Life Science Caucus Meeting
June 23, 2020
7:30am

Co-chairs:
Senators Newton and Woodard
Representatives White and Reives

Meeting will begin shortly

Agenda

- Welcoming Remarks by Chairs
- Presentation – UNC – Chapel Hill (Timothy Sheahan)
- Presentation – ThermoFisher Scientific, Greenville, NC (Alex Graham)
- Life Science Legislation Update
- Discussion
- Adjourn

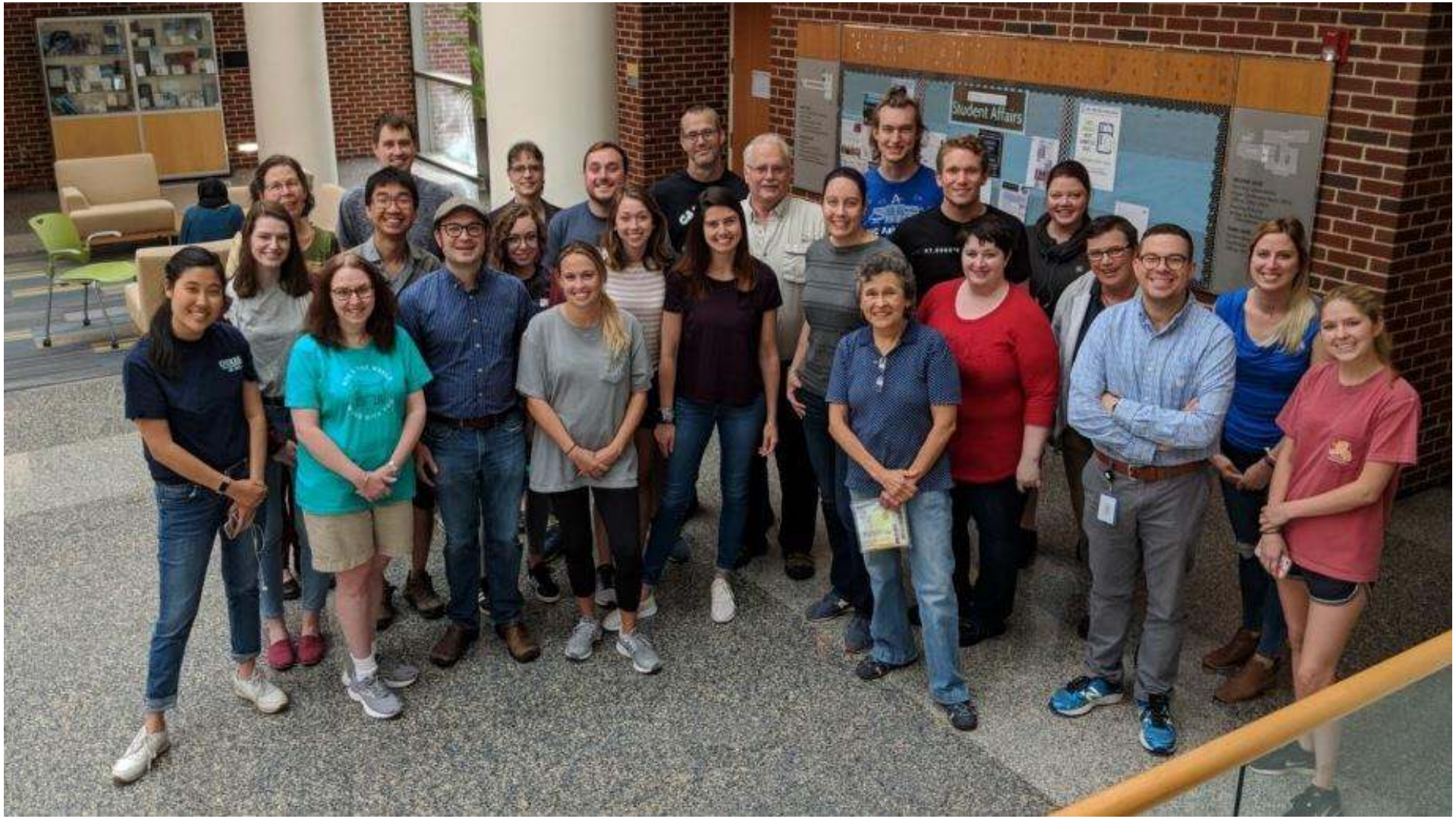
University of North Carolina – Chapel Hill Gillings School of Global Public Health

Timothy Sheahan, Ph.D., is an assistant professor in the Department of Epidemiology at the University of North Carolina. He is an expert virologist whose research is focused on understanding emerging viral diseases and developing new means to stop them. After pursuing graduate studies on the original SARS Coronavirus with Dr. Ralph Baric at UNC-CH, he left in 2009 for postdoctoral studies at The Rockefeller University working on the hepatitis C virus. After a stint at GlaxoSmithKline, he joined the faculty of the Gillings School in 2015. He is currently engaged in multiple interdisciplinary research projects at UNC to address the immediate public health emergency of Covid-19.

