan in 1977.
- **Robert Forgey, MBA, President and Chief Operating Officer** - Mr. Forgey graduated Beta Gamma Sigma from Olin School of Business, Washington University in 2001. He holds both a Bachelor's and a Master's degree in Biology from the University of North Dakota. He has 15 years pharmaceutical industry experience in research and development with G.D. Searle, Pharmacia and Pfizer development. His responsibilities have been in molecular biology methods development, project support, business management and financial control of discovery research organizations. Mr. Forgey most recently served as Manager, Discovery Financial Business Administration/Senior Financial Analyst with Pfizer-Pharmacia. Prior to this he served as Leader, Oncology Operations in Pharmacia Discovery.
- **Donald C. Anderson, MD, CMO** - Dr. Anderson has over 32 years of prestigious and award-winning service in life sciences industrial and academic environments, most recently serving as VP Discovery Research at Advancis Pharmaceutical Corporation, following a term as Global Head of Pharmacogenomics at Aventis Pharmaceuticals. Dr. Anderson has also served in executive capacities at Pharmacia & Upjohn, as well as held a 20-year professorship at the Baylor College of Medicine.



## Executive Leadership (continued)

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- **Dr. J. Patrick McGovren, VP, Preclinical Development** - Dr. McGovren is a longtime and well-known cancer research specialist, holding senior positions in big pharma oncology departments, as well as extensive consulting experience. Prior to joining ProNAi, Dr. McGovren was most recently Research Director, Clinical Pharmacology, Medical Development at Pfizer, following a term as Clinical Research Manager, Oncology Medical Affairs at Pharmacia. Between 1976 and 2000, Dr. McGovren held numerous senior research and management posts at Pharmacia & Upjohn.
- **Dr. Wendi V. Rodriguez, VP, Product Development** - Dr. Rodriguez, whose therapeutic research expertise includes cardiovascular disease, oncology, diabetes and metabolic diseases, joins ProNAi after most recently serving at Novartis Institute of Biomedical Research, Inc. (NIBRI) as Director, Product Management, Cardiovascular Disease Area. Prior to NIBRI, Dr. Rodriguez held numerous senior research positions at both CuraGen and Esperion Therapeutics (now a division of Pfizer Global Research and Development).



## Latest Press Releases

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### Press Contacts

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## ProNAi Therapeutics Announces First DNAi® Mechanism of Action Studies for PNT2258 Oncology Drug Candidate

*Pioneer in DNAi®-based drug development examines role of BCL2 gene in triggering apoptosis of malignant cells*

Kalamazoo, Michigan - August 23, 2007 - ProNAi Therapeutics, Inc., a biopharmaceutical company pioneering a new class of nucleic-acid drugs based on DNA interference (DNAi®), today announced its first mechanism of action studies for its PNT2258 oncology drug candidate, centering on the BCL2 gene's role in triggering cell death in cancer cells.

BCL2 plays a central role in dysregulation of apoptosis in malignant cells, which presents an opportunity for molecular targeted drug discovery. PNT2258 targets a DNA sequence upstream of BCL2 promoters within a region of genomic instability, and ProNAi's preclinical research is currently examining methods for safe and effective delivery of oligonucleotides to regulate BCL2 in difficult-to-treat cancers. Chemotherapy resistance of Non-Hodgkin's Lymphoma and many other tumors are linked to overexpression of BCL2.

To date in preclinical studies in mice, PNT2258 has demonstrated antitumor activity in Non-Hodgkin's Lymphoma, prostate cancer and melanoma xenografts. IND-enabling CMC studies are currently underway, and ProNAi anticipates filing for IND status for PNT2258 in late 2007.

Dr. Richard D. Gill, President and CEO of ProNAi, said, "We are very excited by the positive results of the first mechanism of action studies for our DNAi®-based oncology therapeutic candidate. This discovery highlights the continued progress of PNT2258 toward IND status - while keeping pace with other nucleic acid-based approaches in the quest for safe, effective delivery of therapeutic oligonucleotides."

