3rd International mRNA Health Conference

PROGRAM

November 11-12, 2015 • Berlin, Germany

www.mrna-conference.com

BIONTECH

CUREVAC
the RNA people®

moderna™
messenger therapeutics

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Imprint

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Greeting

Welcome to the 3rd International mRNA Health Conference!

2015 has been a truly momentous year for the mRNA industry as evidenced by the publication of several significant peer-reviewed clinical studies demonstrating the potential and promise of this technology combined with multiple investments totaling more than $1 billion by some of the world's leading multinational corporations and organizations.

Beneath this bright spotlight of promise and potential, we are excited to convene the 3rd International mRNA Health Conference to provide a gathering point for leading innovators, scientists and academia to chart the future of a technology that is being hailed for its potential to treat a wide range of diseases and medical conditions. The two-day event will offer numerous presentations and panel discussions about the significant potential of mRNA, including keynote speeches from Nobel Laureate Harald zur Hausen from the German Cancer Research Center (DKFZ) and Jose Esparza from the University of Maryland School of Medicine.

The successes that we are seeing in 2015 are directly attributable to the collaborative atmosphere that has been in place since the earliest years of mRNA research. The mRNA International Health Conference epitomizes this cooperative philosophy, and it is a testament to the field of mRNA that its innovators are able to work together so closely.

As the International mRNA Health Conference returns to Germany, the place of discovery of mRNA, we look forward to joining with those in attendance to chart a course for 2016 and beyond that will enable this new class of drugs to potentially transform the treatment of many human diseases and disorders.

We hope the conference treats you very well and that the relationships and knowledge you gain allow for even greater success in the years to come.

Warmest Regards,

The Organizing Committee

Ingmar Hoerr
CEO CureVac

Stéphane Bancel
CEO Moderna

Ugur Sahin
CEO BioNTech

Conference Program Overview

Wednesday, November 11, 2015

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Bovine milk and serum factors as risk for colon- and breast cancer?

9:50 AM **José Esparza, University of Maryland School of Medicine**
Harnessing the power of science to develop the vaccines of the future

Vaccines Session

10:20 AM **Chair Introduction by Ingmar Hoerr, CureVac**

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Lessons regarding Nucleic Acid Vaccine Technology From Studies of Synthetic DNA Vaccines

10:45 AM **Jeffrey B. Ulmer, GSK Vaccines**
Self-amplifying mRNA vaccines

11:05 AM ***Coffee Break***

11:25 AM **Dan Wattendorf, DARPA**
Novel Nucleic Acid-Based Immunoprophylaxis Technologies

11:45 AM **Ugur Sahin, BioNTech**
Individualized RNA Immunotherapies

12:05 PM **Stéphane Bancel, Moderna**
Vaccine approaches at Moderna Therapeutics

12:25 PM ***Lunch Break with Poster Session***

1:25 PM **Hans-Georg Rammensee, University of Tübingen**
Impact of the immunogenic landscape of cancers on immunotherapy

1:45 PM **Thomas Hinz, Paul-Ehrlich-Institute**
Regulation of RNA-Based Medicines

2:05 PM **Panel Discussion Vaccines**
Chaired by Ugur Sahin, BioNTech
Speakers from Session
and Christian Mandl, Consultant. Formerly, Global Head of Research and Exploratory Development at Novartis Vaccines

2:50 PM ***Coffee Break***

Delivery Session

3:10 PM	**Chair introduction by Katalin Karikó, BioNTech RNA Pharmaceuticals**
3:15 PM	**Pierrot Harvie, PhaseRX** *Development of a Polymeric Delivery System Enabling Targeted mRNA Delivery to the Liver and Therapeutic Efficacy in an Orphan Liver Disease Model*
3:35 PM	**Philip Santangelo, Georgia Institute of Technology** *Characterizing therapeutic mRNA at the level of single cells and single molecules*
3:55 PM	**Pad Chivukula, Arcturus Therapeutics** *Recent Advances in the Design and Delivery of Messenger RNA*
4:15 PM	***Coffee Break***
4:35 PM	**Michael J. Hope, Acuitas Therapeutics** *Development of a Lipid Nanoparticle (LNP) Platform to Enable mRNA Therapeutics*
4:55 PM	**Joseph Rosenecker, University Children's Hospital Munich** *Nebulisation of IVT mRNA Complexes for Intrapulmonary Administration*
5:15 PM	**Joanna Rejman, Ludwig-Maximilians-University Munich** *Modulation of cell functions by means of mRNA encapsulated in lipid and polymer particles*
5:35 PM	**Panel Discussion Delivery** Chaired by Susan Sobolov, Alexion **Speakers from Session**

Closing of Conference Day 1

6:20 PM	Closing remarks Day 1 by the Organizing Committee
6:30 PM	End of Conference Program Day 1

Networking Evening

7:00 PM	Departure of the coaches to the Networking Evening Enjoy an exclusive networking evening with the mRNA community in ParkInn's Panorama37 (Alexanderplatz 7, 10178 Berlin) with a great view over Berlin. Busses will bring you to the evening location and back to the HILTON.

Thursday, November 12, 2015

9:00 AM **Welcome remarks by the Organizing Committee**

Therapeutics Session

9:15 AM **Chair Introduction by Stéphane Bancel, Moderna**

9:20 AM **Jan Weiler, Novartis Institutes for BioMedical Research**
Therapeutic messenger RNA to produce prophylactic antibodies

9:40 AM **Carsten Rudolph, ethris**
Stabilized non-immunogenic messenger RNA for transcript therapy

10:00 AM **Michael Kormann, University of Tübingen**
Chemically modified RNAs for efficient and safe genome editing

10:20 AM **Romesh Subramanian, Alexion**
mRNA Therapeutics at Alexion

10:40 AM ***Coffee Break***

11:00 AM **Nigel Horscroft, CureVac**
Sequence-engineered mRNA enables an effective protein therapy

11:20 AM **Katalin Karikó, BioNTech RNA Pharmaceuticals**
Why RNA is immunogenic - and how to change that?

