
Consumer and Investment Management Division

SARS-Coronavirus-2 / COVID-19: An Update on Testing, Therapies, Vaccines, and the Healthcare System (Fifth in a Series)

March 20, 2020

Investment Strategy Group

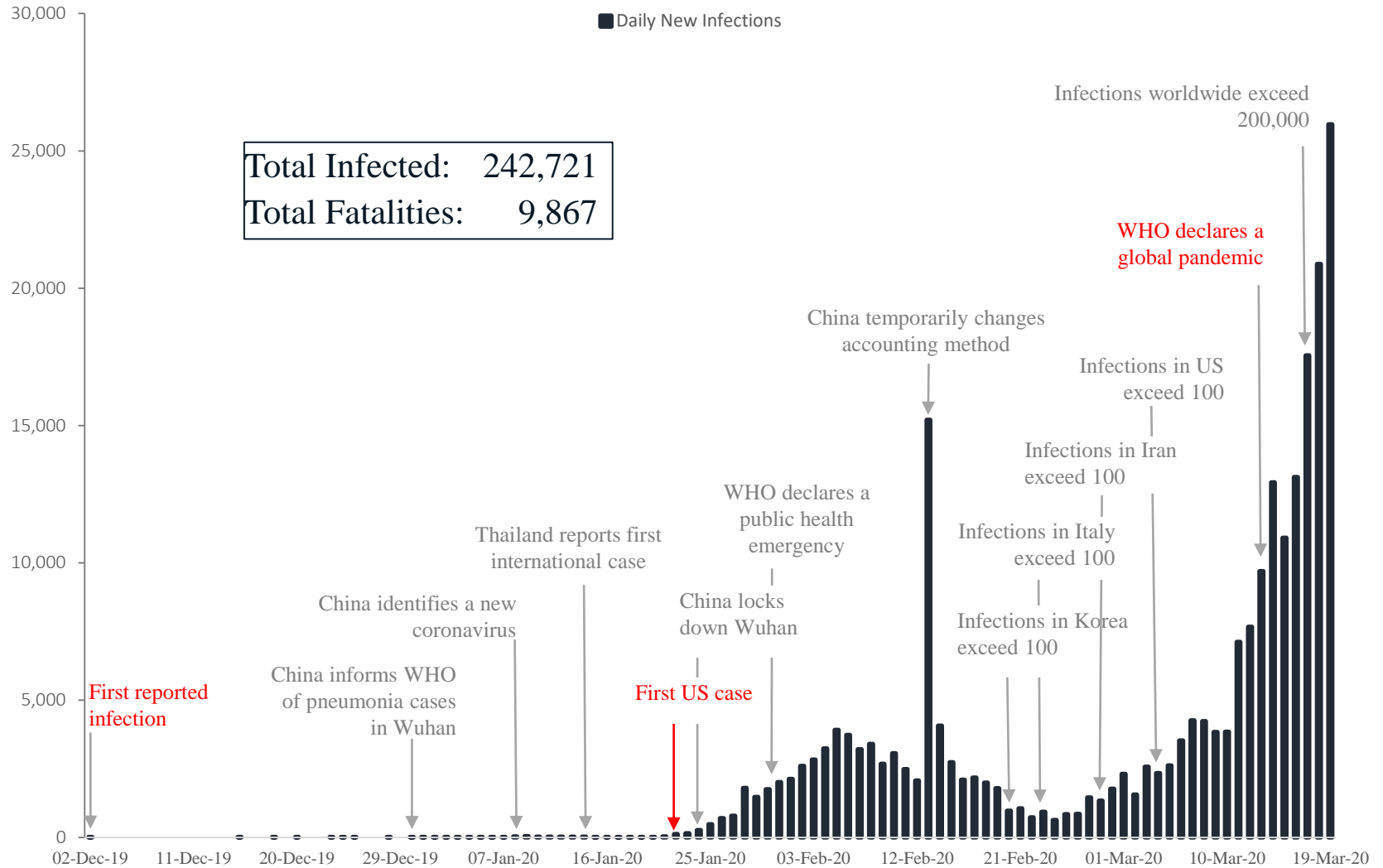
- **Addressing Testing Challenges** Dr. Thomas Schinecker, CEO of Roche Diagnostics
Steve Rusckowski, CEO of Quest Diagnostics
- **Potential Therapeutics** Dr. Leonard Schleifer, MD, CEO of Regeneron
- **Potential Vaccines** Stéphane Bancel, CEO of Moderna
Pablo Tebas, MD, University of Pennsylvania and National
Institute of Health Supported Investigator
- **US Healthcare Preparedness** Peter Slavin, MD, President, Massachusetts General Hospital
- **Outlook and Risks of A Second Wave** Dr. Barry Bloom, T.H. Chan School of Public Health,
Harvard University

Forward-Looking Statements

Today's presentations include forward-looking statements. These statements are not historical facts, but instead represent only the Firms' presenting beliefs regarding future events, many of which, by their nature, are inherently uncertain and outside of the Firms' control. Forward-looking statements include statements about the potential efficacy of diagnostic kits, therapies, vaccines and their potential impact on the global outbreak of a novel strain of coronavirus (COVID-19). Any impact of these measures on the results of the companies presenting or on financial markets or national economies more broadly is uncertain. As at the time of these presentations, the COVID-19 outbreak is resulting in widespread disruption to financial markets and normal patterns of business activity across the world and has led to significant market volatility and accommodative monetary policies by global central banks and companies around the world activating business continuity planning (BCP) strategies to safeguard the well-being of employees, the continued operation of critical functions and the support of clients. The extent of the impact of these measure on the COVID-19 outbreak and on the companies' operational and financial performance, and on the markets and national economies more generally, will depend on future developments including the efficacy of these measures and the duration and continued spread of the outbreak.

