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Overview of Capabilities

Who are We?

Lovelace Biomedical is a contract research organization (CRO) who's mission is to advance human health through meaningful collaboration with innovator companies.

- We perform non-GLP and GLP programs from early concept, IND, NDA, CARCI
- We have a single site with broad & specialty expertise capabilities
- We are a small company with big company ability
- We are leaders in nonclinical development for both respiratory and gene therapy

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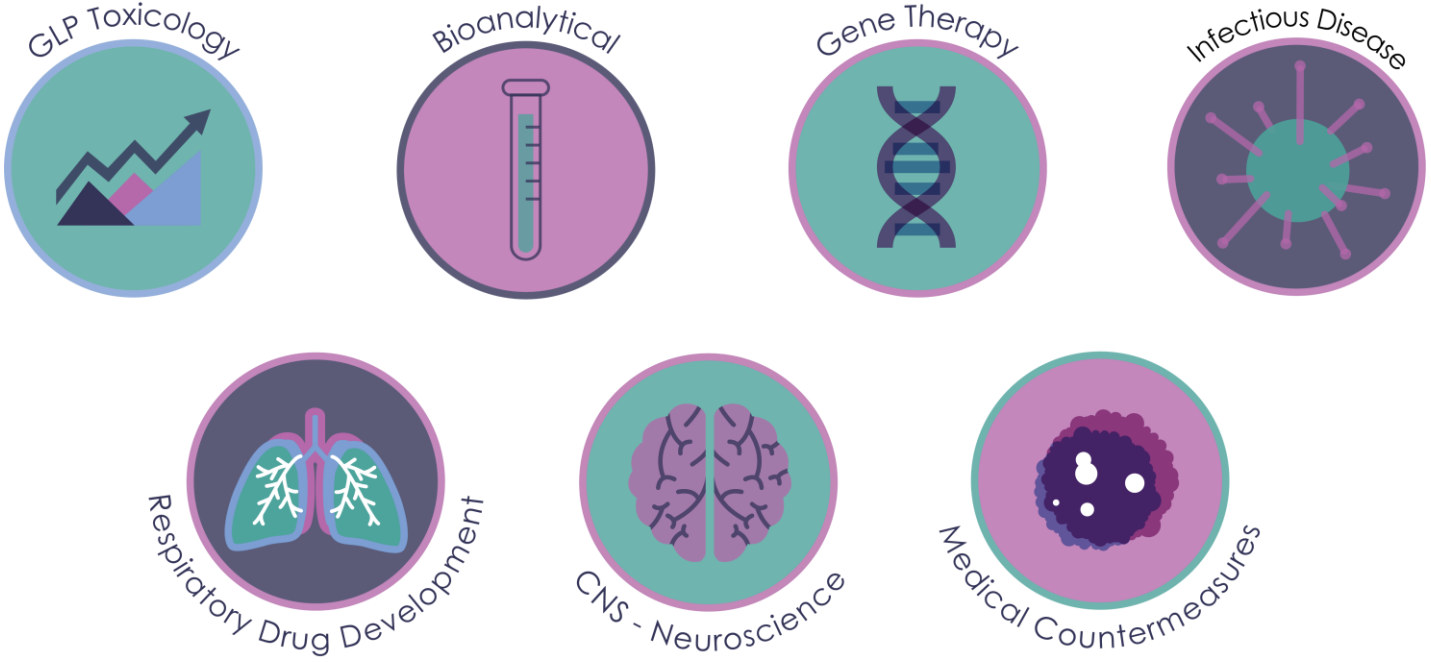
Key Areas of Expertise



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Key Areas of Expertise

- Inhalation/respiratory, Gene therapy, Infectious Disease, Pharmacology, Pharmacokinetics, Complex animals models and IND/NDA enabling toxicology
- Quality, compliance, and transparency are paramount to delivering research services
- Our People matter - talent, passion for service and execution allows us to deliver on commitments

