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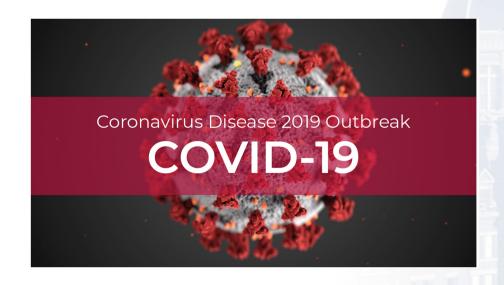
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# COVID-19: A year's perspective



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Johns Hopkins University School of Medicine and
Bloomberg School of Public Health





## **Global Cases**

Cases by Country/Region/Sovereignty

US

India

Brazil

France

Russia

Turkey

United Kingdom

Italy

Spain

Germany

Argentina

Poland

Colombia

Iran

Mexico

Ukraine

Peru

Indonesia

Czechia



**Global Deaths** 3,049,180

568,733 deaths

378,003 deaths Brazil

213,048 deaths Mexico

182,553 deaths India

127,577 deaths **United Kingdom** 

117,997 deaths Italy

104,937 deaths Russia

102,040 deaths France

80,720 deaths Germany

Global Deaths

Total Test Results in US 419,722,893

58,075,920 tests California US

49,224,295 tests New York US

22,494,107 tests Texas US

22,059,218 tests Florida US

21,839,226 tests Illinois US

20,522,711 tests Massachusetts US

> 13,035,565 tests New Jersey US

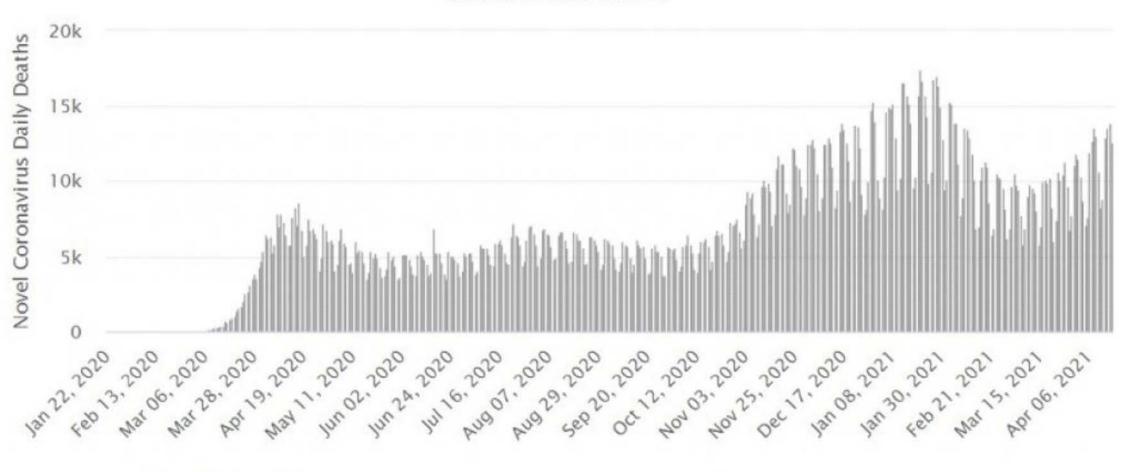
12,568,901 tests Pennsylvania US

12.371.644 tests Michigan US

↓ US Test Results



Deaths per Day
Data as of 0:00 GMT+0



7-day moving average

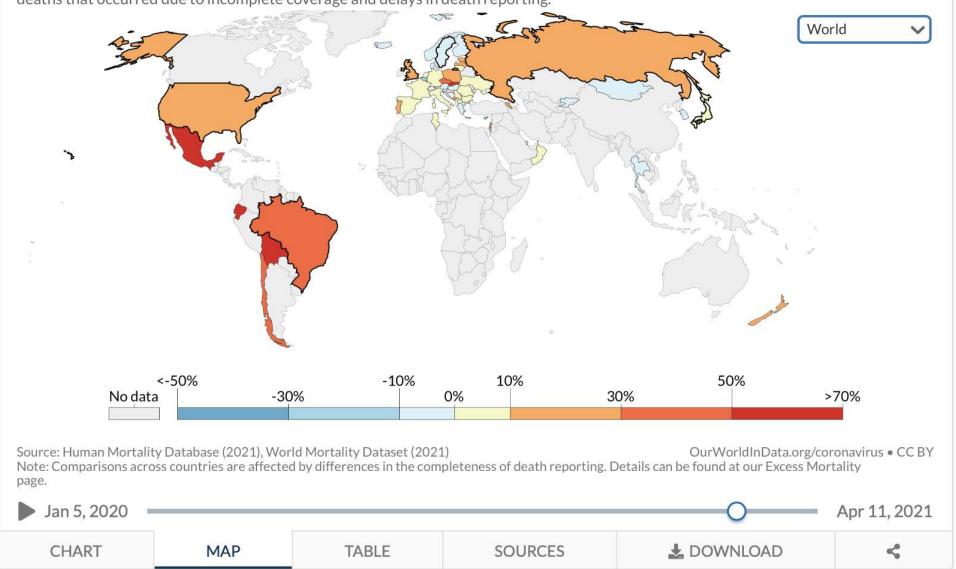
- 3-day moving average

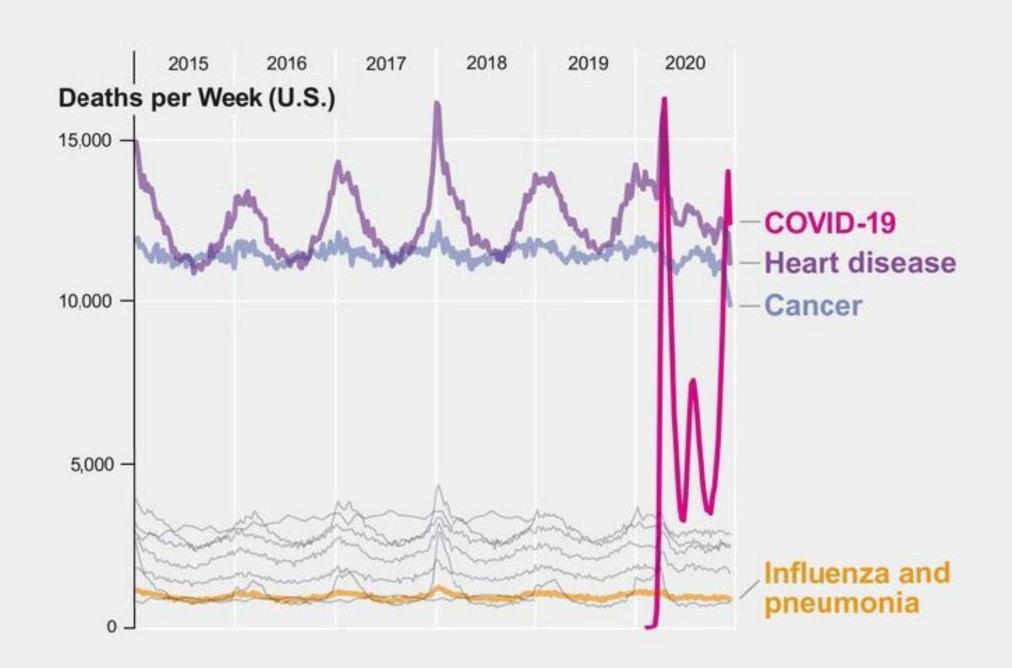
**Daily Deaths** 

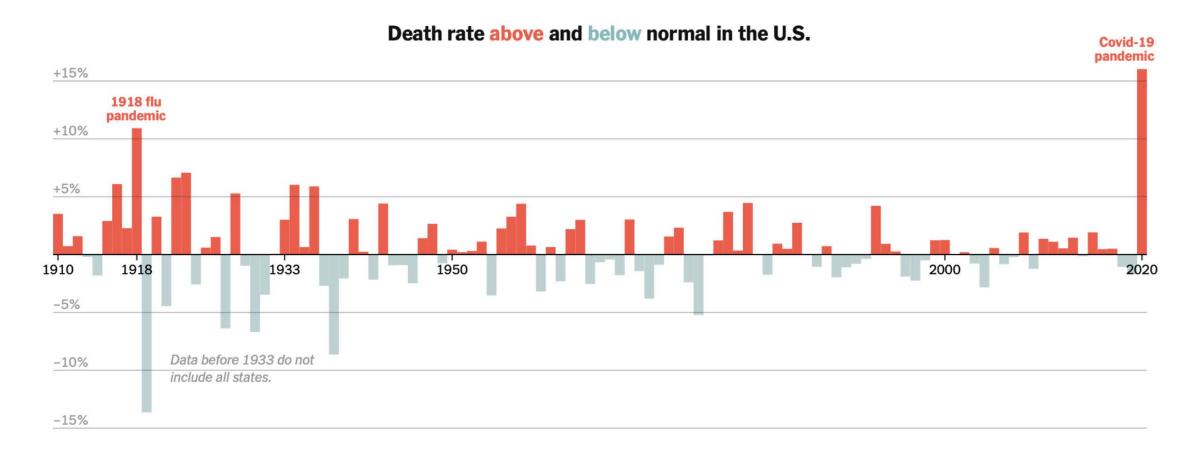