The statements in the presentations are current only as of their date, March 20, 2020. For a discussion of some of the risks and important factors that could affect the Firms' future results and financial condition, please refer to their quarterly reports filed on Form 10-Q and their Annual Reports filed on Form 10-K along with their other public reporting, including in particular the "Risk Factors" included therein.

SARS-CoV-2 Pandemic Timeline

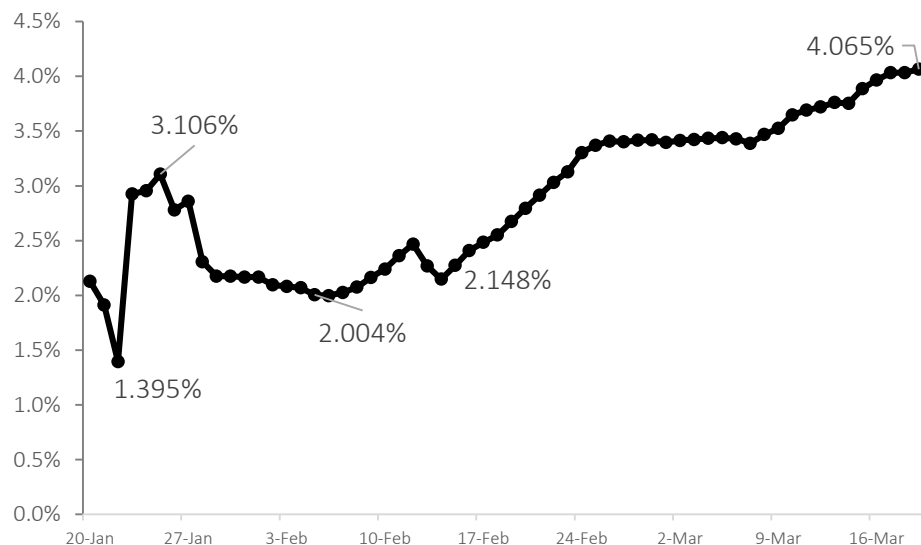


* As of March 19, 2020

Source: Investment Strategy Group, WHO, CDC, National Health Commission of People's Republic of China, John Hopkins University.

The Estimated Case Fatality Rate has Increased Since the Initial Days of the Outbreak, but Varies Considerably by Location and Age

1. Estimated Case Fatality Rate for SARS-CoV-2 Over Time (%)



2. Case Fatality Rate by Location

Location	Infected	Fatalities	CFR
Worldwide	242,721	9,867	4.07%
Worldwide (ex mainland China)	161,793	6,622	4.09%
Wuhan	50,005	2,496	4.99%
Hubei	67,800	3,130	4.62%
Hubei (ex Wuhan)	17,795	634	3.56%
China (mainland)	80,928	3,245	4.01%
China (mainland, ex Hubei)	13,128	115	0.88%
Italy	41,035	3,405	8.30%
South Korea	8,565	91	1.06%
Iran	18,407	1,284	6.98%
United States	13,560	159	1.17%

- The estimated case fatality rate of SARS-CoV-2 has increased steadily, reaching 4.07% based on current data, but continues to remain significantly lower than for SARS (10%) or MERS (34%). As the outbreak evolves, the fatality rate is likely to fluctuate.
- In mainland China, the highest case fatality rate has been recorded in the city of Wuhan (4.99%). Internationally, some of the countries with the highest fatality rates, based on current data, are Italy (8.30%) and Iran (6.98%).
- Fatality rate is generally higher among older adults, among males, and those with pre-existing conditions (cardiovascular disease, diabetes, and chronic respiratory disease).

Testing Challenges

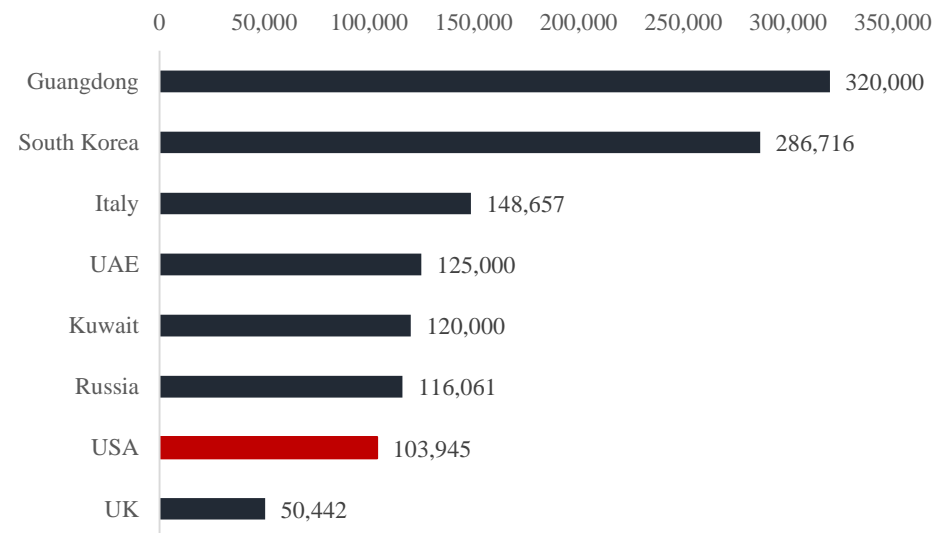
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The system... is not really geared to what we need right now... That is a failing... The idea of anybody getting it easily the way people in other countries are doing it, we are not set up for that. Do I think we should be? Yes, but we are not.

