La Investigación Clínica Farmacológica en COVID-19:
Los retos y oportunidades para México y el mundo.

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Covid-19 Background

❑ COVID-19 is the name of the "novel coronavirus" disease

❑ SARS-CoV-2 is the name of the virus that causes COVID-19

❑ Coronaviruses cause mild respiratory illnesses, such as the common cold

❑ Severe Acute Respiratory Syndrome (SARS)

❑ Middle East Respiratory Syndrome (MERS)

❑ COVID-19 is a new coronavirus disease

❑ Emerged from Hubei Province, China in December 2019

❑ The immediate risk to the general public has become a Global pandemic Since March/2020 until today Nov/30th, 2020

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Global Situation

56,623,643
confirmed cases
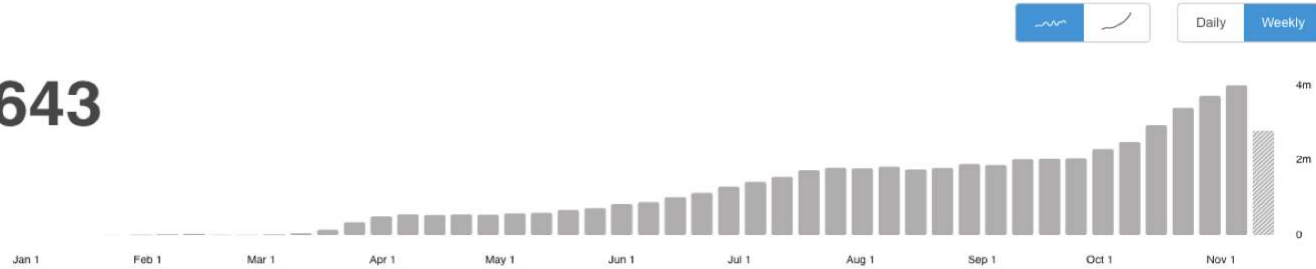
1,355,963
deaths
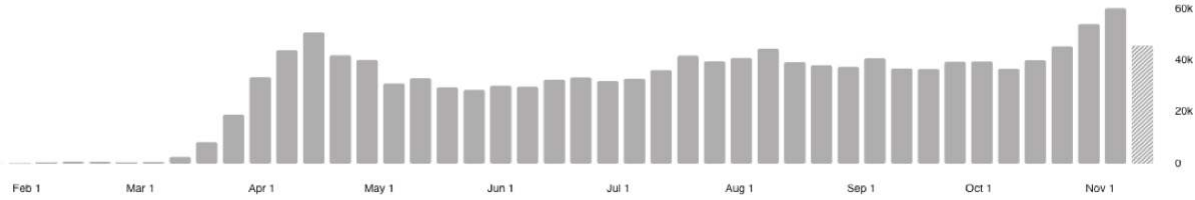
Source: World Health Organization
Data may be incomplete for the current day or week.

Region	Confirmed
Americas	24,035,426 confirmed
Europe	16,353,141 confirmed
South-East Asia	10,254,537 confirmed
Eastern Mediterranean	3,725,280 confirmed
Africa	1,431,795 confirmed
Western Pacific	822,723 confirmed