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Culture and Core Values

- Ethical, responsible and compliant animal welfare
- Scientific and ethical leadership and integrity in everything we do
- Quality, compliance, and transparency are paramount to delivering research services
- Our People matter - talent, passion for service and execution allows us to deliver on commitments

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Fast Facts

- **Rich history of innovation**
- **Single Site focused on nonclinical drug development**
- **Specialty Expertise:**
  - GLP Toxicology/Pharmacology
  - Gene Therapy and Regenerative Medicine
  - Infectious Disease and Vaccine Development
  - Disease Models / Pharmacology
  - Aerosol Delivery and Inhalation Toxicology
  - Lung Biology & Respiratory Disease
  - Neuroscience, Imaging and Advanced Data Analysis
  - Dermatitis
  - Medical Countermeasures

- 70 year history
- 50+ PhDs, DVMs, MD
- 250 employees
- 375,000ft^2 facility

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Employees (Abbreviated)

Jacob McDonald, PhD.
CSO

Phillip Khuel, PhD.
Director Scientific Core Labs

Ted Barret, PhD.
Director of Pharmacology

Melanie Doyle-Eisle, PhD.
Director of Life Sciences

Steve Belinsky, PhD.
Vice President of Research

Larry Mallis, PhD.
Director Analytical/Bioanalytical

Sharla Birch, DVM, PhD.
DACVP
Veterinary Pathology

Meghan Vermillion, DVM, PhD. ACLAM
Lab Animal Veterinarian

Joanna Mleczko, DVM, PhD.
Research Veterinarian

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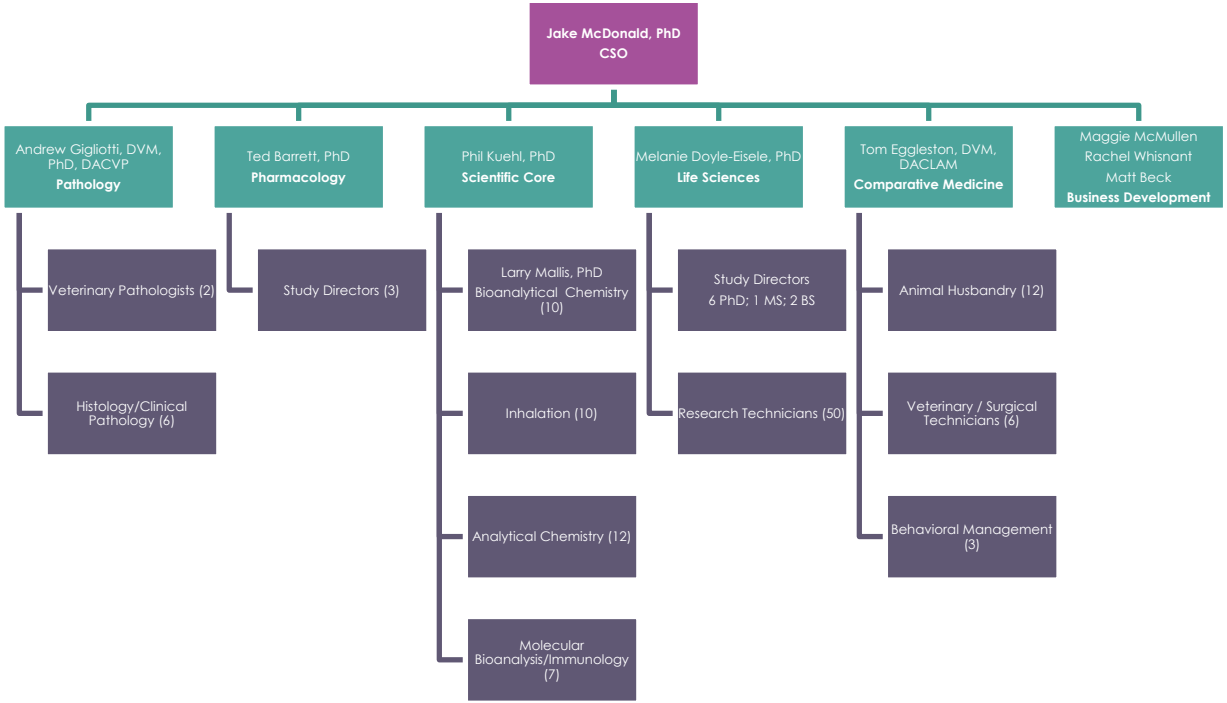
Organizational Structure