Dr. Anthony Fauci
Director, National Institute of Allergy and Infectious Diseases
Testimony before US Congress
12 March 2020

1. Working through the Testing Challenges

- Challenge 1 – CDC was the only entity that initially could confirm infections
- Challenge 2 – Inconclusive results due to reagent performance
- Challenge 3 – Restrictive testing guidelines by CDC
- Challenge 4 – Restrictive FDA regulations
- Challenge 5 – Availability of lab materials

2. Number of Tests Performed



Data for Guangdong is from 26 Feb; for UAE from 16 Mar; for US from 19 Mar, for all others 17 Mar

Addressing Testing Challenges: Roche Diagnostics

- On March 12, the Food and Drug Administration authorized emergency use of the cobas SARS-CoV-2 test.
- On March 13, Roche began shipping the initial 400,000 test kits, expected to be completed this week.
- 900,000 tests manufactured per week. Roche plans to ship an additional 400,000 tests per week to the laboratory testing sites across the nation that are set up to run the test.
- Roche can support 5 million tests per month. Emergency task force in place to increase production in short-term.



cobas 6800

1,440 results in
24 hours



cobas 8800

4,128 results in
24 hours



MagNA Pure 24



**LightCycler 480
Instrument**

Addressing Testing Challenges: Quest Diagnostics

- On March 9, 2020, Quest Diagnostics introduced a new lab-developed test for COVID-19.
- Quest Diagnostics currently performs its tests at its Infectious Disease laboratory in San Juan Capistrano (CA).
- Quest is bringing up its test in the high-complexity laboratories in Chantilly (VA) and Marlborough (MA) this week.
- Quest expects to significantly expand testing at several regional laboratories by the end of March, located in Dallas; Teterboro (NJ); Miami; Los Angeles; Chicago; Kansas City; Pittsburgh; and Phoenix.
- Quest expects to have capacity to perform approximately 10,000 tests a day by the end of the week and approximately 20,000 tests a day by the end of the month.



Potential Therapeutics Pipeline — Milken Institute

Subset of Potential Therapeutical Candidates (as Ordered by Milken Institute)

Count	Treatment	Producer	Current stage of development	Anticipated Timing
1 of 50	Remdesivir	Gilead	Clinical and expanded access	Phase 3 trial results expected April 27th
2 of 50	Scanning anti-viral compounds previously in development	Pfizer	Pre-clinical	Screening completed March, start Phase 1 by end of 2020
3 of 50	TAK-888; Polyclonal hyperimmune globulin	Takeda	Pre-clinical	To patients in 6-18 months
4 of 50	Antibodies from recovered US patient	Lilly/Ab-Cellera	Pre-clinical	Start phase 1 in late July
5 of 50	Antibodies from mice; REGN3048-3051	Regeneron	Pre-clinical	Start phase 1 late summer
6 of 50	Corticosteroids	Peking Union Medical College Hospital	Clinical	Primary study ends April 25, 2020
7 of 50	Kevzara	Regeneron/Sanofi	Clinical	Start phase 2/3 in March/April
8 of 50	Antibody from recovered patients	Celltrion	Pre-clinical	Start phase 1 ~ Sept 2020
9 of 50	ebastine; lopinavir; interferon alpha	Wuhan Red Cross Hospital	Clinical	Primary trial ends March 31, 2020
10 of 50	Recombinant ACE2	The First Affiliated Hospital of Guangzhou Medical University	Clinical	Primary trial ends April 1, 2020
11 of 50	Washed microbiota transplantation	The Second Hospital of Nanjing Medical University	Clinical	Primary trial ends April 2, 2020
12 of 50	PD-1 blocking antibody; Thymosin	Southeast University, China	Clinical	Phase 2 primary trial end April 30, 2020
13 of 50	APN01	University of British Columbia/Apeiron Biologics	Clinical	In Phase 1 pilot in China

Therapeutics: Regeneron



Kevzara Clinical Trial

- On March 16, 2020, Regeneron and Sanofi announced the initiation of phase 2/3 trial, with immediate enrollment of patients.
- Regeneron is leading U.S. trials, Sanofi will lead upcoming ex-U.S. trials.
- Kevzara is a fully-human monoclonal antibody that inhibits the interleukin-6 (IL-6) pathway by binding and blocking the IL-6 receptor.
- The U.S.-based trial will begin at medical centers in New York, one of the epicenters of the U.S. COVID-19 outbreak, and will assess the safety and efficacy of adding Kevzara to usual supportive care.



Novel COVID-19 Antibody Program

- On March 17, 2020, Regeneron announced that it had identified hundreds of virus-neutralizing antibodies.
- Regeneron plans to initiate large-scale manufacturing by mid-April with antibody cocktail therapy. Potential to enter human clinical studies by early summer.
- Regeneron scientists have isolated virus-neutralizing, fully human antibodies from the company's VelocImmune mice, which have been genetically-modified to have a human immune system. Regeneron has also isolated antibodies from humans who have recovered from COVID-19.