Source: World Health Organization
Data may be incomplete for the current day or week.
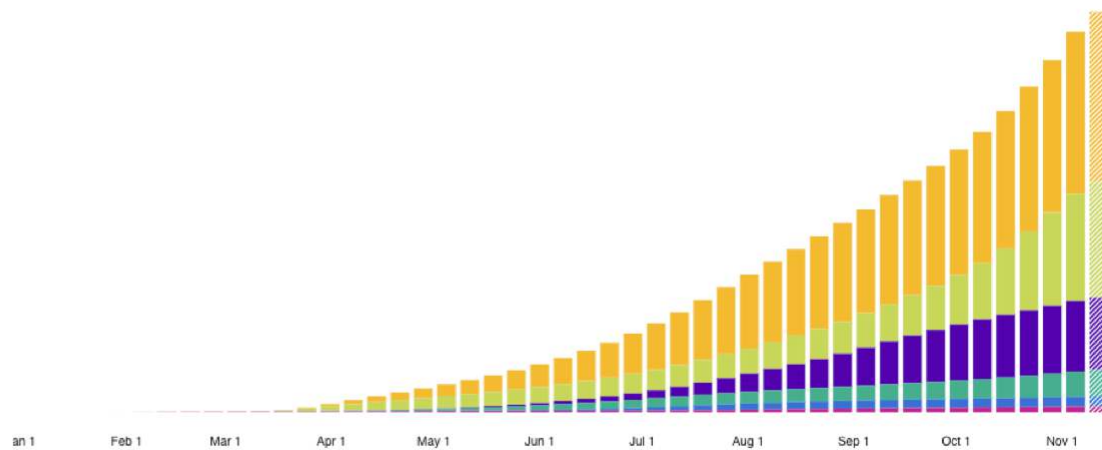
Source: Source: WHO Covid 2020 Data

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1.
United States of America
11,413,788
confirmed cases

2.
India
9,004,365
confirmed cases

3.
Brazil
5,945,849
confirmed cases

4.
France
2,048,857
confirmed cases

5.
Russian Federation
2,039,926
confirmed cases

10.
Mexico
1,049,358
confirmed cases
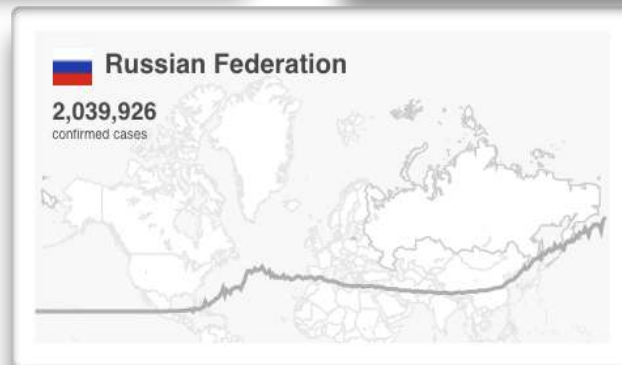
Source: WHO Covid 2020 Data

The current Covid Vaccine R&D Pipeline
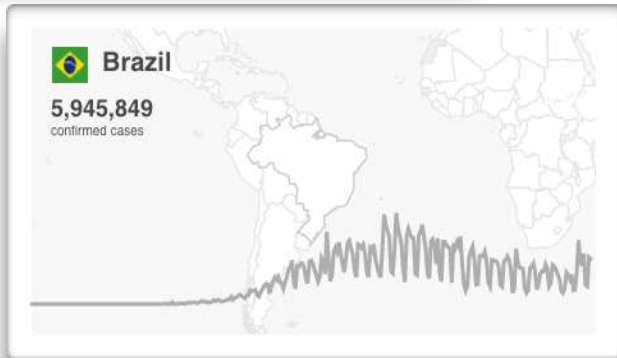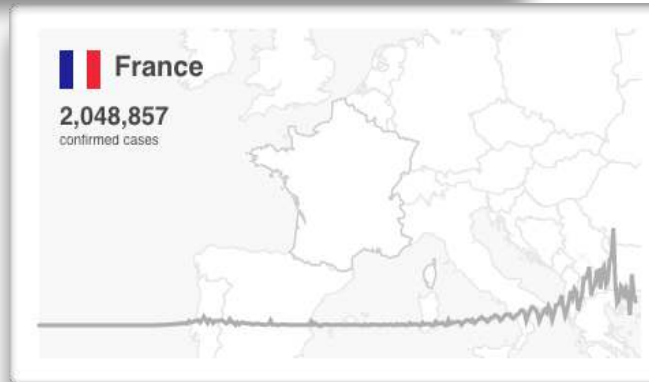
Sanofi*	J&J*	Pfizer	Moderna*	AZ/ Oxford*	Novavax*	Inovio	Merck	Clover Bio-pharm	U. of Queens-land	CureVac	U of Hong Kong
France	USA	USA	USA	UK	USA	USA	USA/ Austria	China	Australia	Germany	China
DNA	Viral Vector	mRNA	mRNA	Viral Vector	Protein	DNA	Viral Vector	Protein	Protein	mRNA	Viral Vector
Ph 1	Ph3 Start 9/2020	Ph 2/3 Start 7/2020	Ph 3 Start 7/2020	Ph 3 Start 9/2020	Ph 2 Start 8/2020	Ph1	Pre-Clinical	Ph1	Ph1	PH1	Pre-Clinical
US: 2.1B	US 1.45B	US 1.9B	US 2.48B	US 1.2B CEPI 750M EU 923M	US 1.6B CEPI 388M	US 83M CEPI 17.3M EU 5M	US 38M	CEPI 3.5M	CEPI 10.6M	CEPI 8.3M EU 421M	CEPI 620K