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***Quality Assurance Reports to CEO**
Operations Reports to COO

Facilities

- 375,00 square feet facility
- Multispecies Animal Housing
- Surgical Suites
- Indoor/outdoor canine options
- Inhalation/containment facilities
- Specialized Laboratories
  - Histopathology
  - Clinical Pathology
  - Analytical and Bioanalytical Chemistry
  - Microbiology and virology
  - Cell / Molecular Biology

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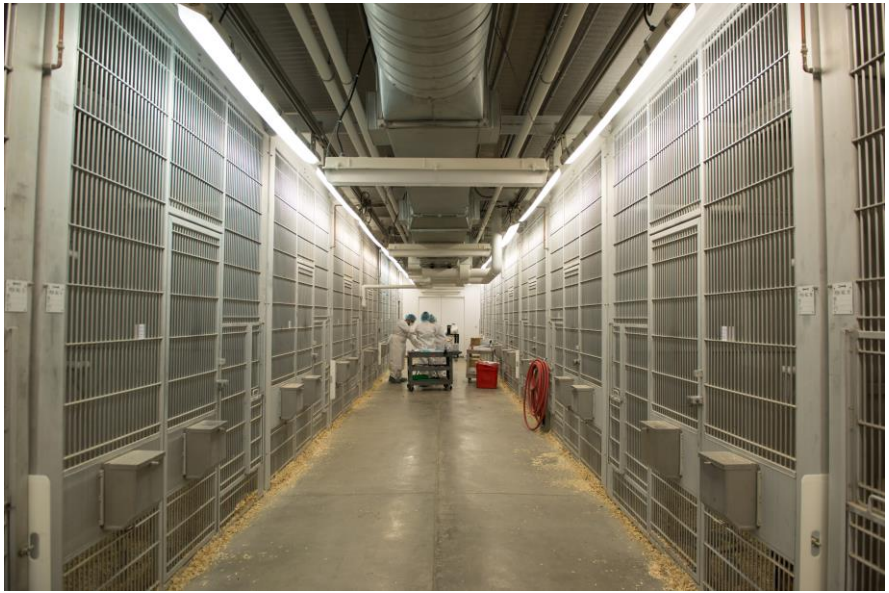
Vivarium

- ~250,000 ft2
- 93 Animal Rooms/ Kennels
  - Primate (3 species) 2276
  - Dog 906
  - Pig 728
  - Ferret 1656
  - Rabbit 524
  - Rat 3360
  - Mouse 6720
  - Guinea Pig 909
  - Goats 12 designated
- ABSL3 animal facility
- Surgical Suites
- Onsite clinical pathology, histopathology
- Large and small animal necropsy suites



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Specialized Capabilities

- Dosing Routes
  - IV, IM, SC, PO, IP
  - Inhalation (nose-only, head-only, whole body)
  - Nasogastric
  - Arterial (hepatic, carotid, coronary, femoral artery)
  - Intracerebral or intraventricular
  - Intrathecal, lumbar
  - Intracameral/Ocular
  - Others: we specialize in the development of novel techniques for dosing as required for gene therapy

- Endpoints
  - Serum chemistry, hematology
  - Telemetry (HR, BP, ECG, etc.)
  - Serum or tissue-based biomarkers
  - Clinical Pathology/Hematology
  - Histopathology
  - PK / TK and biodistribution
  - Ocular pharmacology and toxicology
  - Imaging
    - Radiography
    - SPECT
    - MRI / fMRI

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Core Competency

- **PK**
  - All species
  - PK Modeling / WinNonLin
- **Biodistribution**
  - Radiolabeling
  - Gamma scintigraphy
  - Scintillation counting
- **Toxicology**
  - All species
  - Up to lifetime studies
- **Pharmacology**
  - Respiratory
  - Dermatitis
  - Medical Count.
  - Infectious Disease
  - Genetic Models