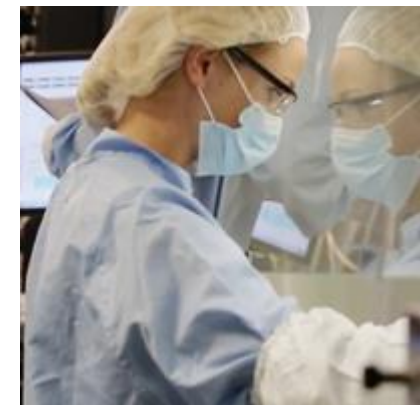
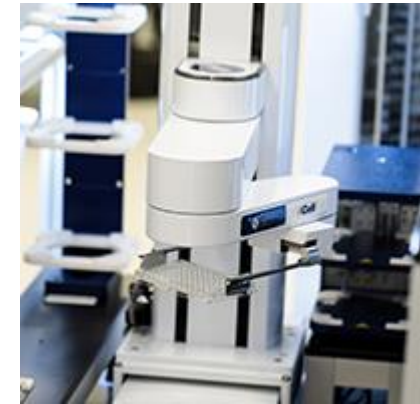
Potential Vaccines Pipeline — Milken Institute

Subset of Potential Vaccine Candidates (as Ordered by Milken Institute)

Count	Vaccine	Producer	Current stage of development	Anticipated Timing
1 of 41	mRNA 1273	Moderna/NIAID	Pre-clinical	Phase 1 started March 2020 at Kaiser Permanente Washington Health Research Institute in Seattle
2 of 41	DNA plasmid; INO-4800	Inovio Pharmaceuticals	Pre-clinical	Start Phase 1 in April
3 of 41	Deoptimized live attenuated virus	Codagenix	Pre-clinical	Animal data in summer 2020
4 of 41	Non replicating viral vector; Ad26	Janssen Pharmaceutical Companies	Pre-clinical	Start phase 1 by end of 2020
5 of 41	Protein subunit; S protein, baculovirus production	Sanofi Pasteur	Pre-clinical	Start phase 1 March 2021
6 of 41	mRNA	Curevac	Pre-clinical	Start phase 1 in a few months
7 of 41	RNA; BNT162	BioNTech/Fosun Pharma	Pre-clinical	Start phase 1 late April

Vaccines: Moderna

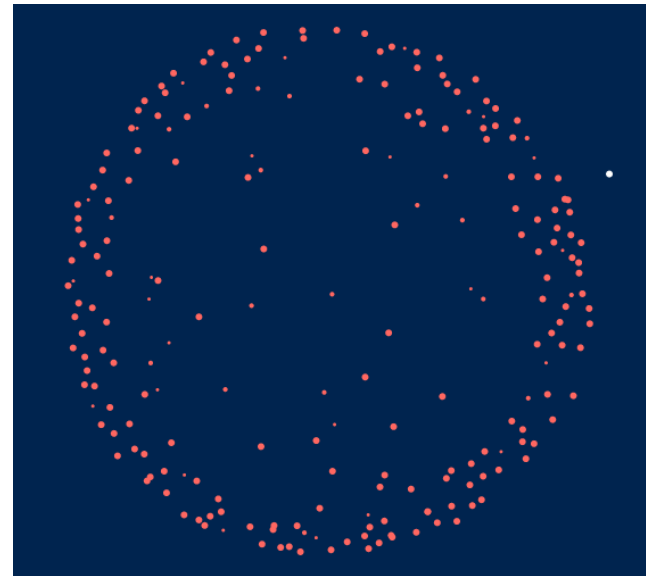
- On March 16, 2020, the National Institute of Health announced that the first participant in its Phase 1 study for Moderna's mRNA-1273 vaccine was dosed, a total of 63 days from sequence selection to first human dosing.
- This Phase 1 study will provide important data on the safety and ability of the mRNA-1273 vaccine to induce an immune response in participants.
- The open-label trial is expected to enroll 45 healthy adult volunteers ages 18 to 55 years over approximately six weeks.



Vaccines: Rapid Response Platform by CEPI

- On February 1, CEPI – the Coalition for Epidemic Preparedness Innovations – invited funding applications for proven vaccine technology that could be used to rapidly develop a vaccine against SARS-CoV-2.
- To date, CEPI has struck partnerships with 8 potential vaccine developers: Institut Pasteur, Curevac, Inovio, Moderna, Novavax, the University of Hong Kong, the University of Oxford, and the University of Queensland.
- In a first step, CEPI will support the preclinical testing, initial manufacture of vaccine materials, and preparatory work for phase 1 studies.

CEPI



The Best Hospitals 2019-20 Honor Roll

These 21 hospitals outperformed all others in U.S. News' Best Hospitals rankings.

By U.S. News Staff July 29, 2019, at 11:45 p.m.

2. Massachusetts General Hospital

Where: Boston

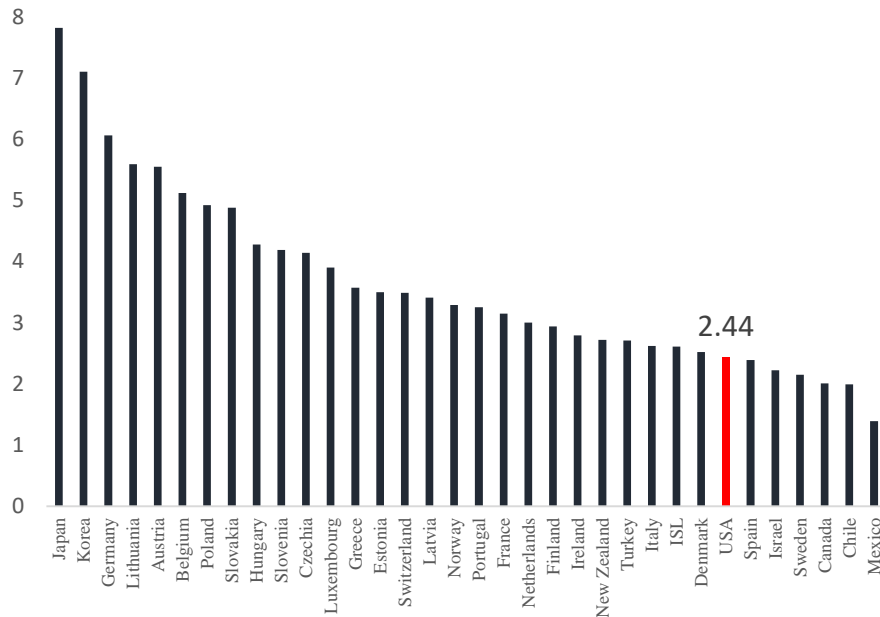
Honor Roll points: 369

Ranked second on the U.S. News Best Hospitals Honor Roll, MGH's specialty rankings include No. 1 in Psychiatry, No. 2 in Diabetes & Endocrinology and No. 2 in Ear, Nose & Throat.