Overlapping USG and COVAC investments

US Gov Funding
Operation Warp Speed Finalist

COVAX Portfolio / Coalition For Epidemic Preparedness & Innovation

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Source: AVAC Org Covid Data

When will a COVID-19 Vaccine be ready?

❑ Vaccine development is a lengthy and expensive process which normally takes more than ~ 13 years

❑ Developing a vaccine more "rapidly" as a response to the COVID-19 outbreak requires a different approach and has been estimated to take around "12 to 18" months. This includes:

❑ A rapid start of development by using novel platforms like mRNA and DNA, that use synthetic processes that are faster than traditional platforms that recreate the virus

❑ Vaccine development steps that are executed in parallel, e.g. initial trials in humans (phase 1 clinical trials) may proceed in parallel with animal studies

❑ To proceed rapidly beyond efficacy trials in humans (phases 2 & 3 clinical trials), large scale manufacturing of vaccines starts earlier in the vaccine development process than in the traditional process

Source: WHO Covid 2020 Data

COVID Vaccine

The Race to Efficacy Data

Experts estimate that in each trial, ~150 infections will be required to demonstrate 60% efficacy with statistical significance. Speed of enrollment and rate of infection will determine when efficacy data will be available

Oxford / AZ – 2B	10K, UK, SA – *started May 2020*
Oxford / AZ - 2B	2K, Brazil – *started June 28 2020*
Pfizer - 3	30K, US, Brazil, Germany, Argentina – *started 27 July 2020*
Moderna - 3	30K, US – *started 27 July 2020*
Novavax – 2B	3k, South Africa – *started 17 Aug 2020*
Oxford/AZ - 3	30K, US – *started 1 Sept 2020*
J & J - 3	60K, US, Argentina, Brazil, Chile, Mexico Peru, Colombia, RSA – *started 23 Sept 2020*
INOVIO – 2B	Q2/3
Novavax - 3	30K, US+
Sanofi -3	40K US+

Q120	Q220	Q320	Q420	Q121	Q221	Q321	Q421	Q122	Q222	Q322	Q422

Source: AVAC Org Covid Data.

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Phase 3 Clinical Trials

Enrolled & Planned Volunteers (2020)
- >100,000
- >25,000
- >5,000
- >5

2020 Ongoing or Planned Ph III Studies

- Moderna - Ongoing
- AstraZeneca – Ongoing
- Pfizer – Ongoing
- Sinopharm – Ongoing
- SinoVac – Ongoing
- CanSino Bio – Ongoing
- J&J – Ongoing
- Gamaleya – Planned
- Sanofi – Planned
- Novavax – Planned

Source: AVAC Org Covid Data.
As of Nov. 20, 2020

COVID 19 Clinical Research Projects

Current COVID 19 Clinical Research Projects Worldwide

Continent / Region	Number of COVID 19 Projects
Americas	1.355
Europe	1.528
Middle East / Africa	450
Asia	401
Oceania	32
Others (No registered)	181
Grand TOTAL Worldwide	3947
*Source: www.clinicaltrials.gov as of November, 20th 2020	