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Bioanalytical Chemistry

- **Biological fluids and tissues**
- **GLP and Non-GLP**
- **Mass Spectrometry (7)**
  - Sciex API 5000, 5500, 4500 – Waters Acquity / Shimadzu uHPLC
  - Sciex API 4000 – Waters Acquity UPLC
- **Liquid Chromatography (5)**
  - Agilent 1100 / 1200; DAD, VWD, RID, FLD detectors
  - UPLC Waters Acquity PDA; FLD, ECD detectors
- **Gas chromatography (3)**
  - Agilent 7890 and 6890, MS, FID, TCD and ECD detectors,
- **Flow Cytometry**
- **ELISPOT**
- **Solid State Analysis**
  - TA Instruments TGA
  - Thermo FTIR
- **Quantitative PCR**
- **Auto-samplers**
  - Tecan / Eppendorf Liquid Handlers
- **Sample Processing**
  - Covaris tissue homogenizer
  - TomTec Quadra Extraction System

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In Vivo Pharmacology Models

- Allergy
- Acute lung injury
- Asthma
- COPD
- Dermatitis
- Infectious disease (influenza, RSV, bacterial, etc.)
- Pulmonary fibrosis
- Cystic Fibrosis
- Pulmonary arterial hypertension
- Radiation injury
- Spinal cord injury
- Traumatic brain injury

- NHP, Canine, Swine, Rabbit, Guinea Pig, Rat, Mouse
- Experts in intensive veterinary medicine and post-operative care

Capability Highlights (Areas of Excellence)

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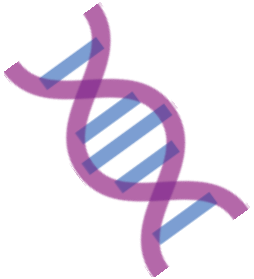
Lovelace Biomedical Gene Therapy Studies (Examples)



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Gene Therapy Center of Excellence

- Established in 2007 by NIH as Center for Gene Therapy Pharmacology/Toxicology in collaboration with Wilson group at Penn. Has successfully operated this Core for over 12 years
- Over 25 IND's and counting in Gene Therapy
- Experienced scientists in working with FDA and innovators to design programs
- Competent veterinary team that develops novel dosing strategies and animal models
- Strategic relationships with animal model resource companies such as Exemplar Genetics, Jackson Laboratories and Penn

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Examples (Lovelace Has Performed >25 Gene Therapy IND Programs)

Vector	Animal Model/Route	FDA Interactions
AAV	Swine model of cardiac failure/ percutaneous catheter delivery to coronary vessels.	Participated in pre-IND meeting and follow-up discussions.
AAV	C57BL/6 mice/IM	NA[a]
AAV	GAA-knockout mice/IV injection	Reviewed pre-IND package and participated in pre-IND meeting.
Adenovirus vector	New Zealand White Rabbits/direct painting to cardiac surface	Reviewed pre-IND packages and participated in pre-pre-IND and pre-IND discussions.
AAV	Swine model of cardiac failure/percutaneous catheter delivery to coronary vessels.	None to date
Lineage-depleted bone marrow cells transduced with lentiviral vector	C57BL/6 mice/IV injection	Pre-IND package input and participated in pre-IND discussions
AAV	African Green monkeys and C57BL/6 mice/Intrapleural injection[d]	NA[a]
AAV	Rhesus macaques/oral inhalation	Participated in pre-pre-IND
AAV	Rats/hind limb knee injection[e]	Reviewed pre-IND package
AAV	NHP isolated limb infusion	Not Applicable
AAV	Cynomolgus monkeys by intramuscular injection once or twice. Included immune suppression	Discussions clarifying and solidifying study design
AAV	GAA knockout mouse dose response study, IM injection once or twice	Discussions clarifying and solidifying study design
AAV	Sprague Dawley rat, intravenous injection	Pre-IND comments from FDA required study conduct