## Excess mortality during COVID-19: Deaths from all causes compared to previous years, all ages, Feb 14, 2021

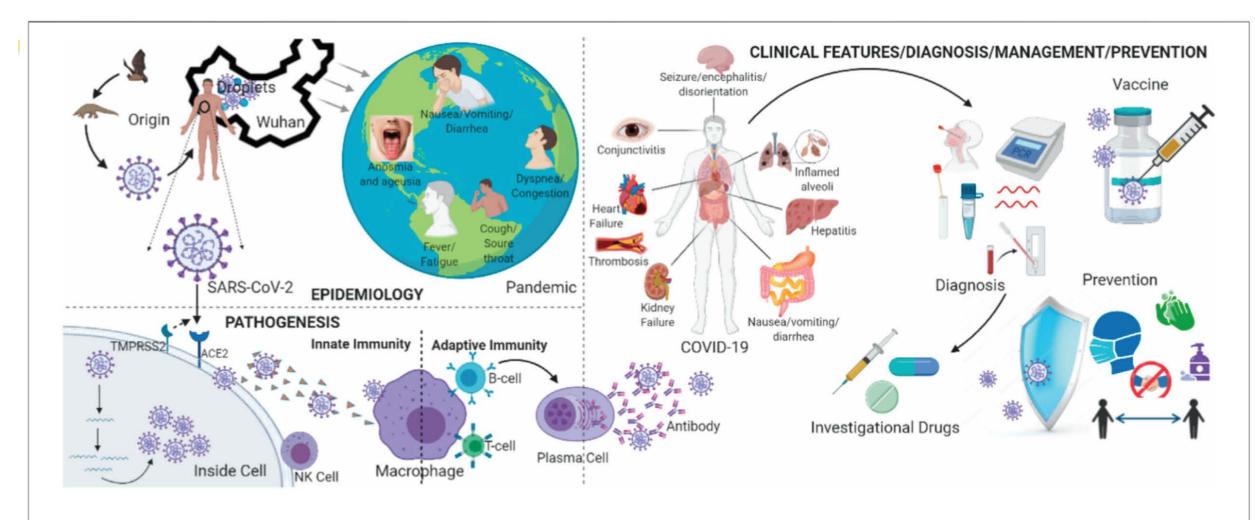


Shown is how the number of weekly or monthly deaths in 2020–2021 differs as a percentage from the average number of deaths in the same period over the years 2015–2019. This metric is called the P-score. The reported number of deaths might not count all deaths that occurred due to incomplete coverage and delays in death reporting.









**FIGURE 1** | Schematic overview of SARS-CoV-2 epidemiology, pathogenesis and clinical features, diagnosis, management, and prevention [Figure created with BioRender, www.biorender.com].