Current COVID 19 Clinical Research Projects in the Americas

Top Covid-19 Trials By Countries	Number of COVID 19 Projects
USA	895
Canada	135
Brazil	123
Mexico	88
Argentina	47
Colombia	32
Chile	25
Central America / Caribbean	23
Others	17
Grand TOTAL Americas	**1385**
*Source: www.clinicaltrials.gov as of November , 20th 2020	

- Less than 12% of pharmaceutical drugs entering phase 1 research will be approved by the FDA / EMEA

- It takes at least ~10/~12 years from the discovery of a new pharmaceutical drug to its approval by the US-FDA, EUMAs & Regulatory Global Agencies.

Pharmaceutical Drug Development & Approval Process

File IND — Phase I — Phase II — Phase III — File NDA

Discovery Research	Preclinical Research	Clinical Development	Approval Phase
3.5 years	1.5 years	5 years	2 years
33.37% of R&D Budget	7.41% of R&D Budget	42.35% of R&D Budget	4.70% of R&D Budget

Source: ESTERN Medical Life Science 2020

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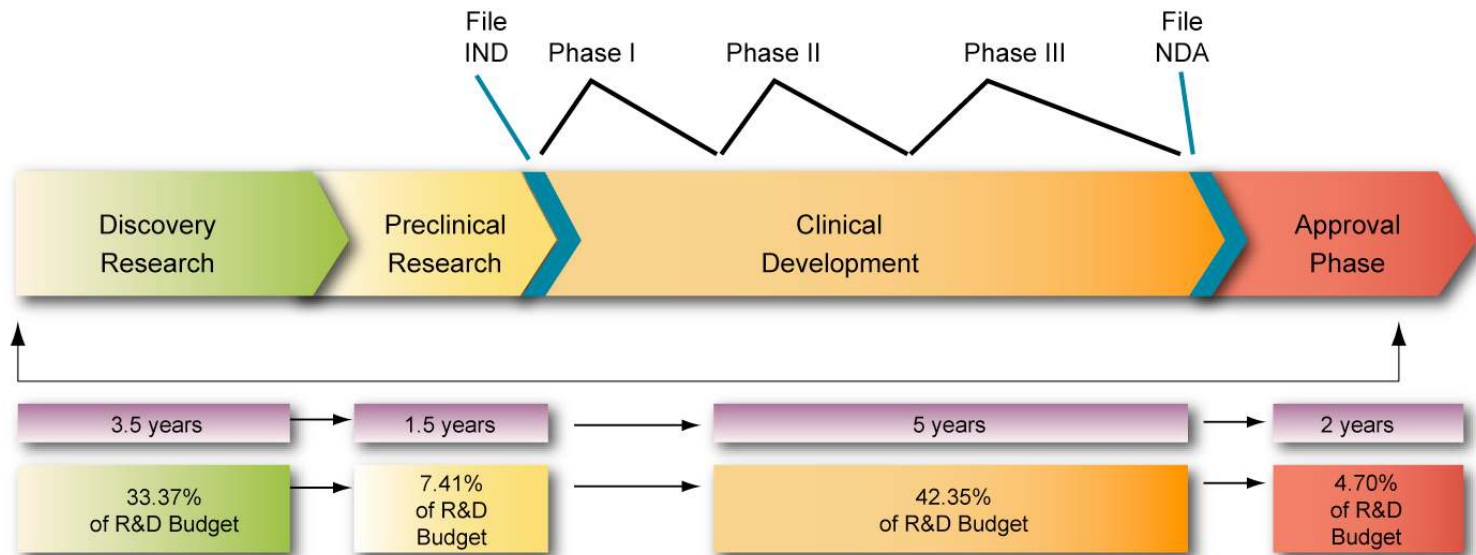
Source: NYT_Covid_2020