Lovelace Biomedical Respiratory Drug Development

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Respiratory Center of Excellence

- Did all nonclinical development animal and early formulation studies that led to Bevespi approval.
- Invented numerous aerosol delivery and measurement devices
- Pioneered pulmonary physiology measurement techniques
- Over 500 publications in respiratory pharmacology, mechanisms and respiratory drug development
- Service on numerous industry panels as Key Opinion Leaders for respiratory hazard and drug development
- Over 10 GLP IND programs in respiratory per year
- Over 50 respiratory pharmacology models in cancer, COPD, infectious disease, asthma, allergic rhinitis, CF, acute lung injury

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Additional Distinguishing Features

- Allergic canine model since 1980's for use in atopic dermatitis/asthma
- Canine colony on aged dogs to study alzheimers/dementia
- fMRI and neurological capabilities to develop translational models in brain injury
- Medical countermeasure models for study of chemical, biological (up to BSL3), radiological, nuclear and explosion threats
- Significant infrastructure and competency in infectious disease, including influenza and many other pathogens
- Key Opinion Leaders in respiratory, CNS, dermatitis, cancer, COPD, animal model development
- Diverse funding experience with both government and commercial clients
- Large federal centers funded in rare diseases, gene therapy, medical countermeasures, HIV, infectious diseases, alternative tobacco, animal model development
- Experience working with large pharma, biotech and start-ups

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Lovelace Biomedical Infectious Disease Drug Development

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Animal Models of Infectious Disease: Supporting vaccine and therapeutic efficacy

- **Viral (seasonal, emerging, ABSL-3)**
  - RSV, influenza virus, adenovirus, parainfluenza, paramixovirus, metapneumovirus, rhinovirus
  - Established viral models in high containment (ABSL-3+)
  - In Development: dengue virus, zika virus, chikungunya virus, WNV, rabies, EEE
- **Bacterial (ABSL-3, MDR)**
  - Established bacterial models in high containment (ABSL-3)
  - In Development: CDC "threat list" AMD, answering the call for "The President's Initiatives" on MDR
  - P. Aeruginosa, K. pneumoniae, A. baumannii, N. gonorrhea
    - Acute (LD/ED50)
    - Subacute to subchronic
    - Institutional experience with "chronic" agar bead model
- **Fungal**
  - Cryptococcus neoformans
  - Aspergillus fumigatus
  - Candida albicans
- **Toxins/Chem**: Ricin, Botulinum, SEB, Sarin, SM

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Select Agent Sampling (ABSL-3)

- F. tularensis (Shu4 strain); (primate, rabbit)
- B. anthracis (Ames strain); (GP, mouse, rabbit, primate)
- Y. pestis (Colorado 92 strain); (mouse, rat, primate)
- Highly pathogenic avian influenza; (mouse, ferret, primate)
- SARS CoV (cynomolgus macaque, rhesus macaque)
- Orthopox viruses: cow, monkey, rabbit, mouse; (animal models: mouse, rabbit, non-human primate, rabbit)

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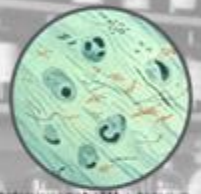
Thank you!

www.lovelacebiomedical.org

Lovelace's Past

William Randolph Lovelace I ("Uncle Doc") goes to medical school in St. Louis.



A photomicrograph of Mycobacterium tuberculosis bacterium. There were several TB sanitariums in New Mexico in the early part of the 20th century.

Dr. Edgar Lassetter

In 1933 Randy married Mary Moulton. Mary's father Earl Moulton came to New Mexico to recover from TB, and Mary was raised in Albuquerque.

Randy becomes Chief of Military Aero Medical Laboratory, Wright Field, OH.

Randy recieves the Distinguised Flying Cross for a parachute jump from 40,200 ft. to test oxygen equipment (his first jump) from General "Hap" Arnold.

After the jump, a shaken Randy Lovelace is tended by a corpsman

In early June 1946 a polio epidemic then raging in Rochester, Minnesota, tragically takes the lives of Randy and Mary's two young sons. The bereaved family returns to Albuquerque.