11:40 AM **Irina Tcherepanova, Argos Therapeutics Inc.**
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12:00 PM ***Lunch Break with Poster Session***

1:00 PM **Nils Bergenhem, AstraZeneca**
Modified RNA as CVMD Therapeutic Modality: opportunities and challenges

1:20 PM **Meltem Avci-Adali, University of Tübingen**
De novo synthesis of extracellular matrix structural proteins for tissue repair by exogenous delivery of mRNA

1:40 PM **Tyler Wagner, Massachusetts Institute of Technology**
RNA-Encoded Synthetic Gene Circuits for Tissue Specific Expression and Small Molecule-Based Dosage Control of Therapeutic Proteins

2:00 PM **Panel Discussion Therapeutics**
Chaired by Brad Guild, ethris
Speakers from Session

Closing of the Conference

3:00 PM Awarding of the Poster Prices
Closing remarks by the Organizing Committee

3:20 PM **End of Conference**

Detailed Program with Abstracts and Speakers' CVs

Wednesday, November 11, 2015

9:00 AM

Welcome remarks by the Organizing Committee

Keynote Session

9:20 AM

Harald zur Hausen, German Cancer Research Center (DKFZ), Nobel Laureate

Bovine milk and serum factors as risk for colon- and breast cancer?

Epidemiological data strongly suggest that dairy cattle meat and milk factors pose the risk for the development of colon and breast cancers. We isolated several novel small circular single-stranded DNAs from cattle sera and milk. They are genetically active in human cells. Two of these agents have also been detected in two lesions of multiple sclerosis. Presently, a concept has been developed which may explain the role of these factors for these diseases.

Harald zur Hausen is a virologist and cancer researcher who discovered the important role that human papillomavirus plays in cervical cancer. His ground-breaking research in the 1970s and 1980s paved the way for the development of the HPV vaccine in 2006 for which he was honored with the Nobel Prize in Medicine in 2008. He also studied the Epstein-Barr virus (EBV).

Zur Hausen studied medicine at the Universities of Bonn, Hamburg, and Düsseldorf. He worked in the virus laboratories of the Children's Hospital in Philadelphia and as a senior scientist at the Institute of Wuerzburg. In 1972, he was appointed chairman and professor of virology at the University of Erlangen-Nuernberg and in 1977 he moved to the University of Freiburg. From 1983 until 2003 he served as scientific director of the German Cancer Research Center. He is an elected member of various research organizations and academies.

9:50 AM

José Esparza, University of Maryland School of Medicine

Harnessing the power of science to develop the vaccines of the future

Vaccines are one the most cost efficient approaches to public health. Their development have paralleled the progress of science. The introduction of tissue culture techniques in the 1950s resulted in the development of numerous attenuated and inactivated viral vaccines. Pioneering work conducted in Tübingen in the 1960s provided the basis for the development of subunit viral vaccines. The potential use of DNA vaccines emerged in the early 1990s and, more recently, mRNA vaccine technologies are being explored. New technologies may be needed to develop the "difficult" vaccines and to make them available to all populations in need.

José Esparza is Adjunct (honorary) Professor at the Institute of Human Virology, University of Maryland School of Medicine. He worked for ten years at the Bill & Melinda Gates Foundation, mostly on HIV vaccines. Previously he was with the World Health Organization in Geneva, Switzerland, promoting the international development of HIV vaccines. From 1974 to 1985 he worked at the Venezuelan Institute of Scientific Research (IVIC). He holds an MD degree from Venezuela (1968) and a PhD in Virology and Cell Biology (1974) from Baylor College of Medicine in Houston. Currently he is a consultant in vaccinology for several companies.

Wednesday, November 11, 2015
Vaccines Session

10:20 AM

Chair Introduction by Ingmar Hoerr, CureVac

10:25 AM

David Weiner, University of Pennsylvania
Lessons regarding Nucleic Acid Vaccine Technology From Studies of Synthetic DNA Vaccines

DNA vaccines represent an important vaccine technology, which has conceptual advantages over traditional vaccine platforms. In humans prior generations were poorly immunogenic. Through multiple improvements including synthetic optimization, genetic adjuvant technology with enhanced EP delivery this technology exhibits improved performance. These synthetic DNA vaccines drive immune responses similar or superior to live viral vectors. We present data in animal models and in human studies that illuminate their immune potency and clinical efficacy. Studies of this technology against several immune targets will be discussed.

Dr. Weiner's laboratory helped found the field of DNA vaccines. With collaborators was the first to move DNA vaccines into the clinic, establishing their initial safety and immunogenicity. His group is instrumental in the renewed interest in the DNA vaccine field through development of advanced DNA technology exhibiting improved immune potency, resulting in clinical efficacy (HPV immune therapy). His laboratory published 380+ scientific publications, 8 books/special volumes. He is an avid supporter of scientific education and graduate and post-graduate training. He serves on advisory boards and as consultant to academic organizations and industry. He is an elected fellow of the American Association for the Advancement of Science in 2011, an elected fellow of the International Vaccine Society 2012, an NIH Directors Transformative Research Award recipient and awarded the Vaccine Industry Associations outstanding Academic Vaccine laboratory - 2015.

10:45 AM

Jeffrey B. Ulmer, GSK Vaccines
Self-amplifying mRNA vaccines

Recent advancements have demonstrated that vaccines based on mRNA have the potential to combine the positive attributes of other types of vaccines, without their limitations. The broad utility of this novel vaccine technology has been demonstrated in multiple animal models, including non-human primates. Furthermore, cell-free synthesis enables vaccine production from sequence information in a matter of days, thereby facilitating a rapid response to newly emerging pathogens. If self-amplifying mRNA vaccines prove safe and effective in humans, this novel nucleic acid vaccine technology will enable a new generation of vaccines able to address the health challenges of the 21st century.

Dr. Jeffrey Ulmer received his B.Sc. with honors from the Department of Chemistry at the University of Regina in 1978 and was the recipient of the Merit Award of the Society of Chemical Industry of Canada. He received his Ph.D. in biochemistry from McGill University in 1985 and completed his postdoctoral training in the laboratory of Nobel laureate Dr. George Palade at Yale University School of Medicine. Dr. Ulmer has held leadership positions at Merck, Chiron, Novartis, and is currently Head of Preclinical R&D US at GSK Vaccines. He has published over 200 scientific articles.