## COVID 19

- 143 million cases globally
- · 3 million deaths
- Disease course
  - Asymptomatic to critical illness
  - Mild Pneumonia to Severe Pneumonia to ARDS
    - » 1/3 hospitalized have Severe COVID-19
- High in hospital mortality
  - 60% NYC April 2020
    - » reduced overtime to 20% secondary to more experienced supportive care

## COVID 19 - Disease Course

· Asymptomatic - number unknown

- Symptomatic
  - » 80% mild
  - » 14% severe illness
  - » 5% critical illness
- Risk Factors
  - » Age
  - » Males
  - » Race (Black, Hispanic, South Asian)
  - » Genetics (Type A Blood group)
  - » Co-morbidities
    - » high blood pressure, diabetes, chronic kidney or liver disease, COPD, cancer, immunosuppression

## COVID 19 - Course

- Incubation: 3-7days
- Initial symptoms: days 1-7
  - » 80% mild
  - » Loss smell and taste
  - » Fevers, cough, headache, muscle aches
- Progression to pneumonia: days 7-10
  - » Shortness of breath
  - » Hypoxia
- Predictors of severity
  - » Leukocytosis, lymphopenia, elevated CRP, thrombocytopenia
- · Death
  - » Respiratory failure

## Initiation of infection

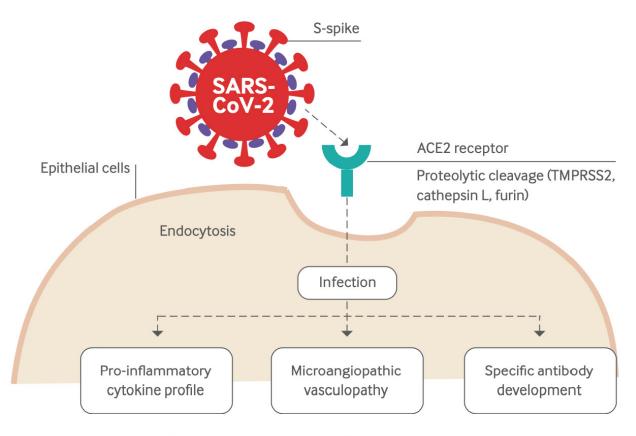


Fig 1 | SARS-CoV-2 S spike protein binds to the ACE2 receptor, which leads to proteolytic cleavage by TMPRSS2, cathepsin L, and furin in the epithelial cell of the respiratory tract. The virus undergoes endocytosis, viral maturation, replication, and release of more virus within the cytoplasm infecting the host cell. Consequences of infected cells include pro-inflammatory cytokine secretion, microangiopathic vasculopathy, and B cell secretion of specific SARS-CoV-2 antibodies

## Pathology in lung

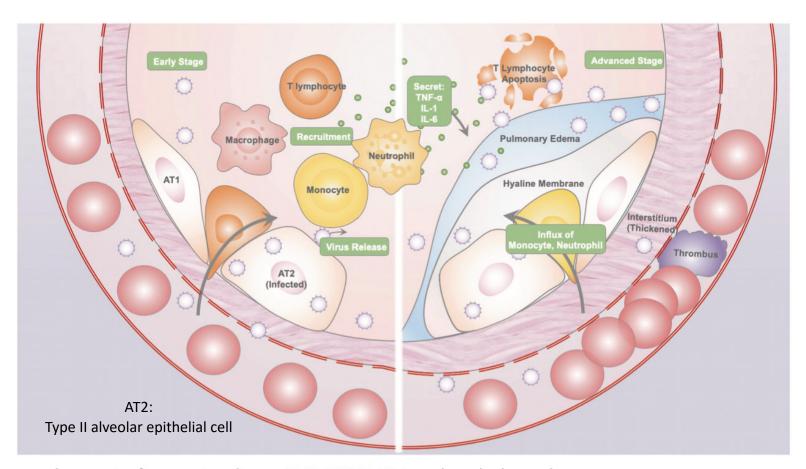


Fig. 1 Immunopathogenesis of coronavirus disease 2019 (COVID-19) in early and advanced stage

### Treatments

 To date no cure to prevent, stop or reverse severe disease

· Clinical trials for COVID-19

Terms	Search Results*	Entire Database**
Synonyms		
covid	5,420 studies	5,420 studies
SARS-CoV-2	1,773 studies	1,773 studies
severe acute respiratory syndrome coronavirus 2	180 studies	180 studies
2019-nCoV	47 studies	47 studies
2019 novel coronavirus	45 studies	45 studies
Wuhan coronavirus	1 studies	1 studies