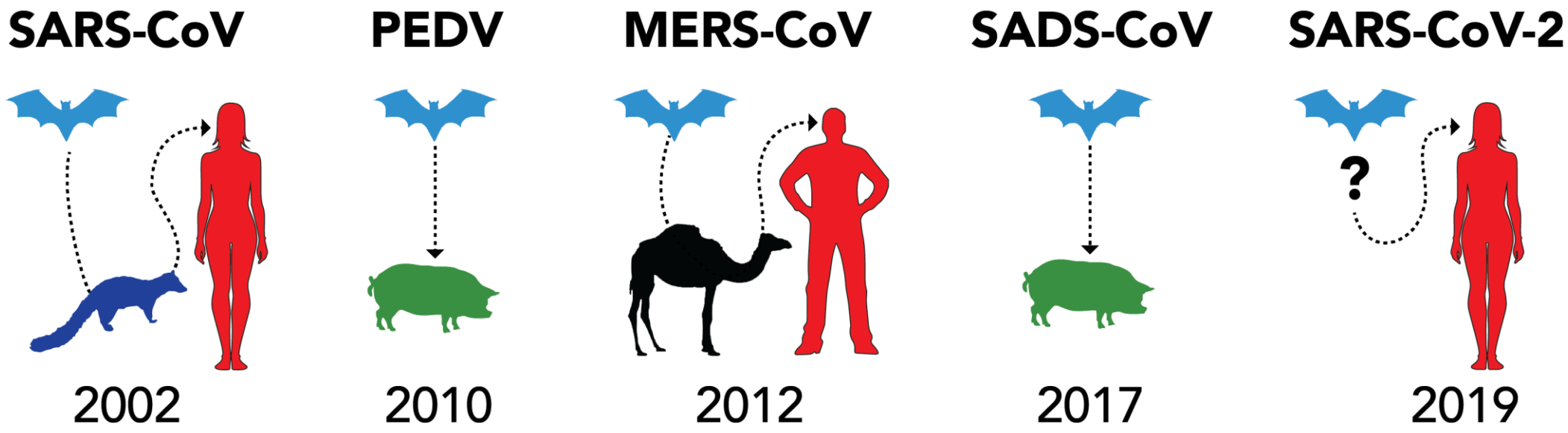
Preparing for tomorrow's pandemics, today

Timothy Sheahan, Ph.D.
@timothysheahan
sheahan@email.unc.edu
Department of Epidemiology
University of North Carolina at Chapel Hill
May 24, 2017