Wednesday, November 11, 2015
Vaccines Session

11:05 AM
Coffee Break

11:25 AM
Dan Wattendorf, DARPA
Novel Nucleic Acid-Based Immunoprophylaxis Technologies

DARPA is investing in rapid immunoprophylaxis approaches through (1) DNA- and RNA-based vaccine antigen gene delivery platforms, (2) DNA- and RNA-based passive antibody gene transfer platforms, and (3) rapid discovery of human-derived potent antibodies. These platforms will decrease the outbreak response timeline, position new platforms for pharmaceutical investment, and, given their synthetic design, can be manufactured rapidly at low cost for population distribution. With successful development and commercialization, these nucleic acid-based platforms can be used to produce immunoprophylaxis drug candidates for emerging pathogens, natural or engineered, more rapidly than current methods.

Col Daniel J. Wattendorf, MC, USAF has been a DARPA Program Manager since 2010. His interests focus on applying methodological advances in genomics and biotechnology to optimize health and prevent disease, including rapid diagnostics, new RNA vaccines, and novel immunoprophylaxis strategies to better outpace the spread of infectious disease. In addition to his DARPA programs, Dr. Wattendorf is a clinical geneticist at the National Naval Medical Center Walter Reed National Military Medical Center and the Cancer Genetics Branch, National Cancer Institute, NIH.

11:45 AM
Ugur Sahin, BioNTech
Individualized RNA Immunotherapies

Mutations are regarded as ideal targets for cancer immunotherapy. As neo-epitopes with strict lack of expression in any healthy tissue, they are expected to be safe. We have recently proposed a personalized immunotherapy approach targeting the spectrum of individual mutations and have shown that vaccination with such poly-neo-epitopic mRNA vaccines induces potent tumor control and complete rejection of established aggressively growing tumors in mice. A first in human clinical study successfully started demonstrating the clinical feasibility of individually tailored “just in time” produced immunotherapies (NCT02035956). Findings of the clinical study will be presented in the meeting.

Ugur Sahin is a doctor of medicine and translational researcher with long-standing expertise in managing projects in the public-private interface. A pioneer in cancer target discovery using high throughput immunological methods and bioinformatics approaches, Prof. Sahin holds more than 70 independent patent applications covering novel cancer biomarkers and targeted therapeutics platforms. His key focus is solving deeply rooted challenges in the multifaceted process of translating innovation from bench to bedside, an interest that was originally prompted by his experiences as a physician. Prof. Sahin’s publications have more than 6000 citations and he is the recipient of prestigious awards from the German Hemato-Oncology Association, German Association for Immunology, German Federal Ministry of Education and Research (BMBF) and American Society of Clinical Oncology.

Wednesday, November 11, 2015
Vaccines Session

12:05 PM

Stéphane Bancel, Moderna
Vaccine approaches at Moderna Therapeutics

Moderna Therapeutics was started with a focus on Therapeutics, but has added several drug modalities with a team at Valera LLC focused on Infectious Disease Vaccines. The company has also partnered with Merck to bring new vaccines to protect important diseases. Between Merck and Valera, there are more than a dozen vaccines in development in the moderna ecosystem in 2015.

Stéphane Bancel has been Moderna founding CEO since 2011. He has built a team of industry leaders and raised more than $1 Billion in funding. He was previously CEO of bioMérieux, a diagnostic world leader. Before, he was Eli Lilly's Belgium Country Manager and executive director of global manufacturing strategy. He holds an University of Minnesota M.Sc. in Chemical Engineering and an Harvard Business School MBA. He was elected Young Global Leader by the World Economic Forum in 2009 and was ranked the number one CEO in the biotech sector according to the 2011 Thomson Reuters EXTEL Study. Stephane serves on Qiagen board, and on Syros Board.

12:25 PM
Lunch Break with Poster Session

1:25 PM

Hans-Georg Rammensee, University of Tübingen
Impact of the immunogenic landscape of cancers on immunotherapy

Analysing the entire detectable landscape of HLA ligands on tumors of intermediate mutation load, in particular hepatocellular carcinomas, renal cell carcinomas, ovarian carcinomas and several leukemia types, consisting of 1000 through 5000 peptides per sample, we do find dozens to hundreds of peptides in germline sequence with apparently tumor specific expression, based on the absence of these peptides on adjacent autologous benign tissue and absence on a large number of normal tissue samples from all organs and tissue types available for analysis, all, of course, within the sensitivity limits of our technology.

Hans-Georg Rammensee studied biology at the Eberhard-Karls-University of Tübingen from 1974 to 1980 and finished his PhD thesis under the supervision of Jan Klein at the Max-Planck-Institute (MPI) for Biology. Since 2008 until present he has been Director of the Interfaculty Institute for Cell Biology. Hans Georg Rammensee is co-founder and member of the Scientific Council of the biotechnology enterprises immatics GmbH, CureVac AG and Synimmune GmbH. He pioneered the identification of peptides bound to the major histocompatibility complex molecules. He currently manages a research network for translational immunology with the aim to develop immunotherapies for the treatment of cancer. This work includes the development of personalised therapies relying on the identification of tumor-specific mutations which are then utilised to manufacture peptide-based medicines for individual patients.

Wednesday, November 11, 2015

Vaccines Session

1:45 PM

Thomas Hinz, Paul-Ehrlich-Institute

Regulation of RNA-Based Medicines

RNA as a drug substance in human medicinal products has become increasingly important during the recent years. Protein-encoding RNAs can either be directly administered to patients or can be used to transfect human cells ex vivo. In this presentation specific regulatory aspects of RNA-based medicines are discussed with an emphasis on marketing authorization via the EMA centralized procedure and the so-called hospital exemption which is a national authorization procedure. Certain GMP aspects are also briefly addressed.

Thomas Hinz is working at the Paul Ehrlich Institute (PEI) in Germany since 1993 where he is head of Section Therapeutic Vaccines since 2005. Regulatory work includes the assessment of clinical trial applications and marketing authorization applications. From 2005-2010 Thomas Hinz was a member of the Cell-based Product Working Party of EMA where he contributed to the development of guidelines for human cell-based medicinal products. From 1993 to 2005 Thomas Hinz worked as a basic scientist and project leader in the research group of the Division of Immunology at the PEI. Special areas of interest were the molecular analyses of T cell receptor gene repertoires in HIV patients and in patients suffering from T cell malignancies. Thomas Hinz studied Biology at the University of Giessen in Germany.