## Treatments

• Therapeutic clinical trials for COVID-19

Terms	Search Results*	Entire Database**
Synonyms		
therapeutic	3,207 studies	265,937 studies
treatment	2,910 studies	251,444 studies
therapy	1,305 studies	92,991 studies
therapeutics	141 studies	5,702 studies
covid	3,207 studies	5,420 studies
SARS-CoV-2	1,046 studies	1,773 studies
severe acute respiratory syndrome coronavirus 2	119 studies	180 studies
2019-nCoV	35 studies	47 studies
2019 novel coronavirus	34 studies	45 studies
Wuhan coronavirus		1 studies

### Treatments

- Supportive Care
- · Anti-virals

- Convalescent plasma
- · Monoclonal antibodies

Immunomodulators

## Supportive Care

- Oxygen
  - » Nasal cannula
  - » High Flow Nasal Cannula
  - » Non-invasive ventilation
  - » Invasive ventilation
  - » ECMO
- Lung protective ventilation
- Proning
- Blood clot prevention
- Dialysis
- Treatment of secondary infections

### Treatments - Anti-Viral

- · Remdesivir
  - » Reduces viral load, 31% faster recovery in hospitalized (11 vs 15 days)
  - » EUA in USA

- HCQ +/- azithromycin, ribavirin + interferon, lopinavir/ritonavir
  - » Inconclusive and contradictory studies
  - » Currently no EUA in USA

## Convalescent Plasma

- · Variable results
- · Overall underwhelming

## Monoclonal Antibodies

#### Bamlanivimab

- » Non-hospitalized within 10 days
  - » decreased virus/hospitalization (6.3% vs 1.6%)
- » No effect hospitalized patients
- »? Prophylaxis in nursing home patients

#### · Casirivimab and imdevimab

- » Similar results in non-hospitalized
- »? hospitalized not on ventilator

## Immunomodulators

- · Anti-IL-6/IL-6R
  - » Tocilizumab and sarilumab
  - » Conflicting study results
  - » FDA panel -
    - » ICU 24h insufficient data to recommend for or against
    - » Non-ICU recommend against
  - Trials with antibodies against
    - » CCR5, GM-SCF, VEGF, Anti-PD1

## Glucocorticoids

#### · Rationale

» Reduce excessive host immune response

#### · Concerns

- » Also suppress overall immune system
- » Increase blood clot risk

### · Open-label study

- » Decreased mortality (29.3% vs 41.1%) on ventilator or oxygen (23% vs 26%)
- » Trend to increase mortality in patients not on oxygen

## COVID-19 looking forward



## COVID-19 looking forward

· Current status

Role of vaccination

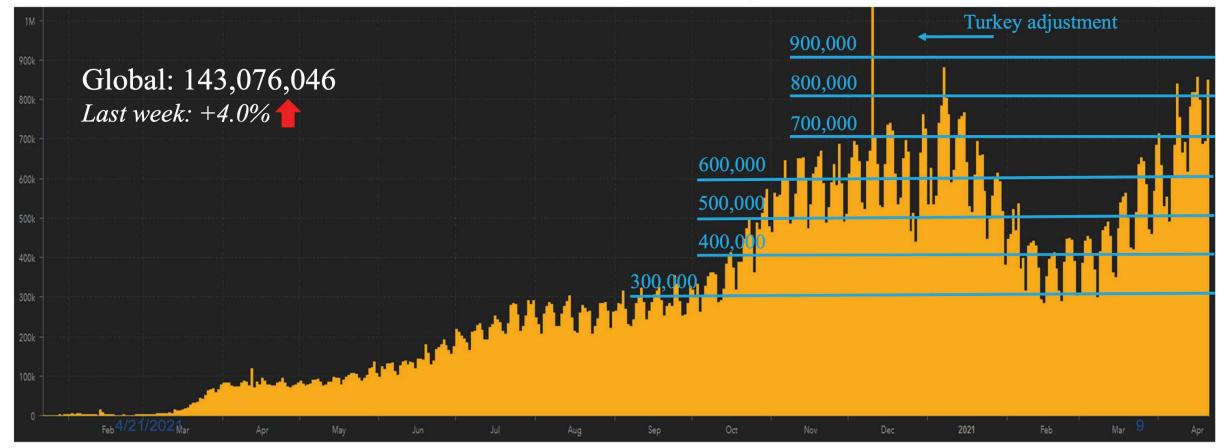
Future therapies

## Situational Awareness Global Updates





- Daily case counts just below record level; rate of increase at 4.0% (from 3.8%) over last week
- Cumulative case count exceeds 140 million; deaths top 3 million