Robert Forgey, Co-Founder and Chief Operating Officer of ProNAi, said, "Using a DNAi®-based strategy to target BCL2 is emerging as a very promising avenue to potentially address certain difficult-to-treat cancers. To date, all alternative approaches to regulating BCL2 in man lack proofs-of-concept, so we are actively pursuing this intriguing possibility, as we continue to advance our preclinical studies."

DNAi® is a novel approach to targeting genomic DNA using sequence-specific therapeutic agents, employing single strands of DNA to target and treat genes responsible for complex genetic diseases, such as cancer.

By acting at the DNA level, where only one or two copies of the gene exist per cell, treatment can be targeted more efficiently by DNAi® drugs. With fewer targets, the activity of a DNAi® drug is expected to last longer at lower doses, and reduce some of the toxicity issues prevalent with other marketed therapies. Additionally, DNA-related therapies are potentially more cost effective to produce.

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ProNAi is based in Kalamazoo, Michigan. For more information, please visit: [www.pronai.com](http://www.pronai.com).

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## Latest Press Releases (Continued)

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## ProNAi Names Polymun as Preferred Manufacturer of PNT2258 DNAi®-based Cancer Therapeutic

*Pioneer in DNAi®-based drug development signs manufacturing agreement with Austrian contract biopharmaceutical developer, to help advance lead oncology drug candidate toward IND*

Kalamazoo, Michigan and Vienna, Austria - June 14, 2007 - ProNAi Therapeutics, Inc., a biopharmaceutical company pioneering a new class of nucleic-acid drugs based on DNA interference (DNAi®), today announced that it has signed a supply agreement with Polymun Scientific GmbH, an Austrian contract biopharmaceutical developer, to manufacture the company's PNT2258 DNAi®-based cancer therapeutic.

Under the terms of the agreement, Polymun will use its proprietary cross-flow injector technology to manufacture ProNAi's liposome-formulated lead drug candidate, which is currently in the final stages of preclinical toxicology testing. ProNAi intends to bring PNT2258 to IND submission later this year.

Dr. Richard D. Gill, President and CEO of ProNAi, said, "Polymun has proven, successful experience in manufacturing drug product for U.S. clinical trials, and we are very happy to be working with them as we advance PNT2258 into the clinic. ProNAi is confident that Polymun's manufacturing processes and

technology are state-of-the-art and up to the task of formulating our oncology drug candidate, which features our novel oligo delivery method for the safe and effective administration of nucleic acid-based therapies.”

Dr. Dietmar Katinger, Vice President of Business Development of Polymun, said, “Polymun is delighted to have the opportunity to work with ProNAi in making this innovative drug candidate. Among our specialties, our company has considerable experience in working with liposomal formulations, and we look forward to this fruitful collaboration to help realize the potential of treating patients with these promising therapeutic nucleotides.”

### **About Polymun Scientific GmbH**

Founded in 1992, Polymun Scientific GmbH is a private company offering contract development and production of liposomal formulations as well as development and manufacturing of biopharmaceuticals. Its patented liposome technology allows efficient manufacturing of constantly high quality in small and large scale. Polymun is investing its revenues in its R&D projects and the further development of technology platforms. As a certified manufacturer of pharmaceuticals Polymun operates in accordance with current GLP, GMP and GCP guidelines. Polymun employs a team of about 40 dynamic and highly qualified scientists, technologists and support staff.

Polymun is based in Vienna, Austria. For more information, please visit: [www.polymun.com](http://www.polymun.com).

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## Latest Press Releases (Continued)

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## ProNAi Announces Preclinical Success for PNT2258 Therapeutic - Curative Events in Xenograft Mice for Difficult-to-Treat Non-Hodgkin's Lymphoma

*Pioneer in DNAi®-based drug development demonstrates single-agent and combination therapy efficacy and drug-dose response in animal studies for lead nucleic-acid-based oncology candidate*

American Association for Cancer Research Annual Meeting, Los Angeles, California - April 17, 2007 - ProNAi Therapeutics, Inc., a biopharmaceutical company pioneering a new class of nucleic-acid drugs based on DNA interference (DNAi®), today announced that its lead oncology therapeutic candidate, PNT2258, has successfully demonstrated preclinical *in vivo* efficacy in xenograft mice for a number of human cancers - including curative events for difficult-to-treat Burkitt's Lymphoma.