2:05 PM

Panel Discussion: Vaccines

Chair: Ugur Sahin, BioNTech

Ugur Sahin is a doctor of medicine and translational researcher with long-standing expertise in managing projects in the public-private interface. A pioneer in cancer target discovery using high throughput immunological methods and bioinformatics approaches, Prof. Sahin holds more than 70 independent patent applications covering novel cancer biomarkers and targeted therapeutics platforms. His key focus is solving deeply rooted challenges in the multifaceted process of translating innovation from bench to bedside, an interest that was originally prompted by his experiences as a physician. Prof. Sahin's publications have more than 6000 citations and he is the recipient of prestigious awards from the German Hemato-Oncology Association, German Association for Immunology, German Federal Ministry of Education and Research (BMBF) and American Society of Clinical Oncology.

Panelists:

Speakers from Session and Christian Mandl, Consultant. Formerly, Global Head of Research and Exploratory Development at Novartis Vaccines

Topics:

Advances in mRNA technologies provide novel options for prevention of infectious diseases and for treatment of cancers. Here we will discuss the key features of these novel product classes, opportunities and challenges in the development of products and their potential pharmaceutical impact.

2:50 PM

Coffee Break

Wednesday, November 11, 2015
Delivery Session

3:10 PM
Chair introduction by Katalin Karikó, BioNTech RNA Pharmaceuticals

3:15 PM
Pierrot Harvie, Phase RX
Development of a Polymeric Delivery System Enabling Targeted mRNA Delivery to the Liver and Therapeutic Efficacy in an Orphan Liver Disease Model

PhaseRx has developed a breakthrough mRNA delivery system using its SMARTT Polymer Technology®. Optimization of the delivery system has led to stepwise improvements in mRNA delivery to the liver using GalNAc targeted polymers. We demonstrated a 5,000 fold improvement in activity over our first generation delivery system. The mRNA was packaged in a nanoparticle allowing mRNA serum stability. We demonstrated a preclinical proof of concept in a well-accepted animal model of a human orphan liver disease by achieving normalization of two well-validated therapeutic biomarkers. The treatment was well tolerated, with no toxicities associated with both single and multiple dosing regimens.

Dr. Pierrot Harvie is Associate Director of Formulation at PhaseRx. He earned a Ph.D from Laval University (Quebec City, QC) and did a post doc on non-viral gene delivery system at the BC Cancer Agency (Vancouver, BC). Dr. Harvie has an expertise in nanoparticles formulation working with lipid and polymer as drug delivery systems. He has over 15 years' experience in the biotech industry formulating small molecules and nucleic acid.

3:35 PM
Philip Santangelo, Georgia Institute of Technology
Characterizing therapeutic mRNA at the level of single cells and single molecules

The use of synthetic messenger mRNA to express specific proteins is a promising therapeutic and vaccine approach that avoids many of the safety issues associated with viral or DNA-based systems. However, in order to optimize mRNA designs and delivery, tools are required to study their distribution and efficiency at the single-cell and whole body level. Here, we present single molecule sensitive tools, which allow for the characterization of delivery pathways, endosomal escape, trafficking (in vitro and in vivo), translational efficiency and innate immune activation. These approaches should assist in overcoming the barriers of delivery and overall efficiency of mRNA therapeutics.

Dr. Philip J. Santangelo is an Associate Professor in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University. He obtained his Ph.D. in Engineering from the University of California at Davis, and was a postdoctoral fellow at both Sandia National Laboratories and Georgia Tech. In his current position, his work is primarily focused on the study of native RNA regulation, RNA virus pathogenesis (hRSV and HIV/SIV), RNA therapeutics and vaccines, and the application and development of imaging technology for these areas.

Wednesday, November 11, 2015
Delivery Session

3:55 PM

Pad Chivukula, Arcturus Therapeutics
Recent Advances in the Design and Delivery of Messenger RNA

Arcturus Therapeutics is focused on RNA medicines incorporating proprietary delivery technology called LUNAR and unlocked nucleomonomer agent (UNA) chemistry. The advent of messenger RNA synthesis using in vitro transcription (IVT) reactions templated by PCR amplicons provides an opportunity for using modified messenger RNA as a novel therapeutic agent to treat diseases. Messenger RNA transcripts turn over rapidly in the cytoplasm, and studies have revealed that only a small fraction of transcript species have half-lifes of 24 hours or more. Finding means to further increase the cytoplasmic half-life of synthetic mRNA would be of value for both in vitro and in vivo applications. We have designed synthetic mRNA containing UNA monomers that show increased cytoplasmic half-life and enhanced delivery in vivo.

Pad Chivukula Ph.D, is the Chief Scientific Officer & Chief Operating Officer of Arcturus Therapeutics, Inc. At Arcturus he is responsible for research and development activities for all of Arcturus's medicines. He brings over 15 years of experience in drug delivery and therapeutic drug development. He led the scientific development of both siRNA and mRNA platform at Arcturus. Dr. Chivukula has contributor to inventing and writing numerous pear reviewed papers and patents in the field. Dr. Chivukula has a PhD in Pharmaceutical Chemistry from the University of Utah where he specialized in nanoparticle drug delivery technology.

4:15 PM

Coffee Break

4:35 PM

Michael J. Hope, Acuitas Therapeutics
Development of a Lipid Nanoparticle (LNP) Platform to Enable mRNA Therapeutics

Previously we developed a class of LNP suitable for systemic delivery of siRNA drugs that successfully transitioned from research into the clinic with a therapeutic candidate for treatment of transthyretin amyloidosis now in Phase III clinical studies. This type of LNP platform is also well-suited to the delivery of other nucleic acids, such as mRNA therapeutics, which require a carrier to facilitate entry into cells followed by release into the cytoplasm. Using both mRNA reporter and therapeutic payloads we have significantly enhanced the potency of this platform compared to the generation of LNPs currently used in the transthyretin trials.

Dr. Hope obtained his Ph.D. in Membrane Biochemistry from the University of London, U.K. He has held senior academic and industry positions including Assistant Professor the Department of Medicine, University of British Columbia, co-founder and Vice President Research at the Canadian Liposome Company and co-founder and Principle Scientist at Tekmira Pharmaceuticals. He has worked in the field of lipid nanoparticle drug delivery for 40 years, including the delivery of nucleic acid therapeutics. Dr. Hope is an author on over 100 publications in peer reviewed journals and has extensive experience in all aspects of the development of LNPs for clinical applications.