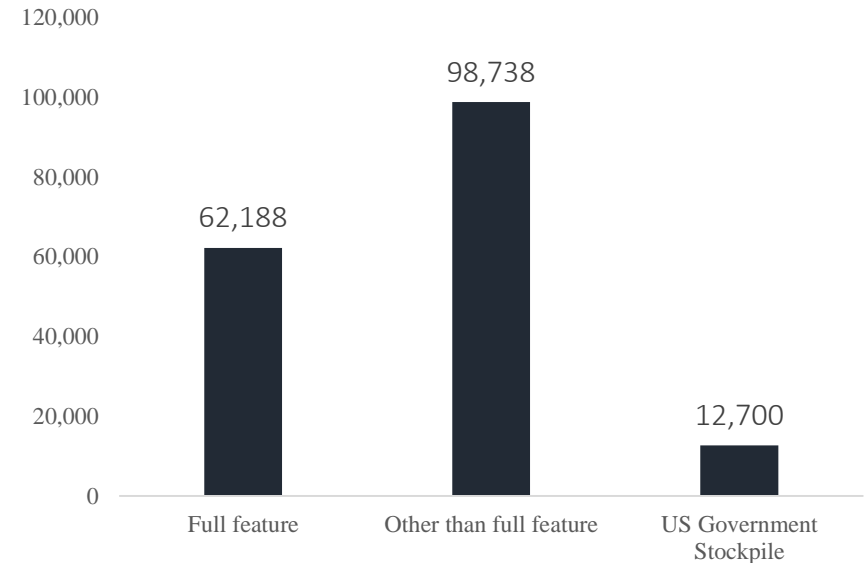


Is the US Healthcare System Prepared?

1. Hospital Beds: Acute Care (per 1,000 inhabitants; 2016)



2. Ventilators (2010 Survey Data; Data on Government Stockpile from 2020)



Note: The median number of full-feature mechanical ventilators per 100,000 population for individual states is 19.7

- According to a comprehensive WHO-China study of 55,924 cases in China (through 20 Feb):
 - 80% of infection cases were mild to moderate (which included non-pneumonia and pneumonia cases);
 - 13.8% were severe (dyspnea, respiratory frequency ≥ 30 /minute, blood oxygen saturation $\leq 93\%$, PaO₂/FiO₂ ratio 50% of the lung field within 24-48 hours); and
 - 6.1% were critical (respiratory failure, septic shock, and/or multiple organ dysfunction/failure).

- About a quarter of severe and critical cases required mechanical ventilation while the remaining 75% required only oxygen supplementation.

Is the US Healthcare System Prepared?

1. Wuhan, China



- Medical workers in protective suits in Wuhan, Hubei Province (China).

2. Kirkland, Washington State



- Kirkland Fire and Rescue ambulance workers at the Life Care Center in Kirkland, near Seattle.

Is the US Healthcare System Prepared?