COVID-19 Vaccine: *"Warp Speed/ Fast track"* R&D & Clinical Development Process
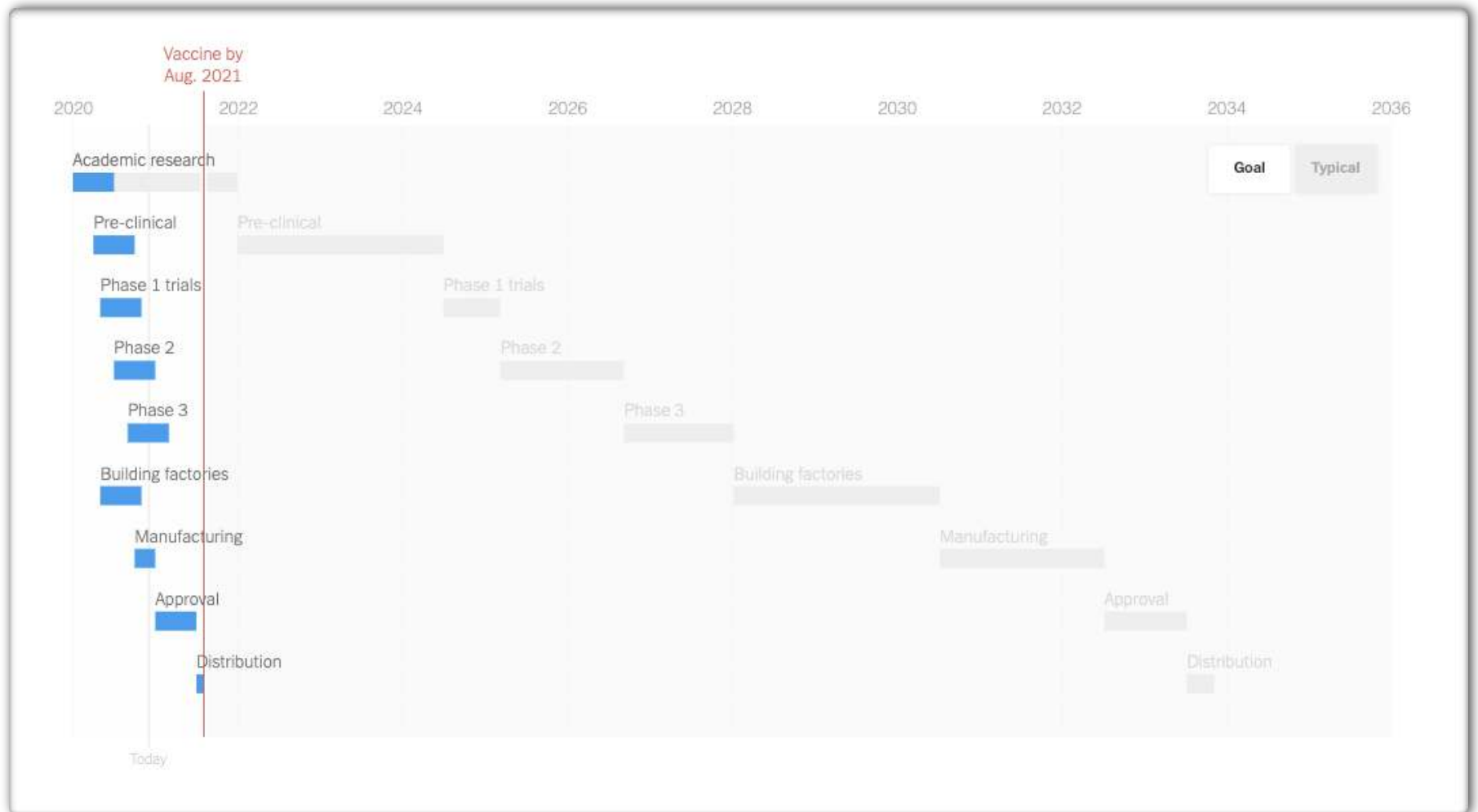
Source: NYT_Covid_2020