1902-1905 | **1906** | **1907-1918** | **1919-1922** | **1933-1936** | **1937-1942** | **1941** | **1943** | **1946-1947** | **1950s**

Uncle Doc contacted Lantry & Sharp Co. about a job as company surgeon on the new Santa Fe Railroad construction in New Mexico.

William Randolph Lovelace II (Randy) is born to Uncle Doc's brother and his wife in 1907. In 1908 they move to New Mexico.

Uncle Doc moves to Albuquerque and opens an office above the Kistler-Collister Department Store on Central Avenue. He assumes responsibility for Santa Fe Railroad health operations and becomes heavily involved with St. Joseph Hospital.

Dr. Edgar Lassetter marries Uncle Doc's sister Lora and becomes a medical partner.

Lovelace Clinic began.

President Frankly Roosevelt presents the Robert J. Collier Trophy in 1940 for the implementation of the BLB oxygen mask. Standing behind the president is Randy Lovelace, with Dr. Boothby to his right and Army Captain Harry G. Armstrong to his left.

Randy enters the military, is trained as a flight surgeon, and serves during World War II.

Randy and Uncle Doc review the charter documents for the Lovelace Foundation, September 1947.

In 1958, the Lovelace Foundation develops an extensive series of rigorous tests designed to judge the fitness of candidates for the NASA Space Travel Program. From a group of 33 military pilots, the seven Project Mercury astronauts are selected to be the first Americans in space.

Randy recruited Dr. Clayton "Sam" White, a former Navy flight surgeon, to manage research operations and expand their scope beyond aviation medicine.

Lovelace's Present - into the Future

Uncle Doc and Randy, 1963

Under Sam White's direction the Foundation's research expands into additional fields, including therapy for blast injury to the lung and the health risks of inhaled radioactive particles. These projects were housed in government-owned facilities located on what is now Kirtland Air Force Base.

Arial view of Lovelace Facilities in the 1960's

NASA announces that a crater on the moon is named in honor of William Randolph Lovelace II.

The Lovelace Institutes building.

Left to right: Dr. Bruce B. Boecker, Assistant Director; Dr. Robert K. Jones, Associate Director; Dr. Roger O. McClellan, President and Director of LBERI; and Dr. Charles H. Hobbs, Assistant Director

The Lovelace family legacy lives on in the biomedical research conducted at LRRI today.

1960-1964

President Lyndon Johnson appoints Randy as Director of Space Medicine for NASA.

At the White House on April 21, 1964. Left to right: Mary Christine Sellman, Randy and Mary Lovelace's daughter; Randy; President Lyndon B. Johnson; Mary Lovelace; Dr. John Sellman, son-in-law of Randy and Mary Lovelace.

1965-1968

December 12, 1965, Randy and Mary Lovelace tragically die in a plane crash while returning from Aspen, Colorado. Their loss is especially difficult on the 82-year-old Uncle Doc, already in declining health. He passed away in December of 1968.

Dr. Lovelace, Wife Missing

Albuquerque Doctor Via Aircraft Vanishes From Colorado Town

Clouds, Snow Mar Search for Lovelaces

All on Lovelace Plane Are Found Dead

1970

Dr. Sam White is chosen to succeed Dr. Randy Lovelace as President of the Lovelace Foundation. His large interdisciplinary staff earned worldwide distinction in the field of inhalation toxicology research.

1970s-1980s

Robert W. Rubin, PhD, President and CEO of LRRI

1990s

In 1996, Robert W. Rubin, PhD, becomes President and CEO. The Institute redefines its mission to find causes and cures of respiratory disease, becomes a private, nonprofit organization, and changes its name to Lovelace Respiratory Research Institute (LRRI). In 1997 LRRI celebrates its 50th anniversary as a research organization.

2000s and Beyond

Today, LRRI addresses challenging national problems in the fields of basic lung biology as well as treatment and prevention of lung diseases, identifying the most critical environmental air pollutants, and protecting against chemical and biological threats.