Testing kits

Protective gear

Protecting Healthcare staff

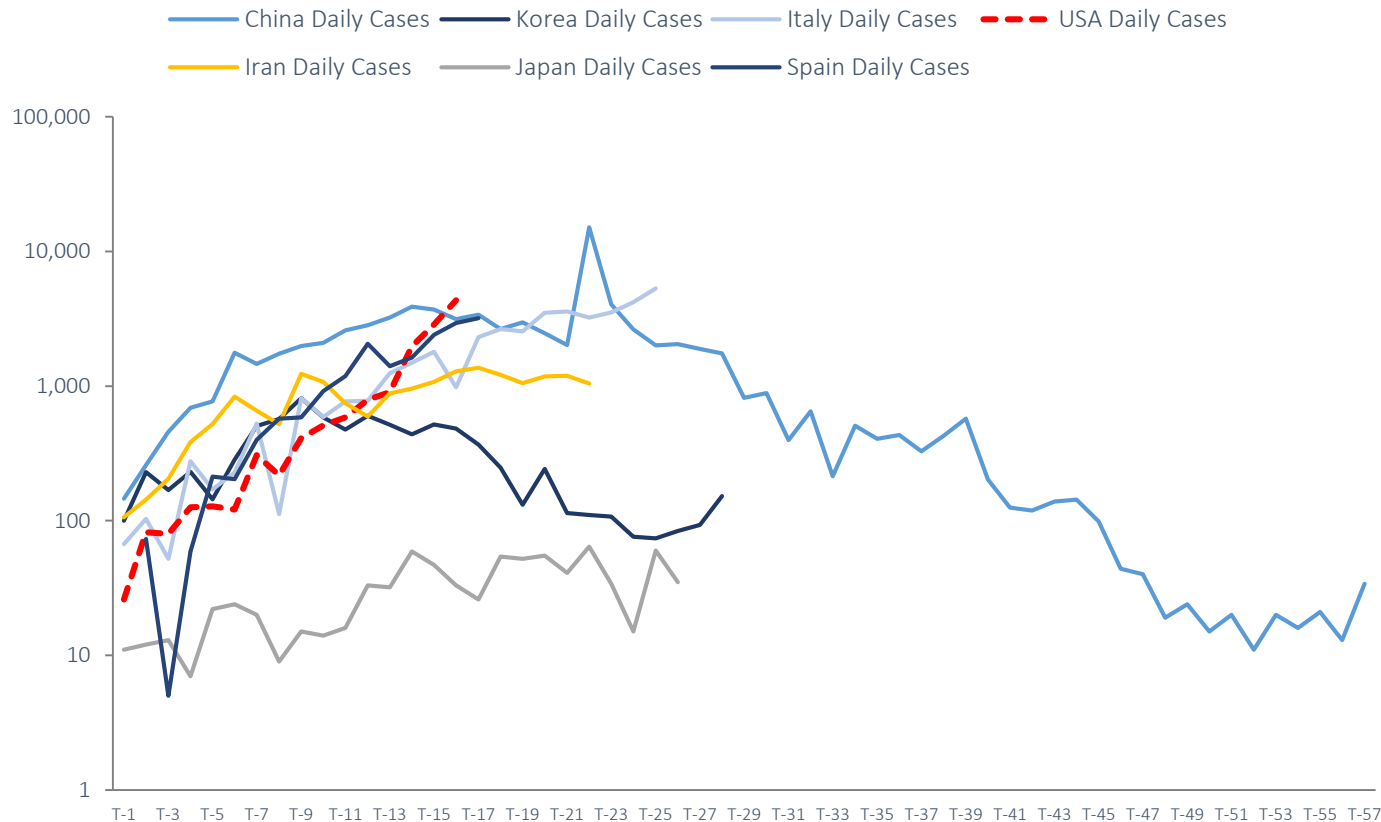
Hospital beds

Respirators/ventilators

Centralized quarantines

What is the Trajectory for the United States?

Number of New COVID-19 Cases by Country (Log Scale; T-1 = Day When Country Reached 100 Cases Cumulative)

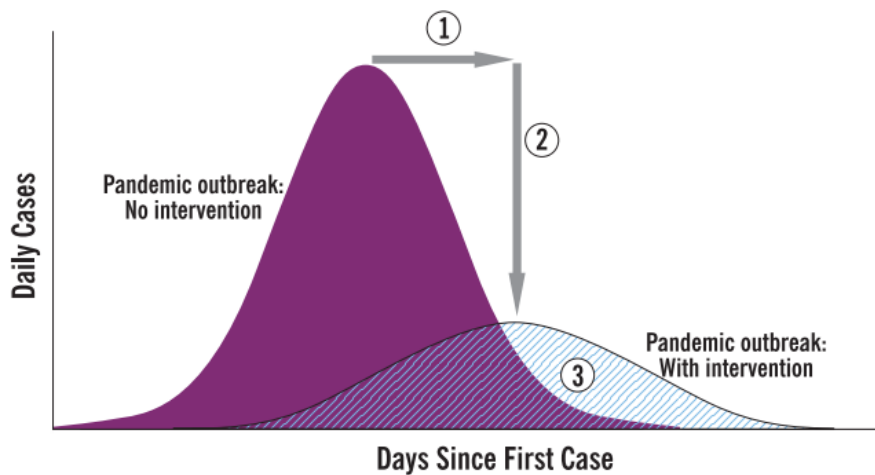


T-1 for mainland China is 23 January when the National Health Commission of the People's Republic of China and the World Health Organization started publishing more comprehensive data.

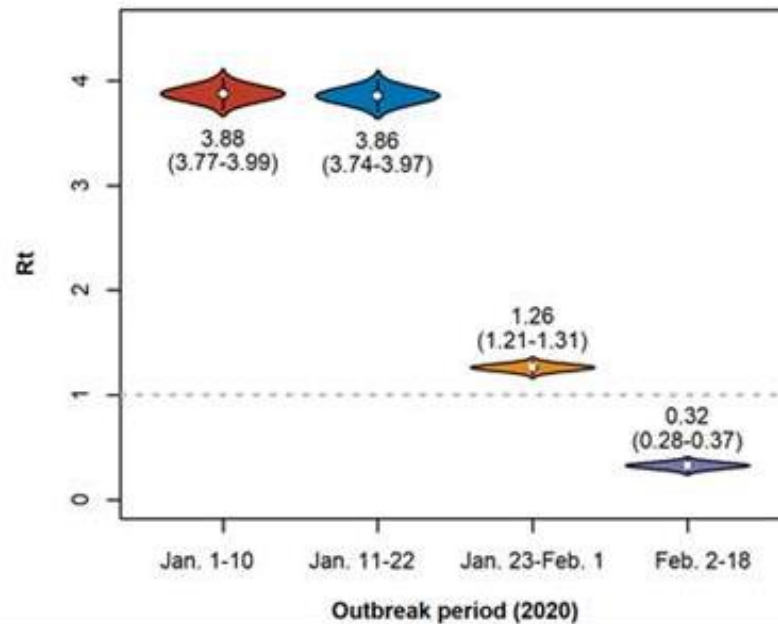
“Flattening the Curve”

1. Goals of Community Mitigation Strategy

- ① Delay outbreak peak
- ② Decompress peak burden on hospitals / infrastructure
- ③ Diminish overall cases and health impacts

