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IN COLLABORATION WITH
Genetic Engineering & Biotechnology News

VANQUISHING THE VIRUS:
Top 160 COVID-19 DRUG & VACCINE CANDIDATES

TUESDAY, MAY 19, 2020 | 1:00 PM – 2:00 PM
VANQUISHING THE VIRUS:
Top 160 COVID-19 DRUG & VACCINE CANDIDATES

ALEX PHILIPPIDIS
Senior News Editor | Genetic Engineering and Biology News
Launched 1981 by Mary Ann Liebert; 1st publication devoted exclusively to biotech field and remains the key driver in the explosion of the industry

Key reader segments are R&D researchers, lab managers, bioprocess development scientists and executive management - including 65,000 qualified magazine subscribers; 180,000 Newsletter subscribers; 230,000 monthly website visitors

GEN delivers critical, high-quality reporting in Bioprocessing, Cancer, Drug Discovery, OMICs, Translational Medicine, Genome Editing
Wreaking Havoc on the World...

As of May 17, according to Center for Systems Science and Engineering at Johns Hopkins:

**DEATHS:**
- 312,381 worldwide
- 88,836 in the U.S.

**CONFIRMED CASES:**
- 4,667,109 worldwide
- 1,471,674 in the U.S.

*Photo: National Institute of Allergy and Infectious Disease (NIAID):*
A Miracle Cure Is Unlikely

Derek Lowe, In the Pipeline (Science Translational Medicine):

“We're not going to have a silver small-molecule bullet.”

C&EN Webinar, ”Can old drugs take down a new coronavirus? The state of COVID-19 drug repurposing efforts”, May 6, 2020
Industry, Academia Take Aim at COVID-19

As of May 17.... 216 Drugs and Vaccines in Development

Stay up to date with GEN’s new COVID-19 resource! Live online this week!
NYC Builds COVID-19 Candidates

Regeneron Pharmaceuticals

Mount Sinai Innovation Partners

Tonix Pharmaceuticals
Common Categories

- **Antibody**: Bind to a specific antigen in order to destroy it.

- **Antivirals**: Inhibit, but do not destroy target pathogen (SARS-CoV-2).

- **RNA-based**: Messenger RNA (mRNA) strands code for a disease-specific antigen. Once strands are inside the body’s cells, the cells use the genetic information to produce the antigen. Once the antigen appears on the cell surface, it is recognized by the immune system.

- **Vaccines** help the body’s immune system to recognize and fight pathogens that include **viruses such as SARS-CoV-2 (COVID-19)**.
Categorizing COVID-19 Drugs & Vaccines

GEN assigns COVID-19 drugs and vaccines to any of four categories:

- Front Runners
- Definitely Maybes
- Keeping An Eye On...
- Too Soon to Tell
COVID-19 Candidates On the Lead Lap

10 Front Runners To Watch This Year (5 Drugs, 5 Vaccines) ... and Why
Antibody “Cocktail”

- **Regeneron Pharmaceuticals**

- Combination of *neutralizing monoclonal antibodies* leveraging company’s VelocImmune® discovery platform

- **Initial** and **backup** cocktails selected from “thousands and thousands of antibodies”

- **Clinical trials** to start in June; Aiming for “couple of hundred thousand doses” by summer
Hydroxychloroquine & Azithromycin

- HCQ sold as Plaquenil® by Sanofi; AZ sold as Zithromax® (Z-Pak) by Pfizer; numerous generics

- FDA advisory cautions against HCQ and chloroquine use in COVID-19 outside hospital settings or clinical trials.

- 1,446-Patient HCQ study: Largest trial to date shows no reduced, increased risk of death or intubation. Conclusion: More trials needed
Remdesivir

- Gilead Sciences

- Emergency Use Authorization granted by FDA on May 1; Approved in Japan

- Phase III NIAID trial: 1,063 participants with mix of symptoms. Median time to recovery of 11 days, vs. 15 for placebo: “Very important proof of concept,” says Fauci, despite change in endpoint.

- Phase III Chinese trial: 158 severe COVID-19 patients treated. No clinical improvement shown.
Also Worth Watching...

- **Avigan (favipiravir)**
  - FUJIFILM Toyama Chemical
  - Approved in Japan for influenza; PM Abe to stockpile 2 million treatment courses

- **Distributed Bio:**
  - Bioengineers broadly neutralizing antibodies based on its SuperHuman platform
  - CEO Jacob Glanville, PhD, featured in Netflix documentary “Pandemic: How to Prevent an Outbreak”
BNT162

- Pfizer & BioNTech

- Up to $748M collaboration

- Phase I/II trial: 7,600 participants, of which 360 in 1st stage, dose level escalation in U.S.