Wednesday, November 11, 2015
Delivery Session

4:55 PM

Joseph Rosenecker, University Children´s Hospital Munich
Nebulisation of IVT mRNA Complexes for Intrapulmonary Administration

Delivery of IVT mRNA to the lung by nebulisation is of great interest. It is not known, if IVT mRNA is stable during the process of nebulisation. Therefore, we investigated the transfection efficiency of non-nebulised and nebulised IVT mRNA polyplexes and lipoplexes. We observed that IVT mRNA lipoplexes showed a slight reduction in transfection efficiency after nebulization. By contrast, the nebulisation process did not affect the cationic IVT mRNA polymer complexes. Furthermore, aerosolisation of IVT mRNA complexes did neither affect the protein duration nor the toxicity of the cationic complexes. Taken together, these data show that nebulisation of cationic IVT mRNA complexes constitute a potentially powerful means to transfect cells in the lung.

Joseph Rosenecker is professor at the Department of Pediatrics, University of Munich. He graduated in Medicine from the University of Munich in 1986. He carried out his M.D. thesis at the Department of Pediatrics in Munich. Residency in Surgery and Pediatrics 1987-1993 at the University of Munich. From there he moved on to UCSF where he was a postdoctoral fellow in the research group of Jay A. Nadel at the CVRI, School of Medicine. Since 1996 Joseph Rosenecker is head of a research group at the Department of Pediatrics which focusses on nucleic acid and gene therapies for pulmonary diseases. Joseph Rosenecker has been principal investigator and coordinator of numerous grant projects that have focussed on nonviral nucleic acid delivery to the airways.

5:15 PM

Joanna Rejman, Ludwig-Maximilians-University Munich
Modulation of cell functions by means of mRNA encapsulated in lipid and polymer particles

In the past decade the potential role of mRNA as a vehicle to deliver genetic information in cells has come into focus. Our research over the last few years has demonstrated that mRNA-based transfection may be employed in such fields as anti-cancer therapy, vaccination strategies, generation of pluripotent stem cells and protein replacement therapy. Our results demonstrated that the duration of protein production following mRNA-based transfection is determined by the delivery method and the carrier system used. In more recent work we showed that nebulisation of mRNA complexes does not lead to significant detrimental effects on the nucleic acid transfection potency.

Dr Joanna Rejman graduated in 2000. She was granted a Marie Curie Individual Fellowship to perform a postdoctoral research project at the Groningen University (The Netherlands). From 2003 till 2007 she was employed as a post-doctoral fellow at San Raffaele Hospital in Milan (Italy) where she worked on gene-therapeutic strategies in the treatment of cystic fibrosis. From 2008 till 2012 she was a research assistant at the Faculty of Pharmaceutical Sciences of Ghent University (Belgium). Her main scientific interests include non-invasive cell labeling, (transient) modification of cell functions, understanding the processes involved in internalization, intracellular trafficking, and processing of nanoparticles.

Wednesday, November 11, 2015
Delivery Session

5:35 PM
Panel Discussion: Delivery

Chair: Susan Sobolov, Alexion

Susan is an executive director, Alexion Pharmaceutical where she is leading the mRNA portfolio of rare disease projects. Prior to this she served as development team leader for Strensiq™ (Asfotase Alfa), an enzyme replacement therapy for hypophosphatasia. Before joining Alexion Susan was Head of PMO at Novartis Institute of Biomedical Research from 2009-2012. She served as Program Executive for Incivek at Vertex from 2007-2009. She began her industry career at Pfizer as a medicinal chemistry and rose through positions of increasing responsibility to Senior Director and Global Development Team Leader. She has more than 20 years of experience in leading projects from preclinical through post-approval in multiple disease areas.

Susan earned her Doctor of Philosophy at Yale University in organic chemistry and then completed an American Cancer Society Post-doctoral fellowship Harvard Medical School.

Panelists:

Speakers from Session

Topics:

A key component to enable mRNA as a therapeutic modality is safe and efficacious delivery systems.

In this panel discussion, topics will be discussed:

- How do mRNA payloads affect the properties of LNP and polymers as delivery systems?
- Do they affect cellular uptake and release mechanisms?
- What are the most promising ways to study and address liabilities and side effects of nanoparticles for acute, intermittent and chronic dosing of mRNA?
- Where do we see the progress being made to have systems for beyond the liver and what are the time horizons?
- Are there testing paradigms that can help speed up the development of new systems?

Closing of Conference Day 1

6:20 PM
Closing remarks Day 1 by the Organizing Committee

6:30 PM
End of Conference Program Day 1

Networking Evening

7:00 PM
Departure of the coaches to the Networking Evening

Enjoy an exclusive networking evening with the mRNA community in ParkInn's Panorama37 (Alexanderplatz 7, 10178 Berlin) with a great view over Berlin. Busses will bring you to the evening location and back to the HILTON.

Thursday, November 12, 2015
Therapeutics Session

9:00 AM
Welcome remarks Day 2 by the Organizing Committee

9:15 AM
Chair introduction by Stéphane Bancel, Moderna

9:20 AM
Jan Weiler, Novartis Institutes for BioMedical Research
Therapeutic messenger RNA to produce prophylactic antibodies

Recently, synthetic messenger RNA (mRNA) has emerged as novel tool in gene therapy and the therapeutic utility of mRNA to trigger a transient boost in expression of gene products associated with human disease is currently being explored by both biotech and pharmaceutical companies. As part of the Defense Advanced Research Projects Agency (DARPA) grant the aim of the project discussed here is to determine if therapeutic mRNA can be used to produce prophylactic antibodies capable of protecting against infectious agents, in a rapid and robust manner. Challenges which have to be overcome to achieve the clinical potential of this project including synthesis, characterization and delivery of antibody expressing mRNA to the site of action in the cells of target tissues will be discussed.

Jan Weiler is a Senior Research Investigator and group leader within the New Technologies Group in the Biologics Center department at Novartis Institutes for BioMedical Research. He received his Ph.D. in Organic Chemistry from the University of Konstanz, Germany in the lab of Prof. Dr. Wolfgang Pfleiderer and was a postdoctoral fellow in the department of Functional Genome Analysis at the German Cancer Research Center DKFZ with Dr. Joerg Hoheisel, where his work focused on developing novel microarray-based expression profiling technologies. Since he joined Novartis Pharma Research in Basel, Switzerland as a lab head in 1997, he has participated in and led antisense-, RNA interference (RNAi) and most recently messenger RNA (mRNA) related projects to assist in prioritizing novel pharmaceutical targets for drug discovery.