COVID 19 Treatments

Clinical Research of Pharmaceutical Products

VIRUS DETECTED ALL PHASES OF ILLNESS

Clinical prognosis and recovery

Lab diagnostic

Isolation/hospitalization

Mild

Moderate

Severe

Critical

Recovery

Isolation/hospitalization

Onset

ICU

Death

Aylward B et al, WHO-China Mission, 2020
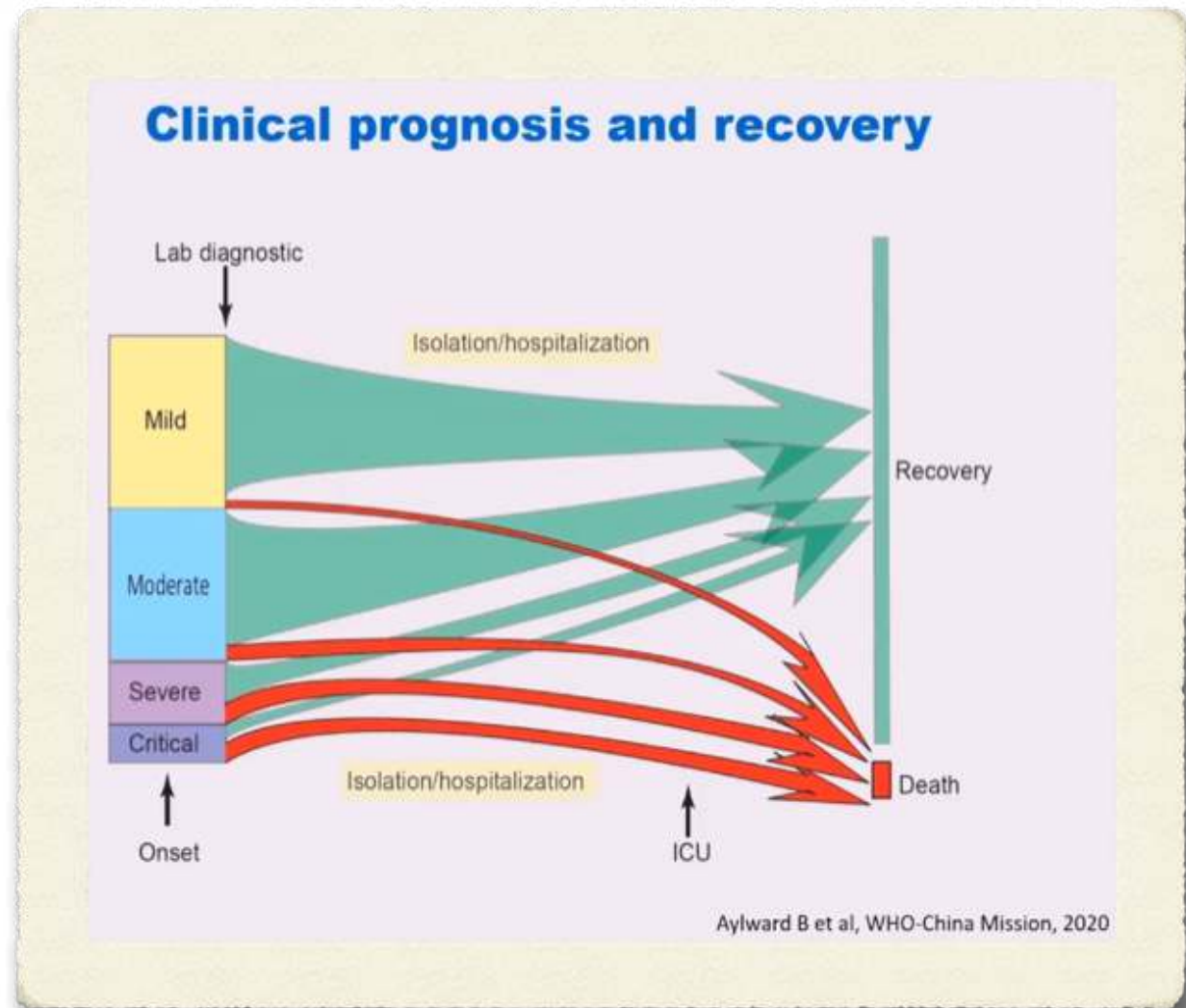
Top CoVid-19 Most Common Treatments as of Nov 2020