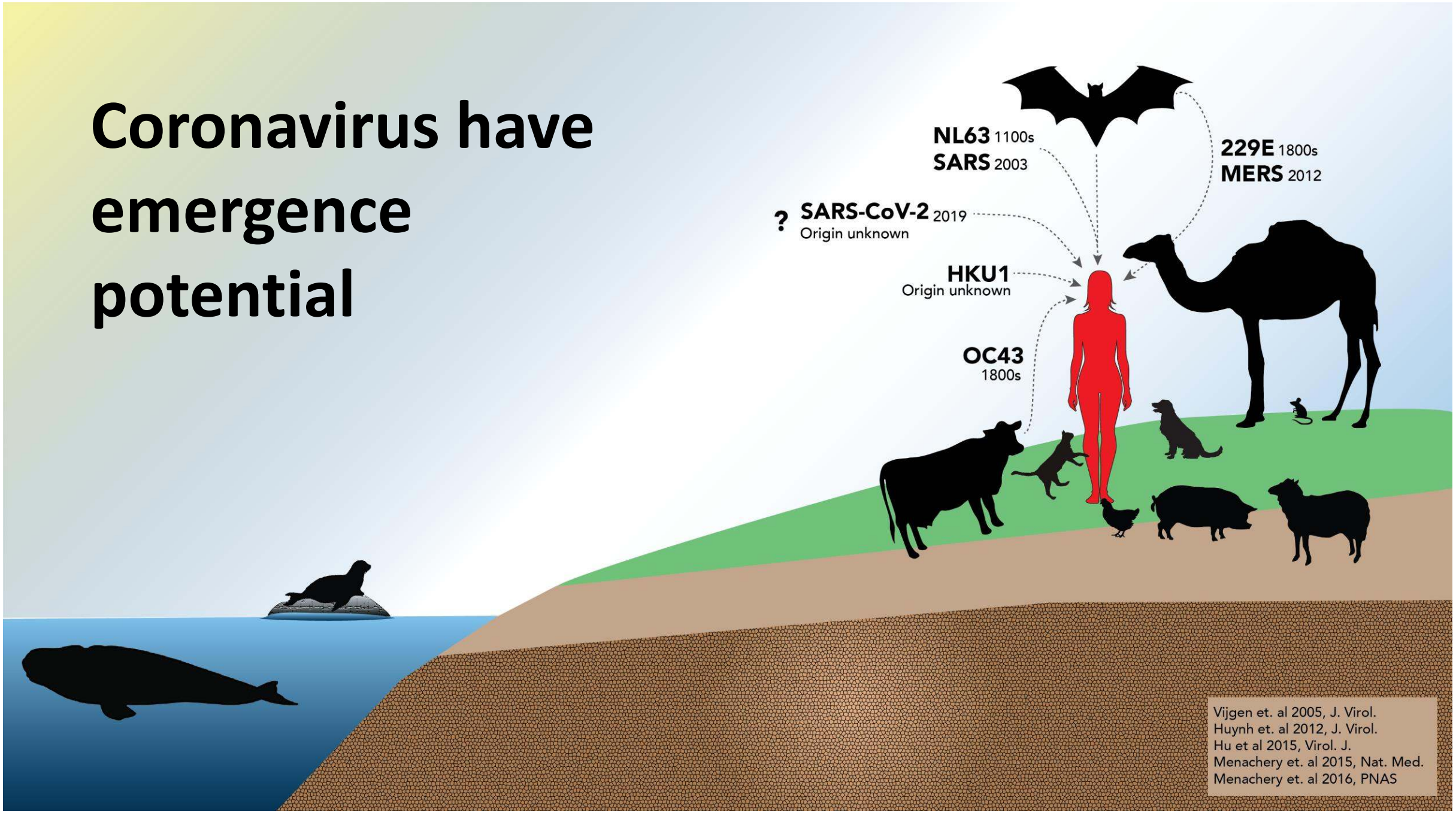
Emerging virus research at Gillings



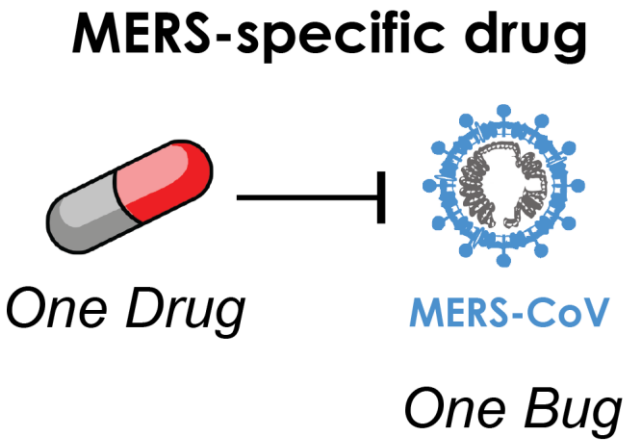
The need for coronavirus therapeutics



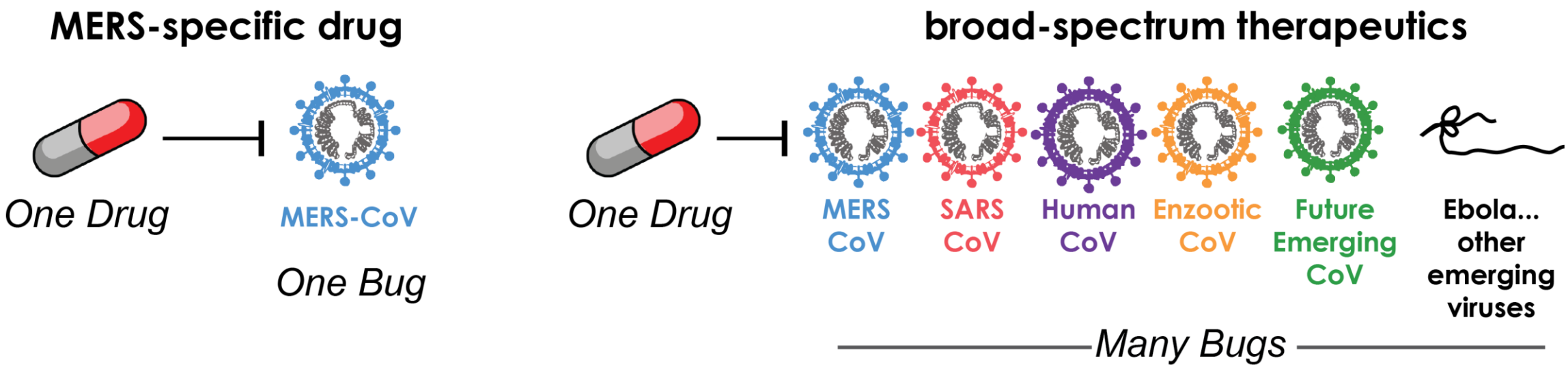
Coronavirus have emergence potential



Why broad-spectrum therapeutics?

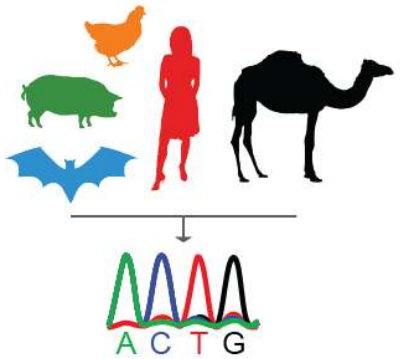


Why broad-spectrum therapeutics?