9:40 AM
Carsten Rudolph, ethris
Stabilized non-immunogenic messenger RNA for transcript therapy

Ethris SNIM® RNA is an enabling platform for “Transcript Therapies” in a broad variety of medical indications, from hereditary or acquired metabolic diseases to regenerative medicine. SNIM® RNA circumvent TLR activation and thus enables repeated administration of mRNA. Because of its precursor function, SNIM® RNA yields sustained protein production within the body and overcomes short duration effects of recombinant proteins. Ethris has developed proprietary delivery systems for pulmonary, systemic and local SNIM® RNA administration and will present preclinical results from its activities. Efficient delivery systems and non-immunogenicity are the keys for making mRNA therapeutics reality beyond oncology applications.

Carsten Rudolph, CEO and president, pharmacist by training, received his PhD from the Department of Pharmacy of the FU Berlin. Since 2003 he is group leader at the Dr. von Haunerschen Kinderspital of the Ludwig Maximilians University, Munich. He is lead inventor of the SNIM® RNA-Technology and co-inventor of numerous drug delivery patent applications. Carsten Rudolph received his post-doctoral lecture qualification at the Department of Pharmacy, FU Berlin in 2009. In 2005 Carsten Rudolph received the prestigious BioFuture Award of the BMBF which is the highest endowed young investigator award in Germany. He is supervising numerous research projects in the field of molecular medicine and gene therapy with a research focus on pulmonary diseases.

Thursday, November 12, 2015
Therapeutics Session

10:00 AM

Michael Kormann, University of Tübingen
Chemically modified RNAs for efficient and safe genome editing

Site-specific endo-nucleases (SSE's) facilitate homologous recombination and represent a promising approach for repairing genomic mutations. We recently demonstrated chemically modified messenger RNA (mRNA) can achieve therapeutic protein expression levels in vivo. Here, we describe nuclease encoded chemically modified mRNA (nec-mRNA) as a novel in vivo delivery tool for short-term expression of site-specific nucleases. Using nec-mRNA and an Adeno-Associated Viral (AAV) vector-template, we demonstrate correction by in vivo genome editing of a mouse lung disease model of Surfactant Protein B (SP-B) deficiency. Nec-mRNA and AAV co-delivery leads to efficient in vivo engineering of the transgenic SP-B promoter, resulting in a significant improvement in survival and pulmonary function. Nec-mRNA offers a potentially improved safety profile for delivery of genome-editing nucleases in vivo, allowing the first therapeutic genome editing using ZFNs in the lung.

Michael Kormann, born 13th of April 1978, studied biology and genetics at the TU and LMU Munich, then received his PhD with summa cum laude. He then moved to the University of Tübingen, under the supervision of Prof. Dominik Hartl and Prof. Rupert Handgretinger, where he soon became Assistant Professor. His work on severe, inherited lung diseases was published in renowned journals such as Nature Biotechnology, winning international prizes such as the Maurizio Vignola Award, and was appointed Editor in journals such as PLoS ONE, Editor for InTech books and regular reviewer for Nature Biotechnology. Michael is specialized in gene therapies for asthma genetics, Cystic Fibrosis and hematopoietic diseases.

10:20 AM

Romesh Subramanian, Alexion
mRNA Therapeutics at Alexion

Currently there are over 5000 – 8000 rare diseases that together affect millions of people worldwide. A large proportion of these rare diseases have an identified genetic origin and 50% of new cases are in children. Advances in genetic research are providing us the knowledge to explain disease patterns that we did not understand before and hence the total numbers of rare diseases are steadily increasing. mRNA therapeutics provides a novel means of providing gain of function strategies for rare diseases. Numerous metabolic diseases exist wherein loss of function of an enzyme results in serious deficits of metabolism during childhood with devastating or life-long deleterious effects. In my talk today I will describe Alexion's current strategy to utilize mRNA therapeutics to benefit rare disease patients.

Dr Romesh Subramanian received a Ph.D. in Pharmacology from Emory University and completed a post-doctoral fellowship at the Dana-Farber Cancer Institute. Dr. Subramanian has extensive experience in the discovery and development of nucleic acid, peptide and small molecule therapeutics targeting rare and orphan diseases. He has developed targets to Phase I at start-up biotechnology companies as well as at large pharmaceutical organizations. Dr. Subramanian co-founded RaNA Therapeutics which investigates epigenetic modulation of genes for gain of function.

Dr Subramanian leads the RNA Therapeutics Division at Alexion Pharmaceuticals and is focused on the treatment of rare and ultra-rare diseases utilizing mRNA Therapeutics. In his current capacity he leads a new state-of-the-art RNA laboratory in Cambridge MA and in collaboration with Moderna Therapeutics he is progressing rare disease clinical candidates to benefit patients.

Thursday, November 12, 2015
Therapeutics Session

10:40 AM
Coffee Break

11:00 AM
Nigel Horscroft, CureVac
Sequence-engineered mRNA enables an effective protein therapy

There is enormous potential for mRNA to revolutionize the way protein and peptide therapeutics are produced and delivered. We have shown that mRNA can achieve therapeutically relevant levels of expression in the absence of immune stimulation, through the use of sequence-engineered molecules. Using erythropoietin (EPO) driven production of red blood cells as the biological model, engineered EPO mRNA elicited meaningful physiological responses in mice, non-human primates and pigs. Our results demonstrate that sequence-engineered mRNA can effectively and safely deliver human protein therapies even without chemical modifications.

Dr Nigel Horscroft is Director Alliance Management at CureVac AG, a global leader in the research and development of mRNA-based drugs. In addition to his alliance management responsibilities he is also the program manager for CureVac's RNArt pipeline of molecular therapeutics. Prior to joining CureVac in 2012 he was Head of Research at Pike Pharma in Switzerland. He has a background in virology and has worked on infectious disease and immunology programs at Pfizer in the UK and Valeant Pharmaceuticals in the US. Dr Horscroft has a BSc in Applied and Industrial Biology from London South Bank University and received his DPhil in Biochemistry from Oxford University.

11:20 AM
Katalin Karikó, BioNTech RNA Pharmaceuticals
Why RNA is immunogenic - and how to change that?