## Situational Awareness Maryland Updates



#### 7-day case rate/100k residents

Spring Peak: 18.03 (5/07)

Summer Peak: 15.55 (7/31)

Fall/Winter Peak: 53.39 (1/13)

- Today: 19.94

#### **Daily positive cases**

Spring Peak: 1,784 (5/19)

Summer Peak: 1,288 (7/25)

Fall/Winter Peak: 3,792 (12/04)

- Today: 1,205

#### 7-day avg positivity (influenced by test volume)

Spring Peak: 26.83% (4/19)

Summer Peak: 4.76% (7/08)

Fall/Winter Peak: 9.47% (1/03)

- Today: 5.28%

#### Hospital bed use

Spring Peak: 1,711 (4/30)

Summer Peak: 592 (8/01)

Fall/Winter Peak: 1,952 (1/12)

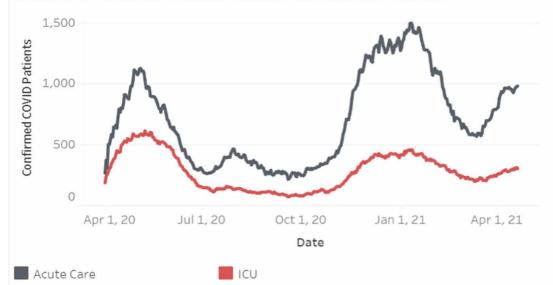
- Today: 1,279

# Situational Awareness Maryland Acute & ICU Census: 04/20



#### Hospitalized COVID-19 Patients

#### Number of COVID-19 Positive Patients in Acute Care and ICU



#### Statewide Occupied Bed Threshold



#### Statewide Occupied Staffed - Adult Acute Care and ICU - Last 10 Days



4/11/21 4/12/21 4/13/21 4/14/21 4/15/21 4/16/21 4/17/21 4/18/21 4/19/21 4/20/21

Available Staffed Beds

Hospitalized Confirmed COVID Patients

Beds Occupied Non-COVID

For more information on bed capacity thresholds please see:

https://phpa.health.maryland.gov/Documents/2020.12.01.01 MDH Order Amended Various Health Care Matters Order Patient Surge ManagementIII.pdf



## Predict who will get COVID-19?

- SARS-CoV-2
  - Airborne spread
  - More infectious than flu
  - New more infectious variants

No ability to predict who will be asymptomatic

No way to predict symptomatic

No ability to predict who will progress to severe disease

## Role of Vaccination

## Vaccination Updates *Global (04/13)*



The New Hork Times

• USA ranks #8 (vs #10 last week) in doses administered per 100 people

Pct. of population

	Doocs administered		i ct. or population	
World	▼ Per 100 people <b>11</b>	Total 824,878,017	Vaccinated _	Fully vaccinated
		024,070,017		
Israel	116	10,290,033	60%	56%
Seychelles	112	108,749	68%	45%
U.A.E.	95	9,156,728	-	-
Chile	65	12,259,848	40%	26%
Bhutan	63	476,740	63%	-
Bahrain	63	989,363	37%	26%
U.K.	60	40,107,877	49%	12%
United States	58	192,282,781	37%	23%
Maldives	55	283,753	52%	3.0%
Monaco	53	20,510	30%	23%