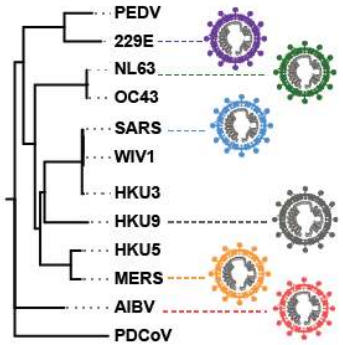


Addressing therapeutic efficacy and breadth

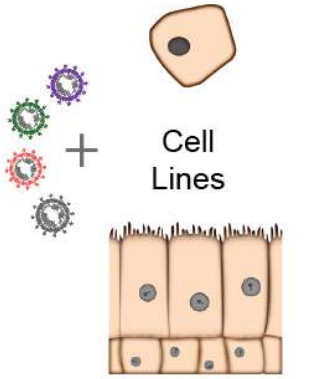
Discovery



Virus reconstruction



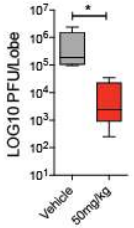
In vitro



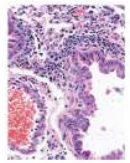
Human Primary
Cell Cultures

In vivo

Prophylactic *Rx* or
Therapeutic *Rx*



Virus growth

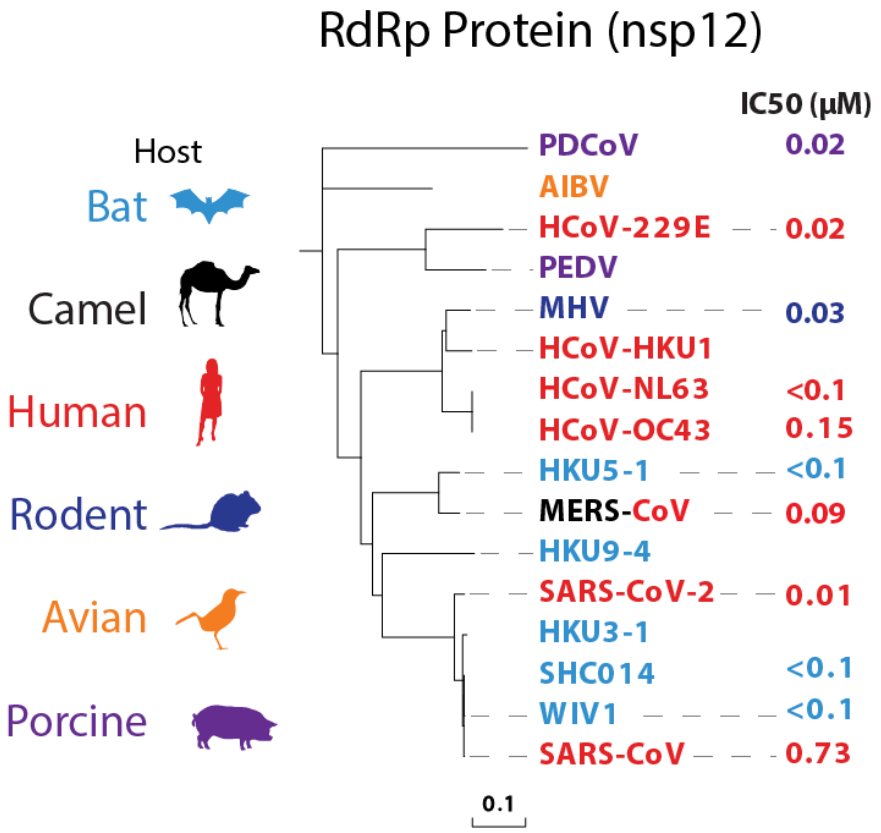


Tissue Pathology

Physiological measures of disease

Safety first: Working at biosafety level 3 (BLS3)

Remdesivir is a broad-spectrum drug for CoV



- An intravenous drug.
- RDV is effective against many CoV in cell culture and in mouse models.
- Our preclinical data positioned RDV for rapid deployment in humans.
- Administered in humans by compassionate use.
- Clinical trials for both severe and moderate COVID-19 in China, USA and elsewhere.

Sheahan et al. Science Translational Medicine 2017
Agostini et al. Journal of Virology 2018
Brown et al. Antiviral Research 2019
Sheahan et al. Nature Communications 2020
Pruijssers et al. In Review 2020

EIDD-2801 is a broad-spectrum drug for CoV

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CORONAVIRUS

An orally bioavailable broad-spectrum antiviral inhibits SARS-CoV-2 in human airway epithelial cell cultures and multiple coronaviruses in mice

Timothy P. Sheahan[1]*†, Amy C. Sims[1]*‡, Shuntai Zhou[2], Rachel L. Graham[1], Andrea J. Pruijssers[3], Maria L. Agostini[3], Sarah R. Leist[1], Alexandra Schäfer[1], Kenneth H. Dinnon III[1,4], Laura J. Stevens[3], James D. Chappell[3], Xiaotao Lu[3], Tia M. Hughes[3], Amelia S. George[3], Collin S. Hill[2], Stephanie A. Montgomery[5], Ariane J. Brown[1], Gregory R. Bluemling[6,7], Michael G. Natchus[6], Manohar Saindane[6], Alexander A. Kolykhalov[6,7], George Painter[6,7,8], Jennifer Harcourt[9], Azaibi Tamin[9], Natalie J. Thornburg[9], Ronald Swanstrom[2,10], Mark R. Denison[3], Ralph S. Baric[1,4†]