	Product Name	Indication Treatment	COVID 19 Treatments	Comments
1.-	REMDESIVIR (Antiviral)**	Developed and tested to treat "*EBOLA, SARS, MERS"	"Mild & Moderate and Severe" COVID 19	Gilead, *Apvd by FDA for Tx compassionate used March/2020 & **Apvd by FDA for Tx on Oct/22 *WHO Warning on Nov/20/20 not be used due to Safety, "No" "meaningful Tx effect" Note: currently being compared as TamiFlu
2.-	FAVIPIRAVIR (Antiviral)*	"Influenza, SARS, H1NI1" -	Randomized trial for COVID 19	Fuji Pharma (investigational, except approved in Japan for influenza) in Apvd by JP: 2014
3.-	RIBAVIRIN (Antiviral)	Primary indication Hepatitis C / Hemorrhagic Fever. Respiratory Syncytial Virus (RSV) infection SARS, MERS	Respiratory Distress Due to COVID-19 but potency still unclear	MSD / Roche 1971 discover & Approved by FDA 1986
4.-	LOPINAVIR (Antiviral)	Approved for HIV	Phase 3 for COVID 19	Abbvie Pharma Drug Apvd by FDA in 2000 Currently in Clinical Trials
5.-	SARILUMAB	Rheumatoid Arthritis	Patients with COVID 19 infection of "Moderate" severity. Currently in Phase 3 Trails	Regeneron / Sanofi – FDA Apvd in 2017 Did not 1 / 2 end point as of Sept/2020 For Covid-19
6.-	BARICITINIB	Rheumatoid Arthritis	Pneumonia by Covid 19	Apvd by FDA in 2017 for RA & Covid-19 combination product Apvd on Nov/19 for adults 7 pediatrics emergency used auth. Combination

	Product Name	Indication Treatment	COVID 19 Treatments	Comments
7.-	OTILIMAB	Rheumatoid Arthritis & Multiple Sclerosis	Covid -related *"Severe"* Lung Disease	Morphosys / GSK Pharm Currently NOT Apvd Please Note: currently in clinical trials process. To target Survival of severe Covid-19 patients. Primary completion date Dec 2020.
8.-	DAPAGLIFOSINA	Diabetes type II Tx / Cardio Heart Failure	Covid-related Respiratory Failure	BSM/AZ Pharma Appv Jan-2014. *Please Note: Currently in a Phase III Cardio Trial to reduce Cardio, Renal metabolic factors according to AZ Trials name Dare-19
9.-	BUDESONIDA	Asthma	Anosmia & Pneumonia	Apvd US FDA / Oct-2001- *Please Note: GlaxoSmithKline (GSK) is set to study investigational rheumatoid arthritis drug Otilimab for the treatment of pneumonia caused by Covid-19 infection
10.-	CHLOROQUINE / HYDROXYCHLOROQUINE	Malaria / Lupus Arthritis	Pneumonia by Covid 19	Apvd FDA in 1955 / *Please Note: Is currently under clinical trials to target Covid Prevent and Treat as of 2020 as of Nov/25 NEJM Ref: as most studies find NO Covid for Preventive HYDROXYCHLOROQUINE of for convalescent plasma. In conclusion NO Compelling Data
11.-	COLCHICINE	Gout Disease /Bechet's System Vasculitis Disease /Preventive Pericarditis	Reduce Cardiac Injury in COVID 19 / others COVID symptoms	Has been used 1500 BC /Apvd by FDA 1961 Covid Protection BD / Cardio Protection / R&D Clinical Trials ongoing

- To date, there are "no" specific Pharmaceutical drug or Pharma-drug combo with proven any efficacy against coronavirus.