Dr. Richard D. Gill, President and CEO of ProNAi, said, "Team ProNAi is quite pleased with our early preclinical results for PNT2258. Particularly encouraging is the fact that PNT2258 has shown promising single agent efficacy and combination therapy efficacy and drug-dose response for multiple cancer types including both hematological and solid tumors."

He added, "However, a very exciting development was our discovery that PNT2258, in combination with Rituximab, demonstrated curative events in treating Daudi xenografts of human Burkitt's Lymphoma in mice. The antitumor effect was rapid and durable. We had 70% complete remissions in two groups of animals dosed with PNT2258 and Rituximab."

In developing its DNAi®-based therapy, ProNAi reports that its successful establishment of *in vivo* efficacy for formulated PNT2258 included:

- Single agent efficacy for DLCL2 Xenografts of Human Non-Hodgkin's Lymphoma
- Combination therapy efficacy with Docetaxel for Human Hormone Refractory Prostate Cancer Xenograft
- Combination therapy with Rituximab in Daudi Xenografts of Human Burkitt's Lymphoma

ProNAi's preclinical research will proceed in 2007. Planned studies include IND-enabling toxicology and ADME studies. ProNAi will file the IND for PNT2258 later this year.

### About DNAi®

DNAi® (DNA interference) is a novel approach to targeting genomic DNA using sequence-specific therapeutic oligonucleotides, employing single strands of DNA to target and treat non-transcribed regions of genomes responsible for complex genetic diseases, such as cancer.

By acting at the DNA level, where only one or two copies of the gene exist per cell, treatment can be targeted more efficiently by DNAi® drugs. With fewer targets, the activity of a DNAi® drug is expected to last longer at lower doses, and reduce some of the toxicity issues prevalent with other marketed therapies. Additionally, DNA-related therapies are potentially more cost effective to produce.

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## ProNAi and Novosom AG Announce Collaboration to Enable Delivery of DNAi®-based Cancer Therapeutics

*Pioneer in DNAi®-based drug development signs licensing deal with maker of Smarticles®, a new class of liposomes, to help advance PNT100 drug candidate toward IND, and overcome key obstacle to delivering nucleotides in vivo to targeted cells*

Kalamazoo, Michigan and Halle, Germany - March 6, 2007 - ProNAi Therapeutics, Inc., a biopharmaceutical company pioneering a new class of nucleic-acid drugs based on DNA interference (DNAi®), today announced a collaboration with Novosom AG to enable successful delivery of DNAi®-based cancer therapeutics.

Under the terms of the collaboration, ProNAi will license Novosom's SMARTICLES® liposome technology for use in all human disease targeted by ProNAi's PNT100 drug candidate. The agreement comprises an upfront payment, milestone payments and royalties, composed of a mixture of cash and equity. ProNAi will also retain an option for four additional DNAi® targets.

Dr. Richard D. Gill, President and CEO of ProNAi, said, "Team ProNAi is very much looking forward to realizing the results of our collaboration with Novosom in this groundbreaking endeavor, as we bring the drug product PNT2258 to IND

submission. The successful delivery of nucleic acid-based drugs has been the 'holy grail' of the industry for many years, and we are confident that our combined approach will yield promising outcomes. With this partnership, we have developed a GMP-enabling oligo delivery method that allows ProNAi to submit an IND, and we expect more significant milestones to be met in the near future."

Elias Papatheodorou, CEO of Novosom, said, "Novosom's technology has been in the forefront of providing a safer, more efficient delivery method available for *in vivo* delivery of nucleotides to targeted cells. We are encouraged by the potential our partnership with ProNAi holds in developing a new class of effective DNA-based drugs."