Coronaviruses (CoVs) traffic frequently between species resulting in novel disease outbreaks, most recently exemplified by the newly emerged SARS-CoV-2, the causative agent of COVID-19. Here, we show that the ribonucleoside analog β-D-N^4-hydroxycytidine (NHC; EIDD-1931) has broad-spectrum antiviral activity against SARS-CoV-2, MERS-CoV, SARS-CoV, and related zoonotic group 2b or 2c bat-CoVs, as well as increased potency against a CoV bearing resistance mutations to the nucleoside analog inhibitor remdesivir. In mice infected with SARS-CoV or MERS-CoV, both prophylactic and therapeutic administration of EIDD-2801, an orally bioavailable NHC prodrug (β-D-N^4-hydroxycytidine-5′-isopropyl ester), improved pulmonary function and reduced virus titer and body weight loss. Decreased MERS-CoV yields in vitro and in vivo were associated with increased transition mutation frequency in viral, but not host cell RNA, supporting a mechanism of lethal mutagenesis in CoV. The potency of NHC/EIDD-2801 against multiple CoVs and oral bioavailability highlights its potential utility as an effective antiviral against SARS-CoV-2 and other future zoonotic CoVs.

In April: Viewed 150K times, PDF downloaded ~30K times
Highest Altmetric "Attention" score ever for this journal.
2020 Sheahan et al. Science Translational Medicine

- An oral drug nucleoside analog.
- EIDD-2801 is effective against many CoV cell culture and in mouse models.
- Our preclinical data positioned EIDD-2801for rapid deployment in humans.
- Now in Phase 1 safety testing. If suitable, will progress to Phase 2 efficacy testing in COVID-19 patients.

Future Directions and Challenges

Immediate goals

1. Reagent and model development.
2. Evaluation of first line therapeutics. Vaccines, small molecules, antibodies.
3. Cross-pollination research opportunities with School of Medicine and School of Pharmacy.

Problems and challenges

1. Occupational safety during a pandemic.
2. Workforce challenges. Training into the lab takes a year.
3. Lots of interest from industry and academia for testing.
4. Acute need for $$$ and staff. Funding needed to manage clinical studies.
5. Need to be preparing for SARS-CoV-3.

Thanks and Acknowledgements

UNC GILLINGS SCHOOL OF GLOBAL PUBLIC HEALTH

Sheahan Lab
Ariane Brown
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Rachel Graham
Lisa Gralinski
Sarah Leist
Alex Shäfer
Trevor Scobey
Amy Sims

Swanstrom Lab
Ron Swanstrom
Shuntai Zhou
Collin Hill

SCHOOL OF MEDICINE
VANDERBILT UNIVERSITY

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Maria Agostini
Jim Chappell
Andrea Pruijssers

ADC3 Antiviral Drug Discovery and Development Center CETR

Rich Whitley
Maaike Everts
Sarah Davis

SR SOUTHERN RESEARCH

Bob Bostwick
Corinne Augelli-Szafran
Ashish Pathak

EMORY UNIVERSITY Emory Institute of Drug Discovery

George Painter
Michael Natchus
Sasha Kolykhalov
George Bluemling

NIH National Institute of Allergy and Infectious Diseases

Michael Schaefer
Erik Stemmy

Antiviral Drug Discovery and Development Center (5U19AI109680)

Partnership R01 (Sheahan/Baric PI) (AI132178)

GILEAD

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Daphne Ma
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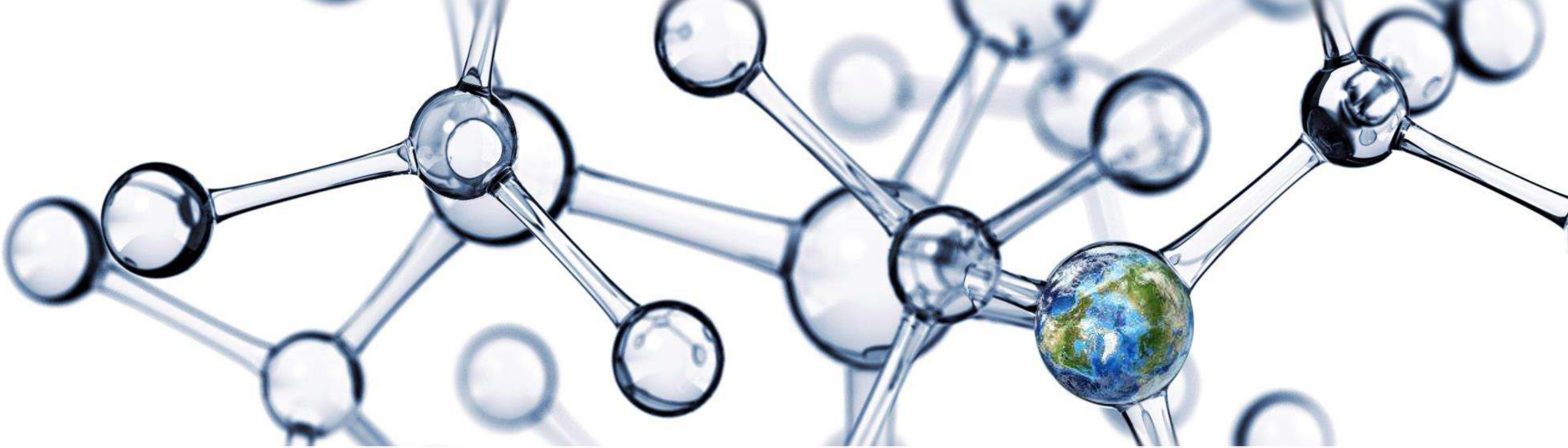
Jamie Spahn
Scott Sellers
Roy Bannister
Yeojin Park
Darius Babusis
Michael Clarke
Richard Mackman
Dustin Siegal