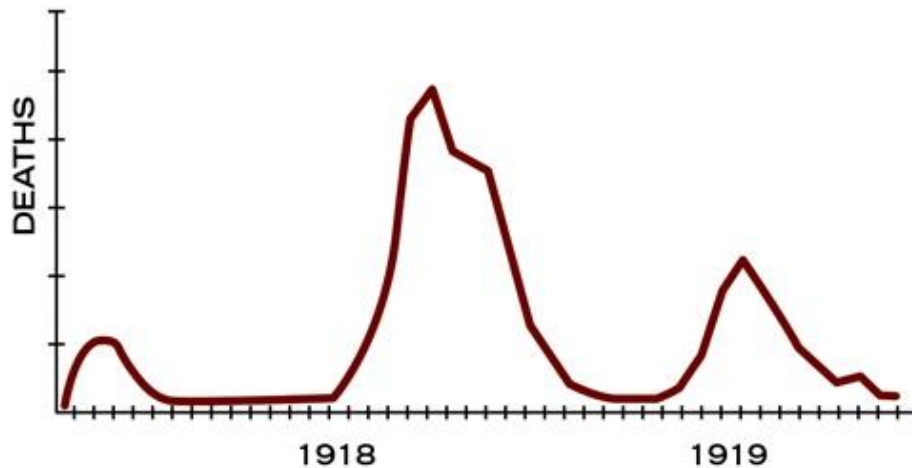


2. COVID-19 in Wuhan: Estimated Reproductive Number Over Time



Another wave?

The 1918 Flu Pandemic (H1N1 Virus) – “Spanish Flu”



- There were 3 different waves of illness during the pandemic, starting in March 1918 and subsiding by summer of 1919.
- The pandemic peaked in the U.S. during the second wave, in the fall of 1918.
- This highly fatal second wave was responsible for most of the U.S. deaths attributed to the pandemic.

Consumer and Investment Management Division

Appendix 1: Potential Therapeutics Pipeline

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Appendix 1: Potential Therapeutics Pipeline (Continued)

1. Remaining potential therapeutical candidates (as ordered by Milken Institute)

Count	Treatment	Producer	Current stage of development	Anticipated Timing
14 of 50	Treatment (scanning compounds to repurpose)	Novartis	Pre-clinical	
15 of 50	Treatment (scanning compounds to repurpose)	Takeda	Pre-clinical	
16 of 50	Treatment (Prezcobix; JNJ)	Chinese hospital testing	Clinical	
17 of 50	Treatment (scanning compounds to repurpose)	Merck	Pre-clinical	
18 of 50	Treatment (antibodies from recovered patients)	Vir Biotech/WuXi Biologics/Biogen	Pre-clinical	
19 of 50	Treatment (hydroxychloroquine), antimalarial	Numerous trials with Chinese research sponsors	Clinical	
20 of 50	Treatment (Truvada)	Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital	Clinical	
21 of 50	Treatment (Jakafi/Jakavi)	Department of Hematology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology	Clinical	
22 of 50	Treatment (PegIntron, Sylatron, IntronA)	Wuhan Jinyintan Hospital (Wuhan Infectious Diseases Hospital)	Clinical	

Appendix 1: Potential Therapeutics Pipeline (Continued)

1. Remaining potential therapeutical candidates (as ordered by Milken Institute)

Count	Treatment	Producer	Current stage of development	Anticipated Timing
23 of 50	Treatment (Xofluza)	The First Hospital Affiliated to Zhejiang University's Medical School	Clinical	
24 of 50	Treatment (Favipiravir or T-705 or Avigan) licensed in Japan for influenza	Numerous trials with Chinese research sponsors	Clinical	
25 of 50	Treatment (Arbidol; umifenovir) licensed in Russia and China for treatment of respiratory viral infections	Numerous trials with Chinese research sponsors	Clinical	
26 of 50	Treatment (Novaferon, Nova) licensed in China for Hep B	The First Affiliated Hospital of Medical College of Zhejiang University	Clinical	
27 of 50	Treatment (Actemra)	First People's Hospital of University of Science and Technology of China	Clinical	
28 of 50	Treatment (Ampligen)	AIM ImmunoTech/National Institute of Infectious Diseases in Japan	Pre-clinical	
29 of 50	Treatment (repurposing antiviral drug candidates)	Materia Medica/Cyclica	Pre-clinical	
30 of 50	Treatment (RNAi - testing 150 RNAis)	Sirnaomics	Pre-clinical	
31 of 50	Treatment (galidesivir)	BioCryst Pharmaceuticals	Pre-clinical	
32 of 50	Treatment (an antiviral)	Toyama Chemical	Clinical	

Appendix 1: Potential Therapeutics Pipeline (Continued)

1. Remaining potential therapeutical candidates (as ordered by Milken Institute)

Count	Treatment	Producer	Current stage of development	Anticipated Timing
33 of 50	Treatment (screening new drugs + library of antiviral compounds)	Enanta Pharmaceuticals	Pre-clinical	
34 of 50	Treatment (anti-corona (COVID-19) IgG from recovered patients)	Kamada	Pre-clinical	
35 of 50	Treatment (Ganovo (danoprevir); ritonavir; interferon)	Numerous trials with Chinese research sponsors	Clinical	
36 of 50	Treatment (mesenchymal stem cells)	Numerous trials with Chinese research sponsors	Clinical	
37 of 50	Treatment (bevacizumab)	Numerous trials with Chinese research sponsors	Clinical	
38 of 50	Treatment (PLX cell product, placenta-based cell therapy)	Pluristem Therapeutics/BIH Ctr for Regenerative Therapy/Berlin Ctr for Advanced Therapies	Pre-clinical	
39 of 50	Treatment (Ryoncil (remestemcel-L), allogenic mesenchymal stem cells)	Mesoblast	Pre-clinical	
40 of 50	Treatment (favilavir)		Approved in China to treat coronavirus	
41 of 50	Treatment (Cerocal (ifenprodil), NP-120)	Algernon Pharmaceuticals	Pre-clinical	

Appendix 1: Potential Therapeutics Pipeline (Continued)