4/21/2021

## Unmet Need

SARS-CoV2 is here to stay

No effective treatment for infected patients



## Dr Rohit Batta MBBS, MRCGP, MFPM

CHIEF MEDICAL OFFICER
Vicore Pharma

#### The Renin-Angiotensin-System (RAS)

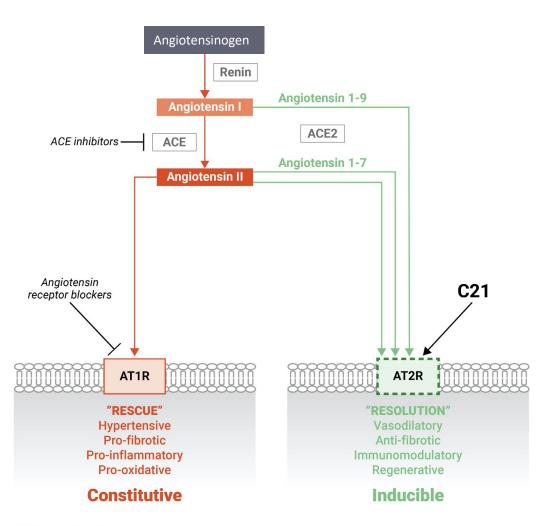


#### **Approved ACE inhibitors, examples**

- Lisinopril
- Enalapril
- Benazepril

#### Approved angiotensin receptor 1 blockers, examples

- Losartan
- Valsartan
- Telmisartan



"A druggable system with untapped potential"

ACE: Angiotensin Converting Enzyme



#### C21 – An angiotensin II type 2 receptor agonist



#### Molecular profile



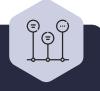
First-in-class angiotensin II type 2 receptor (AT2R) agonist

Potent and highly selective - >5,000x differential affinity AT2R versus AT1R

Reduces TGFβ1 in human IPF tissue

Reduces vasculopathy in pulmonary hypertension-model

#### Milestones passed



Oral, immediate-release dry capsule developed

Phase I; well-tolerated up to 100 mg bid, no GI intolerability

Phase II COVID-19; well-tolerated and reduced risk for oxygen supplementation

Clinically demonstrated increase in peripheral vasodilation

#### Clinical programs



**IPF** - Phase II PoC: 60 pts, single-arm, 9-month study

-Recruitment started Q4 2020-US and EU Orphan Drug designations in IPF

**COVID-19** - Phase III (pivotal): 600 pts, randomized, placebocontrolled clinical study



#### C21 - Phase II ATTRACT trial in COVID-19 design



- Multicenter, randomized, double-blind, placebo-controlled
- 106 patients hospitalized with COVID-19 (C21 n=51; placebo n=55)
  - Acute respiratory infection
  - C-reactive protein at admission (50-150mg/l)
- Disease progression
  - C-reactive protein, disease severity, clinical outcome based on need for oxygen
- Short treatment: 7-day treatment/placebo regime
- Safety and biomarkers

#### **Treatment groups well balanced**

- Age and sex
- Oxygen treatment at baseline
- Vast majority received steroid treatment (well balanced between groups)
- Conducted with clinical centers in India

Screening (n=206)



Randomization (n=106) Treatment

100mg C21 oral capsule twice daily + SoC for 7 days (n=51)

Placebo oral capsule twice daily + SoC for 7 days (n=55)

Follow-up (7-10 days)





#### C21 Phase II ATTRACT Trial: results and analysis



#### **Results**

- Reduced risk of oxygen supplementation need: -58% at day 8; -90% at day 14
- Reduced CRP in O<sub>2</sub> subgroup (p<0.1) on top of glucocorticoid treatment
- Fewer deaths on C21 (1 vs 3); Less mechanical ventilation on C21 (1 vs 4)
- Good safety profile

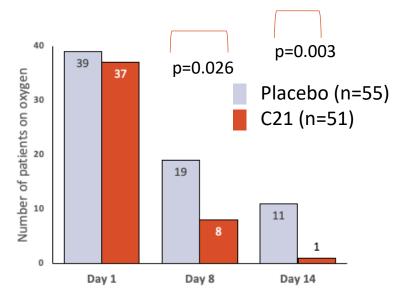
#### Hypoxia and O<sub>2</sub> supplementation

#### Predictive

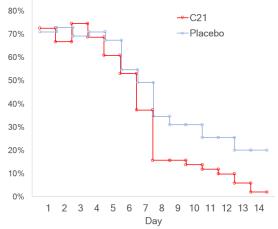
- Predicts DLCO (dyspnea and diffusion capacity of lung for carbon monoxide)
- Predicts total CT score (reticulation and ground glass appearance) 12 weeks later
- May predict long-term implications of COVID-19 infection
- Hypoxia is the most important predictor of life or death, above gender, age, smoking, medical history
- Clinical PoC: C21 improved alveolar function in COVID-19



1. \*Shah AS, Wong AW, Hague CJ, Murphy DT, Johnston JC, Ryerson CJ, et al. Thorax. 2020.