Questions & Answers

ThermoFisher Scientific, Greenville, NC

- **Alex Graham**, is Vice President, Global Sales & Marketing Operations with Thermo Fisher Scientific. He is responsible for leading a team that maximizes the productivity and effectiveness of the Sales and Marketing organization. Includes planning and forecasting, reporting and analysis, process optimization, system selection and configuration, target setting, sales compensation design and implementation, sales training and inside sales. He's been with ThermoFisher since 2012 and had previous sales and financial operations experience. He holds a BA in Psychology from Lyndon State College and an MBA, Finance, from Queens University of Charlotte.



ThermoFisher SCIENTIFIC

Pharma Services

Our Mission and Purpose

We enable our customers to make the world healthier, cleaner and safer

Pharma Services is the Leader in Drug Development, Trial Logistics and Manufacturing

Patheon › ThermoFisher SCIENTIFIC ‹ fisher clinical services

20 billion
solid doses

156 million
sterile doses

representing 75% of all dosage forms

1000+
molecules developed

4,000+
clinical trials supported

50+
large molecule drug substance

200+
small molecule drug substance

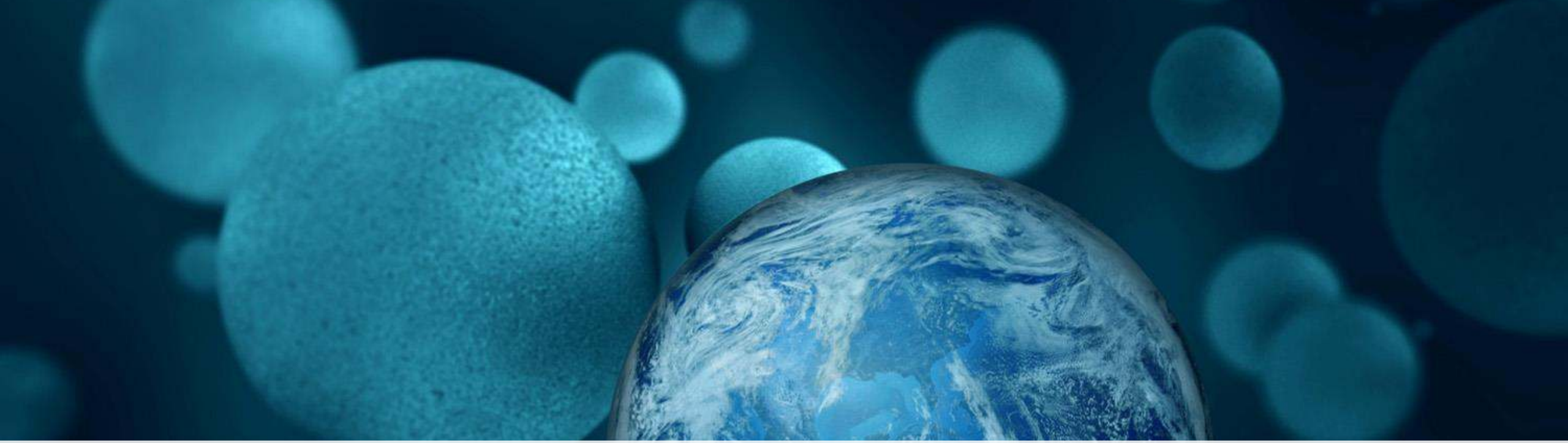
800+
clients

12,000
employees

Flexible business models

Customized to meet your unique needs

ThermoFisher SCIENTIFIC

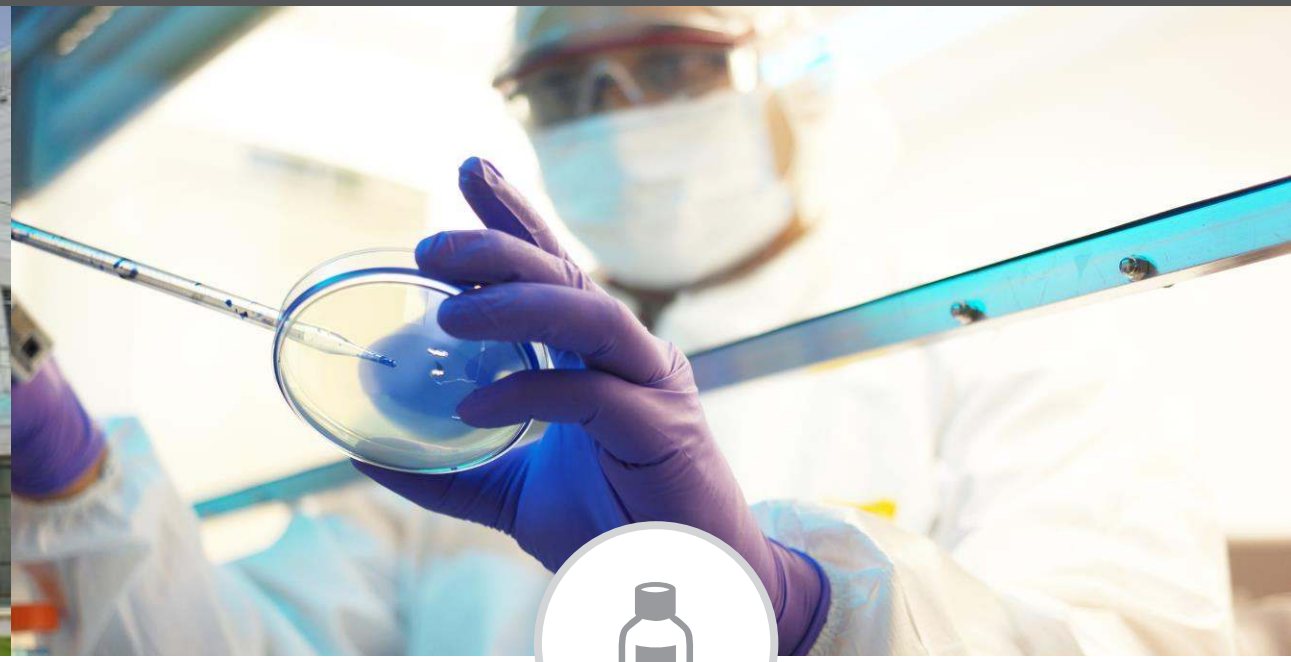


ThermoFisher SCIENTIFIC

Greenville, NC Clinical and Commercial Capabilities Overview

Employees: ~1,500
Total site area: 1.55 million ft^2

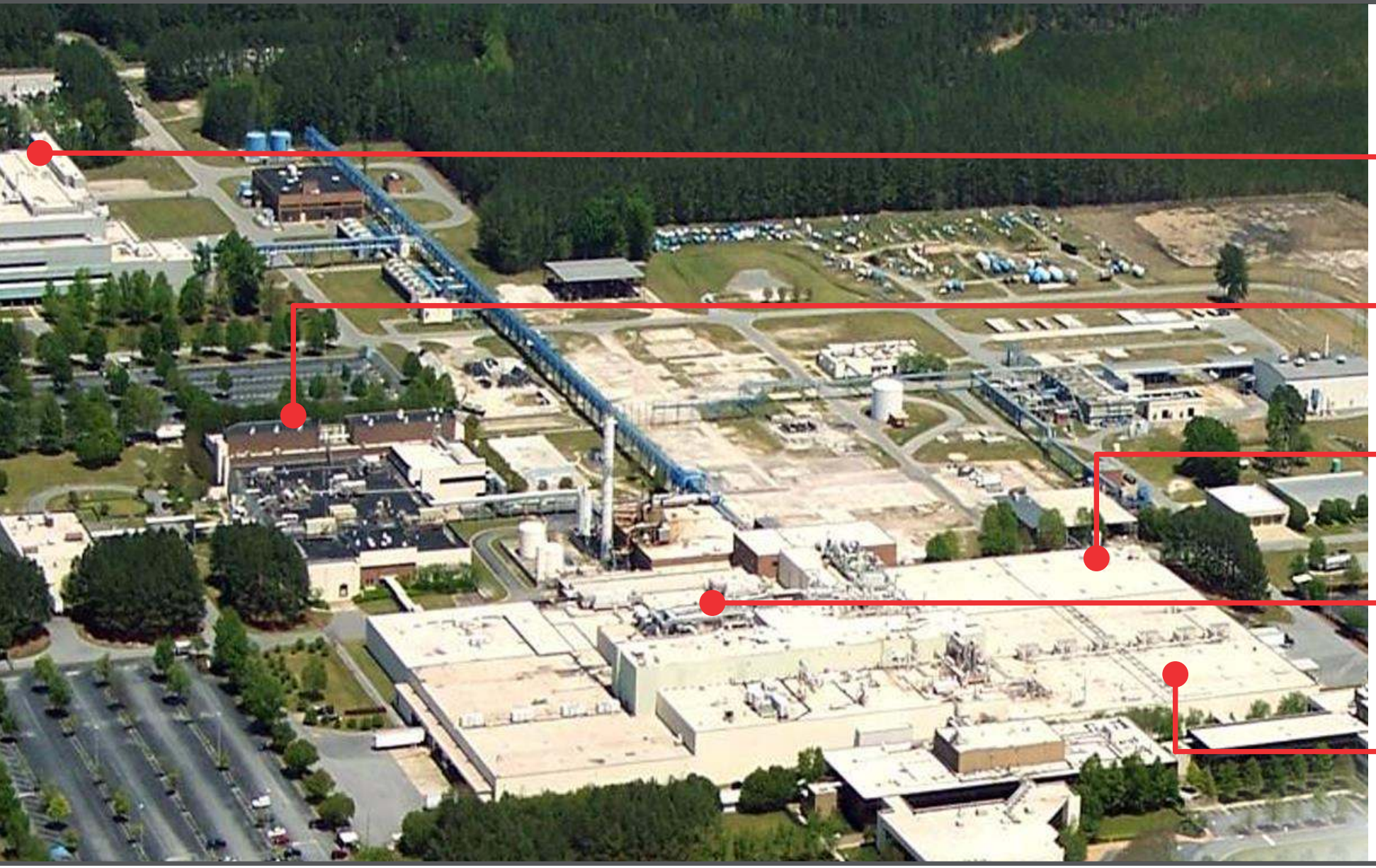
Greenville Overview



Pharma Services Greenville Operations in North Carolina, U.S.A., is a large multipurpose pharmaceutical development, manufacturing, and packaging campus.

The operation provides both development and commercial services for sterile injectables and commercial services for oral solid dose forms.

Clinical and Commercial Operations



- Steriles North
- QA/QC/PDS
- Packaging
- Steriles South
- Commercial OSD