1. Remaining potential therapeutical candidates (as ordered by Milken Institute)

Count	Treatment	Producer	Current stage of development	Anticipated Timing
42 of 50	Treatment (Brilacidin, a defensin mimetic)	Innovation Pharmaceuticals	Pre-clinical	
43 of 50	Treatment (Ieronlimab (PRO 140), a CCR5 antagonist)	CytoDyn	Pre-clinical	
44 of 50	Treatment (BXT-25)	Bioxytran	Pre-clinical	
45 of 50	Treatment (peptides)	CEL-SCI	Pre-clinical	
46 of 50	Treatment (unknown)	Mateon Therapeutics	Pre-clinical	
47 of 50	Treatment (antibodies)	ImmunoPrecise Antibodies	Pre-clinical	
48 of 50	Treatment (screening drug compounds)	Southwest Research Institute	Pre-clinical	
49 of 50	Treatment (unknown)	NanoViricides	Pre-clinical	
50 of 50	Treatment (siRNA candidates)	Vir Biotech/Alnylam Pharmaceuticals	Pre-clinical	

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Appendix 2: Potential Vaccine Pipeline

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Appendix 2: Potential Vaccines Pipeline (Continued)

1. Remaining potential vaccine candidates (as ordered by Milken Institute)

Count	Treatment	Producer	Current stage of development	Anticipated Timing
8 of 41	Vaccine (DNA)	Takis/Applied DNA Sciences/Evvivax	Pre-clinical	
9 of 41	Vaccine (DNA plasmid)	Zydus Cadila	Pre-clinical	
10 of 41	Vaccine (non replicating viral vector; MVA encoded VLP)	GeoVax/BravoVax	Pre-clinical	
11 of 41	Vaccine (non replicating viral vector; ChAdOx1)	University of Oxford	Pre-clinical	
12 of 41	Vaccine (non replicating viral vector; adenovirus based NasoVAX)	Altimmune	Pre-clinical	
13 of 41	Vaccine (non replicating viral vector; Ad5 S (GREVAX™ platform))	Greffex	Pre-clinical	
14 of 41	Vaccine (non replicating viral vector; Oral Vaccine platform)	Vaxart	Pre-clinical	
16 of 41	Vaccine (non replicating viral vector; Viral-vectored)	CanSino Biologics	Pre-clinical	
17 of 41	Vaccine (protein subunit; Drosophila S2 insect cell expression system VLPs)	ExpreS2ion	Pre-clinical	
18 of 41	Vaccine (protein subunit; S protein)	WRAIR/USAMRIID	Pre-clinical	

Appendix 2: Potential Vaccines Pipeline (Continued)

1. Remaining potential vaccine candidates (as ordered by Milken Institute)

Count	Treatment	Producer	Current stage of development	Anticipated Timing
19 of 41	Vaccine (protein subunit; S trimer)	Clover Biopharmaceuticals Inc./GSK	Pre-clinical	
20 of 41	Vaccine (protein subunit; peptide)	Vaxil Bio	Pre-clinical	
21 of 41	Vaccine (protein subunit; Ii-Key peptide)	GenereX/EpiVax	Pre-clinical	
22 of 41	Vaccine (protein subunit; S protein)	EpiVax/Univ. of Georgia	Pre-clinical	
23 of 41	Vaccine (protein subunit; Full length S trimers/nanoparticle + Matrix M)	Novavax	Pre-clinical	
24 of 41	Vaccine (protein subunit; S protein clamp)	University of Queensland/GSK	Pre-clinical	
25 of 41	Vaccine (protein subunit; S1 or RBD protein)	Baylor, New York Blood Center, Fudan University	Pre-clinical	
26 of 41	Vaccine (protein subunit; Subunit protein, plant produced)	iBio/CC-Pharming	Pre-clinical	
27 of 41	Vaccine (replicating viral vector; measles vector)	Zydus Cadila	Pre-clinical	
28 of 41	Vaccine (replicating viral vector; measles vector)	Institute Pasteur	Pre-clinical	
29 of 41	Vaccine (replicating viral vector; horsepox vector; TNX-1800)	Tonix Pharma/Southern Research	Pre-clinical	

Appendix 2: Potential Vaccines Pipeline (Continued)

1. Remaining potential vaccine candidates (as ordered by Milken Institute)

Count	Treatment	Producer	Current stage of development	Anticipated Timing
30 of 41	Vaccine (RNA; mRNA)	China CDC/Tongji University/Stermina	Pre-clinical	
31 of 41	Vaccine (RNA; mRNA)	Arcturus/Duke-NUS	Pre-clinical	
32 of 41	Vaccine (RNA; saRNA)	Imperial College London	Pre-clinical	
33 of 41	Vaccine (unknown)	University of Pittsburgh	Pre-clinical	
34 of 41	Vaccine (unknown)	University of Saskatchewan	Pre-clinical	
35 of 41	Vaccine (unknown)	ImmunoPrecise	Pre-clinical	
36 of 41	Vaccine (modified infectious bronchitis virus vaccine)	MIGAL Galilee Research Institute	Pre-clinical	
37 of 41	Vaccine (unknown)	Doherty Institute	Pre-clinical	
38 of 41	Vaccine (unknown)	Heat Biologics	Pre-clinical	
39 of 41	Vaccine (unknown)	Tulane University	Pre-clinical	
40 of 41	Vaccine (unknown)	ImmunoPrecise Antibodies	Pre-clinical	
41 of 41	Vaccine (unknown)	AJ Vaccines	Pre-clinical	

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The following table provides an example of the effect of management and incentive fees on returns. The magnitude of the difference between gross-of fee and net-of-fee returns will depend on a variety of factors, and the example has been simplified.

Period	Gross Return	Net Return	Differential
1 year	6.17%	4.61%	1.56%
2 years	12.72%	9.43%	3.29%
10 years	81.94%	56.89%	25.05%

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