Immunogenicity of RNA has been recognized for decades, but the underlining molecular mechanisms were only elucidated very recently. The understanding of how RNA sensors such as TLR3, TLR7, TLR8 and RIG-I are activated guides us to generate non-immunogenic RNA for protein therapy. Studies have shown that incorporation of modified nucleotides, optimization of RNA sequences, proper formulation and purification are all greatly enhance therapeutic performance of the in vitro-transcribed mRNA.

Dr. Karikó leads the mRNA-based protein therapy program for BioNTech RNA. Prior to that, she investigated RNA-mediated immune activation at the University of Pennsylvania. She is co-inventor of the first patents related to generation of non-immunogenic mRNA by incorporation of modified nucleotides.

Dr. Karikó received her Ph.D. in Biochemistry from University of Szeged, Hungary. As a postdoc, she studied dsRNA-induced antiviral mechanisms at Temple University in Philadelphia, where she participated in a clinical trial of mismatched dsRNA.

Thursday, November 12, 2015
Therapeutics Session

11:40 AM

Irina Tcherepanova, Argos Therapeutics Inc.

RNA optimization for ectopic protein expression and increased potency of a cell-based immunotherapy

AGS-003 is an autologous immunotherapy for cancer consisting of Dendritic cells electroporated with RNA encoding CD40L and autologous tumor antigens. CD40L RNA causes ectopic expression of CD40L protein which, surprisingly, binds the CD40L receptor intracellularly leading to IL-12 secretion. This assures CD8 T cell maintenance without the need for CD4 T cell signaling, which is impaired in cancer subjects. Secondly, electroporation of amplified patient tumor RNA supports the expression of antigen epitopes specific to each individual, assuring product specificity. The RNA development was aimed at optimizing protein expression, and assuring a consistent manufacturing process.

Dr. Tcherepanova is the Senior Director of R&D at Argos Therapeutics. She received her Ph.D. in Molecular Pharmacology from the Albert Einstein College of Medicine and completed post-doctoral training at the Duke University Medical Center. She joined Argos in 2000 and was instrumental in the development of autologous RNA transfected DC immunotherapy. She is the author of multiple peer reviewed publications and is the inventor on several patents. The most advanced product, AGS-003 is currently being tested in a pivotal Phase 3 clinical trial in advanced Renal Cell Carcinoma.

12:00 PM

Lunch Break with Poster Session

1:00 PM

Nils Bergenhem, AstraZeneca

Modified RNA as CVMD Therapeutic Modality: opportunities and challenges

AstraZeneca is strongly committed to nucleotide drug discovery and development. Our collaboration with Moderna gives AstraZeneca the option to select up to 40 drug targets for clinical development in cardiovascular, metabolic and renal diseases as well as cancer. mRNA as a drug modality has the potential to increase expression of intracellular proteins as well as use tissues as expression machineries for sustained deliver to systemic circulation of labile proteins, increasing the addressable target space. Depending on the protein, tissue targeting and possible need for delivery vehicles will add challenges on the road to successful drug development.

Nils Bergenhem is Director, Strategy & Externalization for CVMD iMed at AstraZeneca, and Alliance Coordinator for the CVMD portfolio in the AstraZeneca – Moderna mRNA collaboration. Prior to joining AstraZeneca, Nils was Chief Scientific Officer or VP Research at several US biotech and start-up companies focused on various aspects of metabolic diseases. Earlier in his career, Nils held positions of increasing importance at Novo Nordisk in Copenhagen. Nils holds an undergraduate degree in Chemistry from Linkoping University, Sweden, a Ph.D. in Biochemistry from Umeå University, Sweden, and has completed post-doctoral work at University of Michigan in Molecular Biology and Human Genetics.

Thursday, November 12, 2015
Therapeutics Session

1:20 PM

Meltem Avci-Adali, University of Tübingen

De novo synthesis of extracellular matrix structural proteins for tissue repair by exogenous delivery of mRNA

Elastin is an important extracellular matrix component for maintaining the elasticity of organs and tissues. The endogenous synthesis is completed in adolescence. Due to genetic or pathological disorders, elastin can be absent or be degraded by aging. Here, we show that synthetic modified mRNA can be used to induce elastin synthesis in desired cells and tissues. Thus, this auspicious strategy of exogenous mRNA delivery can be applied to induce de novo elastogenesis in several regions, such as skin, blood vessels, and alveoli.

PD Dr. Meltem Avci-Adali holds a Master of Science degree in biomedical engineering and a Diploma degree in pharmaceutical technology. She completed her Ph.D. in biology at the University of Tuebingen in 2010. Currently, she is the research group leader of "Aptamer Technology" and "In vivo Tissue Engineering" at the department of Thoracic and Cardiovascular Surgery at the University Hospital Tuebingen, Germany. She has published numerous papers in reputed journals and has extensive research experience in the fields of synthetic mRNA, aptamers, implant surface functionalization, endothelialization, and in vivo tissue engineering.

1:40 PM

Tyler Wagner, Massachusetts Institute of Technology

RNA-Encoded Synthetic Gene Circuits for Tissue Specific Expression and Small Molecule-BasedDosage Control of Therapeutic Proteins

RNA therapeutics are an attractive alternative to traditional DNA-based therapies, providing transient expression with minimal risk of genomic integration. However, the majority of current applications, ranging from vaccination to genetic reprogramming, rely solely upon constitutive expression. We have employed synthetic biology to expand the potential of RNA expression platforms to include cell-type specific expression and small molecule mediated dose control of therapeutic proteins. Synthetic biology aims to create and characterize libraries of highly predictable and modular genetic parts that can be combined to produce genetic circuits. To this end, we establish a collection of RNA-based parts that can modulate translation. We demonstrate that RNA-based circuits can be regulated using either exogenous siRNAs or endogenous miRNAs. Finally, we couple our genetic parts with small molecule responsive elements to form an RNA-only circuit platform that can dynamically control expression of multiple therapeutic proteins using external inputs.

Tyler Wagner received a Bachelor of Science in Chemical Engineering from the Massachusetts Institute of Technology in 2012. He is currently pursuing a Ph.D. in Biomedical Engineering as a joint member of Ron Weiss' lab at MIT and Douglas Densmore's lab at Boston University. Together with Jacob Beal at Raytheon, he developed a quantitative model of gene expression from RNA replicons. His present research focuses on engineering RNA circuits for therapeutic applications, with an emphasis on external regulation and dynamic control.