Strategic Growth Initiatives

- Lab of the future
- North American packaging hub
- Pharmaceutical development services
- Prefilled syringe capabilities
- NC State grant incentive
- Continuous manufacturing
- Modernization of facilities

Thermo Fisher Adding $74 Million Upgrades to Biomanufacturing Site in Greenville

A Thermo Fisher plant in Greenville that has become one of North Carolina's largest pharmaceutical manufacturers, is getting another $74 million upgrade to support the growing global demand for biomanufacturing services and biologics products.

The expansion of the Eastern North Carolina factory's prefilled syringe (PFS) and vial-filling lines is part of a $150 million investment in three global fill & finish plants that also includes two in Italy. The company says the expansions will especially support demand for sterile liquid and lyophilized product development and manufacturing.

The Thermo Fisher Scientific Greenville, NC site
-- Thermo Fisher photos

Lyophilization, also known as freeze-drying, is a process used for preserving biological material by removing the water from it, first freezing it and then drying it, under a vacuum, at very cold temperatures. Lyophilized materials may be shipped more efficiently and stored much longer than untreated biologicals.

"This continued investment in North Carolina facilities and people is a testament to the value companies such as Thermo Fisher see in our trained workforce and in our global life science leadership"

Questions & Answers

Life Science Legislation Update

Sam Taylor
President, NCBIO

2020 Enacted Legislation

- SL 2020-4 (H1043) $85M in funding for COVID-related research at North Carolina universities
- SL 2020-18 (H315) Reduces cost of nitrogen credits needed to treat biomanufacturing and other wastewater in Neuse River Basin
- SL 2020-26 (H472) $2M Matching funds for participation in National Institute for Innovation in the Manufacture of Biopharmaceuticals (NIIMBL)

2020 Pending Legislation