- Currently they are *"2922"* Covid-19 clinical trials in the Pharmaceutical Treatment indications as of Nov 26th 2020 not related to Vaccines as referred by Clinical Trials. Gov

- Mainstay is *"supportive"* management including advanced organ support for patients with "severe" disease

- Both, novel and repurposed therapies, under clinical trials investigation

- Different therapies may be beneficial for different *"disease phases and presentations"* of COVID-19 illness

- Most Common Misconceptions: Antibiotics do not work against viruses; they only work on bacterial infections. Antibiotics *do not* prevent or treat COVID-19, because COVID-19 is caused by a virus, not bacteria

Mexico Most Common Challenges and Opportunities in Clinical Research

- Mexico ranks 21st in the Global Clinical Trials Research Execution

- Mexico Its internationally below in the clinical trials execution "not" only developed countries but also with other "emerging economies like Brazil, Argentina, India & South Africa.

- Changes in the lifestyle such as diet, smoking, & less exercise have contributed to the progression of chronic & other key diseases profiles across Mexico & Latin America , driving the demand in for novel / newer key vanguard treatments

- The largest Cause of Deaths in LATAM are currently Cardiovascular, Oncological & Infectious Diseases

- Growing prevalence of Obesity (~24%) in Latin America correlates to increased risk of Diabetes & Cardiovascular disease.

- Since 2000, Obesity in adults in **Mexico** has risen 8% with now 32% of adults reported Obese in Mexico.

- Prevalence of tobacco use in Latin America (31% men & 17% women smoke) contributes to the progression of cancer, heart disease & certain respiratory disease.

Source: Source: ESTERN Medical Life Science 2020 & SPM

Mexico Barriers in Clinical Research

1. Regulatory Process US/EU/Mexico

United States

- Prior review by FDA is nor required except for Phase I

- The IRB review is "~45" days

European Union

- There is a PARALLEL review process: EC/IRB submission and MoH can be performed simultaneously.

- The EC/IRB - MoH review is "~60" days

Mexico

- The review process is sequential:
1. Research Committee + Ethics Committee
2. UHAP
3. Cofepris (MoH)

- RC/EC Review: ~20 - 30 days
- UHAP + Cofepris Review: ~ 60 days
- Cofepris Review (no UHAP): according Cofepris web ~90 days.
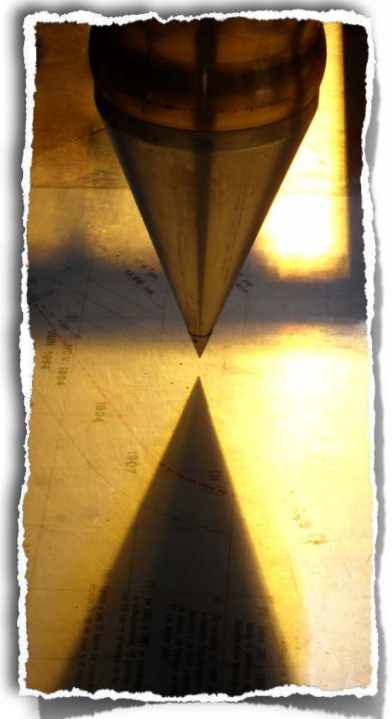- Regulatory Process Time currently "~5-6" Months

Source: ESTERN Medical Life Science 2020

2. Financial Barriers

- Capital Financial investment, Angel or Venture Capital investment for the development of new novel R&D Pharma products in the Mexico & LATAM regions.

- The capital invested in Mexico for the development of new companies is much less than that of other countries in LATAM / Global Emerging Economies

3. Cultural Barriers

- Lack of clinical, R&D synergies between the scientific / academic world vs industry / entrepreneurship with full knowledge and understanding

- Proper Training Programs for Scientists / Research & Medical Centers

- Promote the creation of interdisciplinary teams with:
    - Scientific Experience
    - Commercial Experience
    - Business R&D plans
    - Experience in Intellectual Property
    - Scientific & Biotechnology Incubators and Biotech Corridors

Source: Source: ESTERN Medical Life Science 2020 & SPMVol61

Questions & Answers