### About Novosom AG

Novosom is working with its partners to develop unique antisense, DNAi and siRNA based therapeutics with a current focus in inflammation, oncology and liver diseases. Novosom's Smarticles® liposomal vectors allow partners to deliver their active substance (siRNA, antisense, decoy etc) inside the cell either for topical or systemic applications. Smarticles are an enabler of systemic treatments and an enhancer of topical treatments. The Company has several active therapeutically-relevant collaborations in oncology and inflammation. Novosom AG main investors include IBG Beteiligungsgesellschaft Sachsen-Anhalt mbH and MBG Mittelständische Beteiligungsgesellschaft Sachsen Anhalt.

Novosom AG is based in Halle, Gemany. For more information, please visit: [www.novosom.com](http://www.novosom.com).

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## ProNAi Announces DNA Interference (DNAi®) Drug Development Strategy for 2007

*Pioneer in nucleic acid-based drug development aims to bring PNT2258 therapeutic candidate to IND submission by mid-year - company to formally announce preclinical data in the spring*

Kalamazoo, Michigan - January 8, 2007 - ProNAi Therapeutics, Inc., a biopharmaceutical company pioneering a new class of nucleic-acid drugs based on DNA interference (DNAi®), today announced its drug development strategy for 2007, and its plans to bring its lead therapeutic candidate, PNT2258, to IND submission by mid-year.

DNAi® is a novel approach to targeting genomic DNA using sequence-specific therapeutic agents, employing single strands of DNA to target and treat genes responsible for complex genetic diseases, such as cancer.

By acting at the DNA level, where only one or two copies of the gene exist per cell, treatment can be targeted more efficiently by DNAi® drugs. With fewer targets, the activity of a DNAi® drug is expected to last longer at lower doses, and reduce some of the toxicity issues prevalent with other marketed therapies. Additionally, DNA-related therapies are potentially more cost effective to produce.

In a promising advance for DNA-based drugs, ProNAi has overcome a long-standing barrier to effective DNA therapy delivery - by means of a viable method for the safe, effective delivery of therapeutic oligonucleotides - the keystone to making DNAi® a viable treatment option in humans.

Dr. Richard D. Gill, President and CEO of ProNAi, said, "For many, many years, the promise of DNA-related therapies has gone largely unfulfilled, due to a daunting number of obstacles - lack of specificity and potency, high manufacturing costs, as well as the inability to deliver effective doses of DNA-

based drugs - a problem that also still affects RNAi-based approaches currently in vogue. ProNAi has worked steadily and methodically to overcome each of these barriers to nucleic acid-based therapeutics and we fully expect to have our lead drug candidate, PNT2258, ready for IND submission by mid-year."

Robert Forgey, Co-Founder and Chief Operating Officer of ProNAi, said, "DNAi® is radically different from competing approaches such as antisense, decoy, RNAi, shRNA, triplex, immunostimulators, and other nucleic acid drug approaches, and displays significant potential advantages over each. For example, current RNAi and antisense treatment approaches concentrate on binding to messenger RNA (mRNA) to slow or stop disease progression. However, because mRNA molecules are continually synthesized from a disease gene, the need for destruction of the molecule must be continuous for it to remain effective. This means RNAi drugs need high doses, which in turn means higher toxicity as well as cost - even if they solve their delivery problem. DNAi® eliminates this issue entirely, by focusing on the gene itself, channeling therapies one level up where 'less is more' in terms of drug dose and effectiveness."

Dr. Gill added, "ProNAi is looking forward to demonstrating the viability of DNAi®-based drugs in the coming year, as we announce our very promising preclinical results for PNT2258, which has shown exciting in vivo efficacy in xenograft mice for a number of cancers. Our first drug formulations show promising utility against multiple target genes, and we are targeting well-documented, non-translated genomic sequences. We are also examining the potential for a Dx/Rx combination, and will further develop that possibility."