- 4 versions: Two nucleoside modified mRNA (modRNA) candidates; a uridine containing mRNA (uRNA) candidate; and a candidate using self-amplifying mRNA (saRNA).
ChAdOx1 nCoV-19

- University of Oxford, its spinout Vaccitech, and AstraZeneca

- Based on adenovirus vaccine vector and COVID-19 spike protein.

- Phase I/II trial: Up to 1,100 healthy volunteers.

- £20M pledged by U.K. government to support ChAdOx1 nCoV-19 development.
mRNA-1273

- Moderna

- Up to $483M committed by BARDA

- Lipid nanoparticle (LNP)-encapsulated mRNA vaccine encoding for a prefusion stabilized form of the Spike (S) protein.

- Positive Phase I interim results reported May 18: All 45 participants produce antibodies by day 15 after treatment.
Also Worth Watching...

- **Novavax’s NVX-CoV2373**
  - Up to $388M from CEPI toward clinical trials, large-scale manufacturing
  - **Phase I/II trial** planned: 131-patient Phase I portion set to start this month; topline results expected in July

- **CanSino Biologics’ Ad5-nCoV**
  - China’s most advanced vaccine candidate; Partnered with *Academy of Military Medical Sciences, Institute of Biotechnology*
Looking Ahead: What Can We Anticipate...

- **SPEED** — Timeframes for developing new drugs and vaccines will continue to shorten, as companies chase market opportunity and apply new technologies while regulators eager for therapeutic solutions accommodate them.

- **ACCESS** — Slow global rollout of therapeutics as stakeholders navigate pricing, and nations extract promises to receive first doses of new drugs and vaccines whose development they fund (UK will get Oxford U. vaccine first; China, its own developers’ vaccines; the U.S., Sanofi’s vaccine).

- **R&D REVIVAL** — As COVID-19 leaders (Gilead, Regeneron) applied R&D from Ebola therapeutics, other developers look to SARS-CoV-3, 4, etc.
Thanks for listening. Let’s stay in touch!

• Alex Philippidis
  • Email: aphilippidis@liebertpub.com
  • Twitter: @AlexWestchester
  • Phone: (914) 740-2245

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DAVID WEINREICH
Senior Vice President, Head, Global Clinical Development | Regeneron Pharmaceuticals Inc.
LEVERAGING REGENERON’S PROPRIETARY TECHNOLOGIES AND EXPERTISE TO RESPOND TO THE COVID-19 THREAT

- Over the past 3 decades of investment, Regeneron has built a suite of proprietary technologies for drug discovery, development, and manufacturing that can be leveraged to rapidly respond to emerging threats.

- Regeneron’s end-to-end capabilities and Velocisuite technologies have generated 7 FDA-approved medicines.

- The repeatable and reproducible approach has changed the timelines from years to months, including in infectious disease outbreaks with MERS-CoV, Ebolavirus, and now with SARS-CoV-2.
VELOCISUITE ENABLES RAPID DEPLOYMENT OF INFECTIOUS DISEASE THERAPIES

VeloclImmune® REGENERON’s unique technology for producing fully human monoclonal antibodies.

VelociMab® REGENERON’s rapid isolation of therapeutic antibodies and generation of production cell lines

VELOCIGENE®

VELOCIMOUSE®

VELOCIMMUNE®

VELOCIMAB®

VelociT™

VELOCIHUM™

VELOCI-Bi™

VELOCIMMUNE®

VELOCIMAB®

Immunization

24 days

Ab Isolation

34 days

Cell line Generation

18 days

Speed to clinic

- Unprecedented speed from immunization to GMP production cell lines
- Final molecules chosen from more than 1000 antibodies
- “All hands on deck” effort across multiple departments
RAPID RESPONSE TECHNOLOGIES FOR GLOBAL GOOD

MERS-CoV
- Identification and validation of Spike-protein blocking antibodies
- Phase 1 study completed

EBOLA VIRUS (REGN-EB3)
- Prevented death in major randomized controlled trial in the DRC
- BLA submitted

SARS-CoV-2
- Identifying potent, fully human monoclonal antibodies
- Preclinical activities and manufacturing scale-up being expedited

Discovery and preclinical validation has been compressed to **3-6 months** vs. years in a typical process

Simplification of handoff reduces clinical manufacturing timeframe to **less than 6 months**

OUTBREAK
- Isolation of fully human monoclonal antibodies

CLINICAL TRIALS
- Manufacture of clinical-grade antibodies for human use
Using VelociSuite technologies, discovery and preclinical validation has been compressed to 3-6 MONTHS vs. years with a standard process.