- S848 (COVID-19 Economic Recovery Grants); grants for investment in tangible property in North Carolina; first-of-its-kind opportunity for emerging NC life science companies
- H1099 (Funds for Ag Tech Cluster); $250,000 to support growth of North Carolina agricultural biotechnology cluster
- H1221 (Funds for NC Central University); $6M to support life science research, education and training programs at NCCU

2020 Pending Legislation, cont.

- S432 (Pharmacy Benefits Manager Licensure) (Conference Committee); Give doctors, pharmacists and patients more control over how prescriptions are filled; give consumers credit against deductibles for discount coupon amounts against cost of brand name medicines without a generic equivalent
- S361 (Healthy NC) (Conference Committee) Establish consistent and transparent process for patients and their doctors to request exceptions from step therapy.

Next Steps

- New products, existing products, and repatriated products will be manufactured where there is an existing workforce
- North Carolina has one of largest life science workforces in the nation; with concentration in area from Research Triangle to Greenville
- North Carolina has established workforce training with capacity to meet new demand
- North Carolina has an opportunity to play an important role in the nation's life science response to COVID-19

Next Steps, cont.

- Provide funding to the NC Biotechnology Center for
  - Loans to companies with COVID-19 related technologies
  - Marketing to US companies seeking to relocate production and supply chain to the United States
- Provide funding for One NC Small Business Fund
  - Grants to match federal SBIR grants for novel life science technologies
- Provide funding for universities and community colleges to
  - Bring manufacturing workforce training on-line
  - Provide hands-on training while observing appropriate COVID-19 mitigation practices

FOR MORE INFORMATION

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(919) 281-8960

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Representatives White and Reives

Meeting adjourned