Thursday, November 12, 2015
Therapeutics Session

2:00 PM

Panel Discussion: Therapeutics

Chair: Brad Guild, ethris

Brad Guild joined Ethris in April 2015 as the Head of International Operations. In 2008 he spearheaded studies on transcript therapy at Shire Pharmaceuticals and co-developed with Ethris proof of principle studies on CFTR transcript therapy. In 2012 he advanced mRNA therapy for the treatment of rare diseases at Pfizer. Previously, he developed therapeutic antibodies in the Department of Ophthalmology at Novartis, served as the Head of Protein Sciences at Millennium Pharmaceuticals, and was a founding scientist of one of the first gene therapy companies, Somatix, where he constructed the MFG vector that was used in the treatment of SCID-X1.

Panelists:

Speakers from Session

Topics:

Transcript therapy is poised to become a disruptive technology for the delivery of biologics. Just as there is promise there are also questions and challenges which the Therapeutics Session Panel will address.

Among the topics for discussion:

- Regulatory considerations in the delivery of transcript therapy
- CMC and process considerations for RNA manufacture and nanoparticle formulation
- RNA chemistries: their advantages and risks for controlling inflammation
- Is there an ideal design for transcript engineering?
- Strategies for tolerance induction for the protein products of chronic transcript therapy
- Anti-infectives, vaccines and protein replacement – Which are best first applications of transcript therapy?
- Genome editing by transcript therapy – What are the prospects and limitations for delivery and efficiencies?
- Systemic delivery of transcript therapy and off-target considerations
- Challenges/advantages posed by various modes of delivery for transcript therapy: intravenous, pulmonary, subcutaneous and intramuscular

Closing of the Conference

3:00 PM

Awarding of the Poster Prices

Closing remarks by the Organizing Company

3:20 PM

End of Conference

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BioNTech AG is an immunotherapy leader with bench-to-market capabilities, developing truly personalized, well-tolerated & potent treatments for cancer and other diseases. Established by clinicians and scientists, the Group is pioneering disruptive technologies ranging from individualized mRNA based medicines through innovative Chimeric Antigen Receptors / T-cell Receptor-based products and novel antibody checkpoint immunomodulators. BioNTech's clinical programs are supported by an in-house molecular diagnostics unit whose products include MammaTyper®, a molecular in-vitro diagnostic kit marketed under CE and IVD marking in Europe and certain other countries. Founded in 2008, BioNTech is privately held, with Strüngmann Family Office as a majority shareholder.
www.biontech.de

CureVac has more than 15 years of expertise in handling and optimizing the versatile molecule mRNA for medical purposes and the most advanced product pipeline and IP portfolio in the industry. Since 2008, CureVac has applied its mRNA technology in more than 350 humans in seven clinical trials in eleven countries, including an ongoing Phase IIb trial in prostate cancer.
CureVac's mRNA programs include novel mRNA-based cancer immunotherapies and prophylactic vaccines against infectious diseases (RNActive®), molecular therapies designed to trigger the body's own production of therapeutic proteins (RNArt®), and RNA encoded antibodies (RNAntibody®).
CureVac has entered into various collaborations with multinational corporations and organizations, including agreements with Boehringer Ingelheim, Sanofi Pasteur, DARPA, Johnson & Johnson, the Bill & Melinda Gates Foundation and IAVI.
In 2006, CureVac successfully established the first GMP facility worldwide for the manufacturing of mRNA. In 2016 CureVac will start the construction of an industrial scale production facility with a capacity of 30 million doses per year.
www.curevac.com

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messenger therapeutics

Moderna is pioneering messenger RNA Therapeutics™, an entirely new in vivo drug technology that produces human proteins, antibodies and entirely novel protein constructs inside patient cells, which are in turn secreted or active intracellularly. This breakthrough platform addresses currently undruggable targets and offers a superior alternative to existing drug modalities for a wide range of disease conditions. The company currently plans to develop and commercialize its innovative mRNA drugs through a combination of strategic relationships as well as newly formed ventures. Cambridge-based Moderna is privately held and currently has strategic agreements with AstraZeneca, Alexion Pharmaceuticals and Merck.
www.modernatx.com

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Aldevron offers custom plasmid (supercoiled or linear), mRNA, and IVT enzyme production to support the growing mRNA field. We also offer a genetic immunization technology that allows for the generation of high-affinity antibodies directly from a DNA sequence. Our services and methods provide consistency at all levels with a deliberate pathway from research to clinical manufacture. Visit with our team to learn how Aldevron's custom services can support and advance your scientific platform.

AstraZeneca is a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of cardiovascular, metabolic, respiratory, inflammation, autoimmune, oncology, infection and neuroscience diseases. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information please visit: www.astrazeneca.com.

Ethris – Enabling Therapies develops innovative therapeutics based on proprietary platform technologies with high diversification potential that enable therapies for diseases with currently dissatisfying treatment options and high unmet need.

SNIM® RNA is a first-in-class biopharmaceutical platform for therapies of rare diseases, alternative for recombinant proteins, and for "Transcript Therapies" in regenerative medicine. ethris enabling therapies provide access to highly profitable markets.

Ethris was founded at the end of 2009 by Dr. Carsten Rudolph (CEO) and Prof. Dr. Christian Plank (CSO) and was later joined by Dr. Walter Schmidt. The goal of ethris is to rapidly and continuously translate its Technology.

ThermoFisher SCIENTIFIC

Thermo Fisher Scientific is a developer and manufacturer of standard and customized phosphoramidites (including TheraPure™ and DyLight™ phosphoramidites) used in the production of oligonucleotides and modified specialty nucleic acids for research, diagnostics and therapeutic applications. Thermo Fisher Scientific is your industrial partner of choice offering over 25 years of manufacturing experience, a mature quality system and proven sustainability. Our Milwaukee-based facility is dedicated to meeting the growing needs of the market.

TriLink BIOTECHNOLOGIES

TriLink has been facilitating customer success for 20 years as the industry leader in manufacturing high quality nucleoside triphosphates, mRNAs, and oligonucleotides for the research, diagnostic, therapeutic, and OEM markets. Our extensive experience with specialty modified nucleic acids and our commitment to quality result in the best products and services available. We offer ISO/QSR compliant cGMP mRNA manufacturing for discovery and early-phase clinical trials. TriLink has established a Start-Up and Emerging Companies Program that provides a dedicated project manager to oversee all aspects of your commercial project including scientific, scale-up, and documentation consultation. At TriLink our expertise is your success.

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