**OUTBREAK**
- Isolation of fully human antibodies (no need for human survivor samples)
- Creation of and preclinical testing in genetically-humanized mice
- Creation of manufacturing-ready cell lines (18 days vs. 6-9 months)

**CLINICAL TRIALS**
- Manufacture of clinical-grade antibodies for human use

Simplification of handoff reduces clinical manufacturing to LESS THAN 6 MONTHS

**APPLIED TO DATE:**

**EBOLA**
- In WHO-run clinical trial, REGN-EB3 was dramatically superior at preventing Ebola deaths vs. ZMapp control
- Under FDA review; Orphan Drug & Breakthrough Therapy Designation

**MERS**
- ID and validation of REGN3048-3051 spike-protein blocking antibodies against MERS coronavirus
- Phase 1 clinical testing completed
- Collaboration with BARDA and coronavirus experts at UMD

**SARS-COV-2 & OTHER PATHOGENS**
- Ongoing collaboration with BARDA to discover and develop antibody therapies for various infectious diseases
- Includes influenza and novel coronavirus, SARS-CoV-2
MOVING RAPIDLY WITH SARS-COV-2/COVID-19 RESPONSE

ANTICIPATED TIMELINE OF REGENERON DRUG DISCOVERY, DEVELOPMENT & MANUFACTURING EFFORTS:

**Jan:** Began coronavirus discovery program, building on success with related coronaviruses & diseases

**March:** Screening for most potent antibody candidates for prophylactic and therapeutic medicine

**Early summer:** Small quantities available for initial clinical trials

**Late summer:** Goal is for hundreds of thousands of doses for human testing; prophylaxis and treatment

**Feb:** Expanded collaboration with U.S. Health and Human Services to develop novel coronavirus antibodies

**April onward:** Manufacturing scale-up of selected antibody therapy; animal testing

**March:** Initiated Phase 2/3 trial of Kevzara® (sarilumab) in severe COVID-19 patients

JAN  FEB  MAR  SPRING/SUMMER  LATE SUMMER

All timelines are estimated and subject to vary depending on many scientific and technical factors. The use of Kevzara to treat the symptoms of COVID-19 is investigational and has not been fully evaluated by any regulatory authority.
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VANQUISHING THE VIRUS:
Top 160 COVID-19 DRUG & VACCINE CANDIDATES

SETH LEDERMAN, MD
Co-Founder, CEO & Chairman | Tonix Pharmaceuticals
Cautionary Note on Forward-Looking Statements

Certain statements in this presentation regarding strategic plans, expectations and objectives for future operations or results are “forward-looking statements” as defined by the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as “anticipate,” “believe,” “forecast,” “estimate” and “intend,” among others. These forward-looking statements are based on Tonix’s current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to failure to obtain U.S. Food and Drug Administration clearances or approvals and noncompliance with its regulations; our need for additional financing; delays and uncertainties caused by the global COVID-19 pandemic; substantial competition; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. The forward-looking statements in this presentation are made as of the date of this presentation, even if subsequently made available by Tonix on its website or otherwise. Tonix does not undertake an obligation to update or revise any forward-looking statement, except as required by law. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2019, as filed with the Securities and Exchange Commission (the “SEC”) on March 24, 2020, and periodic reports and current reports filed with the SEC on or after the date thereof. All of Tonix’s forward-looking statements are expressly qualified by all such risk factors and other cautionary statements.
Potential COVID-19 Vaccine

TNX-1800 (modified horsepox virus)²,³

- Pre-clinical and pre-IND stage
- Live virus vaccine designed on our horsepox vaccine platform⁴ to express the SARS-CoV-2 Spike (S) protein
- Milestones:
  - ⁴th Quarter 2020 – Non-human primate testing results expected⁵

¹COVID-19 = Coronavirus disease 2019
²Collaboration with Southern Research and University of Alberta
³Experimental new biologic, not approved for any indication
⁴TNX-801 is unmodified horsepox virus, which is in development as a vaccine to protect against smallpox and monkeypox
⁵We cannot predict whether the global COVID-19 pandemic will impact the timing of these milestones
Considerations in SARS-CoV-2 Vaccination Strategies: Choice of Antigen

- CoVs are characterized by spike (S) proteins projecting from the virion surface.\(^1\)
- Antibodies generated against S proteins in SARS-CoV provide full protection against infection, though the duration of protection is unclear.\(^2, 3\)

An optimal SARS-CoV-2 vaccine would also induce a potent T cell response to **improve** viral clearance and **promote** long-lived protection.\(^4, 5\)

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TNX-1800 is Based on a Horsepox Virus (HPXV) Vector Designed to Express SARS-CoV-2 S Protein

Horsepox
sHPXV
~200,000 Bp

TNX-1800*
rHPXV/SARS-CoV-2S
~200,000 Bp

*TNX-1800 is at the pre-IND stage of development

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The TH1/TH2 Decision: The Immune System Chooses a Cellular or Humoral Response

- TH1 (cellular) and TH2 (humoral) responses are characterized by unique cytokine patterns.1,2
- The immune response favors TH1 or TH2 immunity, a decision based in part on which cytokines (e.g., IFNs or IL-4) are produced early in the adaptive response.1,2
- Some infections are only well controlled by TH1 T cell-mediated immunity.1,3
- In 20 healthy recovered CoV-2 volunteers, only TH1 T cell-mediated immunity was observed.4


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Advantages of Live, Replicating HPVX as a Vector Platform for Vaccines

- TNX-1800–infected host cells are designed to produce SARS-CoV-2 S protein, activating an immune response against those proteins.
- TNX-1800 is based on a live, replicating vaccine (HPXV) platform, which induces a robust immune response.