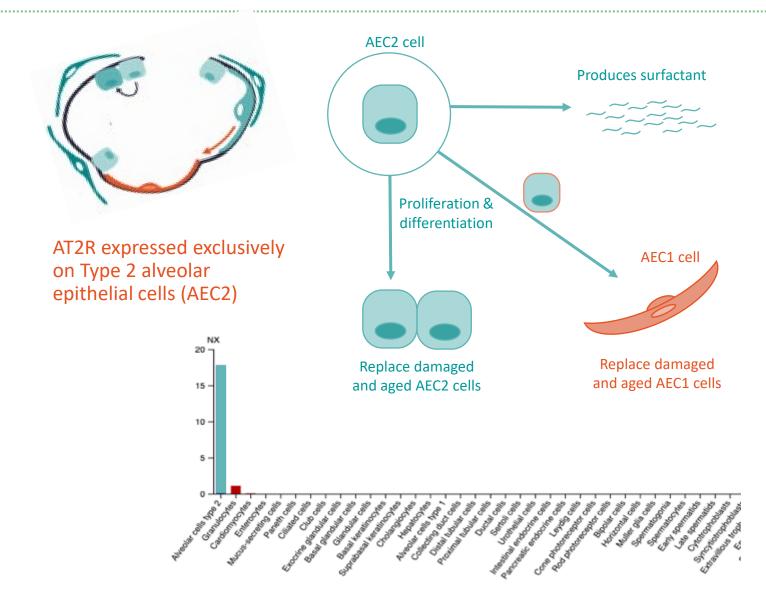






#### C21 in COVID-19







#### Study design phase III in COVID-19



Randomized, double-blind, placebo-controlled, multicenter, phase III study to investigate efficacy and safety of C21 in patients hospitalized with COVID-19

#### **DESIGN HIGHLIGHTS**

- COVID-19 severity of moderate to severe with high medical need
  - Exclusion: Moderate-severe ARDS (Berlin criteria: PaO2/FiO2 < 200)</li>
- Placebo-controlled design: in pre-IND advisory discussions
- 600 patients (300 + 300)
  - Powered to assess clinically relevant recovery outcomes
- Rapid; first patient in Q3 2021, data Q1 2022
- Potential for EUA with compelling data
- Multinational study

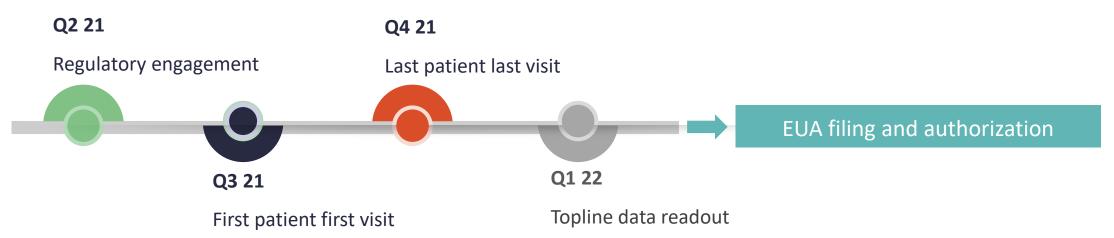
#### **COMPARISON WITH PHASE 2 ATTRACT STUDY**

- Slightly broader patient segment
- Earlier intervention (within 72h of hospitalization)
- Screening: 48h versus 72h (includes patients not on O<sub>2</sub>)
- Improved characterization of disease
- Longer treatment (14 vs 7 days) and follow-up periods (60 vs 14 days)
- Global recruitment (N + S hemisphere)
- Global CRO with extensive COVID-19 experience



#### C21 COVID-19 trial outline and timeline







#### **COVID-19: the opportunity for Vicore**





Clear clinical findings



- Positioning early interventional of hospitalized patients
- Preventing patients requiring O<sub>2</sub> treatments and ventilation
- Oral administration potential for home treatment
- Controlling the impact of the disease
- Increases confidence that C21's specific agonism of AT2R can restore lung conditions
- Priced as one-off emergency intervention, seasonal sales, expansion potential
- Provides positioning for follow-on molecules addressing AT2R



- Phase II funded by LifeArc charity
- Phase III fully funded