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## ProNAi Closes Successful Bridge Funding Round, Secures \$6.65 Million Total

*Pioneer in DNAi-based drug development raises additional financing to further develop PNT-100 cancer therapeutic candidate toward FDA IND submission*

Kalamazoo, Michigan - October 24, 2006 - ProNAi Therapeutics, Inc., a biopharmaceutical company pioneering a new class of nucleic-acid drugs based on DNA interference (DNAi), today announced that it has successfully closed its bridge funding round, securing \$6.65 million in additional financing.

The bridge funding round included investments from Apjohn Ventures, Grand Angels, Amherst Fund, Sigvion Ventures and a previously announced investment of \$3.3 million from the Michigan Economic Development Corporation, which closed on September 12. Since its founding in 2004, ProNAi has successfully raised \$11 million to date.

Dr. Richard D. Gill, President and CEO of ProNAi, said, "Team ProNAi is delighted at the success of our bridge financing round, which will help us bring our lead drug candidate, PNT-100, toward submission to the FDA as an Investigational New Drug sometime in mid-2007. Our drug development team is making remarkable progress in developing this very promising therapeutic, and we look forward to additional compelling efficacy and safety outcomes."

Robert Forgey, Chief Operating Officer of ProNAi, said, "ProNAi has demonstrated a solid track record of scientific progress to date, and it is clear that the investment community has responded strongly to our team's potential for creating and commercializing an innovative class of drugs for the treatment of cancer through DNAi-based discovery."

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## ProNAi Announces New Scientific Advisory Board

*Pioneer in DNAi-based drug development brings aboard top experts in genomics, oncology, oligonucleotides, preclinical and clinical development*

Kalamazoo, Michigan - October 12, 2006 - ProNAi Therapeutics, Inc., a biopharmaceutical company pioneering a new class of nucleic-acid drugs based on DNA interference (DNAi), today announced that it has named its new Scientific Advisory Board team, composed of distinguished researchers and professionals in genomics, oligonucleotides, preclinical and clinical drug development.

Dr. Richard D. Gill, President and CEO of ProNAi, said, "ProNAi is delighted to have such a remarkable and highly experienced Scientific Advisory Board team working closely with us as we bring our PNT100 cancer therapeutic candidate into the clinic. With such a vast range of distinguished expertise in both our core scientific and business segments, our SAB members represent the top-tier of research, drug development and market expertise that ProNAi has brought to bear in support of developing a new class of DNAi-based drugs."

Robert Forgey, Chief Operating Officer of ProNAi, said, "The prominence of each of our Scientific Advisory Board members in their respective fields speaks for itself. Each is a noted and respected leader in genomics, oncology, oligonucleotides, preclinical and clinical drug development, hailing from prestigious institutions. We look forward to creating compelling and fascinating scientific research and results together."

ProNAi's new Scientific Advisory Board team comprises:

- **Tod Woolf, Ph.D.** Founder and CEO, IPIFINI, Inc. Sudbury, MA; Founder Sequitur, sold to Invitrogen

- **Cy Stein, MD, PhD**, Professor and Head Genitourological Cancer, Albert Einstein College of Medicine, New York, NY
- **Mace Rothenberg, MD**, Ingram Professor of Cancer Research and Professor of Medicine, Vanderbilt Medical School, Nashville, TN
- **Ayad Al-Katib, MD**, Head Oncology, St. Johns Medical Center, Detroit, MI; Professor of Medicine, Wayne State University Medical School, Detroit, MI
- **David Olson, PhD**, Vice President Research PanCell, Co-founder Gentera, Ann Arbor, MI; Chief Business Development Officer, Accuri Instruments, Inc., Ann Arbor, MI; Co-Founder, President and Chief Executive Officer, The Fund for Autoimmune Research, Ann Arbor, MI
- **Craig Webb, PhD**, Director and Principal Investigator, Tumor Metastasis and Angiogenesis Laboratory; Director, Multiple Myeloma Laboratory, Van Andel Research Institute, Grand Rapids, MI
- **John Schimenti, PhD**, Professor and Director, Vertebrate Genomics, Cornell University, Ithaca, NY
- **Terry Magnuson, PhD**, Professor and Chair Genetics, University of North Carolina, Chapel Hill, NC

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