HPXV can serve as a platform for general vaccine development:

- Capacity for large and diverse viral DNA inserts
- Vaccines can be rapidly generated and readily manufactured at scale

TNX-1800 Replication Cycle

- TNX-1800 is designed to infect host cells and reprogram them to express SARS-CoV-2 S protein.
- TNX-1800’s HPXV platform uses host cell machinery to produce more virus, which infects more host cells and potentiates the immune response.
TNX-1800 is Designed to Induce Robust T\textsubscript{H}1 Cellular Immunity

Scarification with live replicating orthopoxviruses evokes innate and adaptive immunity, including T\textsubscript{H}1 and strong CD8 T cell responses\textsuperscript{1,2}.

Vaccination by scarification\textsuperscript{1}

\textsuperscript{1}Example of major cutaneous reaction, or "take," resulting from a replication-competent live-virus vaccine delivered via scarification, indicating successful vaccination\textsuperscript{1-3}


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Relationship Between Horsepox, Certain Vaccinia Strains and Variola

Legend: Alignment of orthopoxvirus genomes and location of horsepox (HPXV) genes within telomeres. Orthopoxvirus genomes were aligned using the program GView (https://server.gview.ca). The actual nucleotide sequence of each gene within the genome was compared to the coding sequence (CDS) of each gene within the horsepox (HPXV) reference genome (NCBI Accession DQ792504) and the following orthopoxvirus genomes (VACV Mulford 1902 - MF477237; VACV Lister - AY678276; VACV ACAM2000 - AY313847; VACV Copenhagen - M35027; VACV IOC-B141 - KT184690; VACV TianTan - KC207810; Rabbitpox virus (RPXV) Utrecht - AY484669; MVA-BN - DQ983258; VACV LC16m8 - AY678275; Variola virus (VARV) (Bangladesh 1975 - L22579). The white gaps in the HPXV reference sequence represent non-coding sequences within the genome. The percent identity (PID) cutoff was set to 85%, meaning that only matches with PID values over 85% are displayed. Abbreviations: BLAST = Basic Local Alignment Search Tool; LITR = left inverted terminal repeat (ITR); RITR= right ITR.
Development of TNX-1800 as a COVID-19 Vaccine

Collaboration with Southern Research
- Southern Research will develop and test TNX-1800, which is designed to express Spike (S) protein from the virus that causes COVID-19, which is called SARS-CoV-2.
- We plan to test whether vaccination of animals with TNX-1800 will elicit an immune response to the S protein from SARS-CoV-2 and if so, whether such an immune response will protect mice and non-human primates against a challenge with SARS-CoV-2 virus.
- We expect to receive data from small animal experiments and from primates in the fourth quarter of 2020\(^1\)

Further Development
- The further development of TNX-1800 for human clinical trials will require manufacturing according to Good Manufacturing Practice, or GMP.
- TNX-1810, TNX-1820 and TNX-1830\(^2\) are in early development as vaccines to elicit almost pure T cell responses vaccines.

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\(^1\)We cannot predict whether the global COVID-19 pandemic will impact the timing of these milestones

\(^2\)TNX-1810, -1820 and -1830 are experimental new biologics, at the pre-IND and pre-clinical stage of development and are not approved for any indication.
Thank you!
Vanquishing the Virus: Top 160 COVID-19 Drug & Vaccine Candidates

Erik Liim, PhD
President | Mount Sinai Innovation Partners
COVID-19 Innovation: Antibody Test

- Anti-SARS-CoV-2 Enzyme Linked Immunosorbent Assay (ELISA) Assay
- Granted FDA Emergency Use Authorization
- Utilizing two antigens: Receptor Binding Domain (RBD) and Full-Length Spike protein
- Measuring titers (levels) of antibodies a person has produced
Distinguishing characteristics the Mount Sinai COVID-19 Antibody Test

- Developed in response to patient needs, and first utilized in Mount Sinai’s convalescent plasma program
- Performed on over 30,000 patient samples
- No proprietary equipment needed
- Potential uses in vaccine and therapeutics
- Developing additional advanced features of the assay
- 100% PPV, 99.6% NPV, 100% specificity, 94% sensitivity