Webinar:



## **Antibodies to Watch in a Pandemic**

# YUMAB's approaches to anti-SARS-CoV-2 antibody therapeutics

Corat Therapeutics – Fast track against COVID-19

**Dr. Thomas Schirrmann, CEO/Managing Director** 





#### **Overview:**

## YUMAB<sup>®</sup> platform – Fast track from target to lead





### Case study: YUMAB contract research supported client's \$1Billion deal





https://www.genengnews.com/news/boehringer-ingelheim-enleofen-ink-1b-per-product-anti-il-11-partnership-focused-on-nash-lung-disorders/

## **Status: SARS-CoV-2** Pandemic (28.06.2020)



🐨 COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)

NORT

North Atlantic



Last Updated at (M/D/YYYY) 6/28/2020, 10:33:50 nachm.



countries/reaions

Lancet Inf Dis Article: Here, Mobile Version: He Lead by JHU CSSE. Technical Support: Esri Living Atlas team and JHU APL. Financial Support: JHU and NSF. Click here to donate to the CSSE dashboard team, and other JHU COVID-19 Research Efforts, FAQ, Read more in this blog, Contact US,

Incidence Rate

Case-Fatality Ratio

Testing Rate

Hospitalization Rate

AFRICA

AUSTRALIA

Esri FAO NOAA

Global Deaths	LIC Ctata Laval		
500.108	Deaths, Recovere		
5.747 deaths	31.397 deaths, 70.010 recovered New York US		
2.070 deaths	14.975 deaths, 29.967 recovered		
azil	New Jersey US		
3.634 deaths	8.040 deaths, recovered		
nited Kingdom	Massachusetts US		
I.738 deaths	6.888 deaths, recovered		
Ily	Illinois US		
2.781 deaths	6.606 deaths, <mark>65.808</mark> recovered		
ance	Pennsylvania US		
3.343 deaths	6.158 deaths, 51.099 recovered		
Dain	Michigan US		
5.381 deaths	5.901 deaths, recovered		
exico	California US		
6.095 deaths	4.311 deaths, 8.053 recovered		
dia	Connecticut US		
0.508 deaths	3.419 deaths, recovered		
in	Florida US		
732 deaths	3.199 deaths, 39.792 recovered		
elgium	Louisiana US		
135 deaths	3.168 deaths, 4.935 recovered		
Global Deaths Global Recovered	↓ US Deaths, Recovered		



## Status: **SARS-CoV-2** Pandemic (28.06.2020)

**R** 



COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU) Total Confirmed 10.063.319 Confirmed Cases by Country/Region/Sovereignty Brazil Russia India United Kingdom Peru No vaccine and Chile Spain Italy no curative medicine/treatment Mexico Pakistan France are available! Turkey Germany Saudi Arabia South Africa Bangladesh Canada Qatar Colombia Egypt Hospitalization Rate Cumulative Confirmed Cases Active Case Case-Fatality Ratio Testing Rate Sweden Admin1 Admin2 Lead by JHU CSSE. Technical Support: Esri Living Atlas team and JHU APL. Financial Support: JHU and NSF. Click here to donate to the CSSE dashboard team, and other JHU COVID-19 Research Efforts, FAQ, Read more in this blog, Contact US Last Updated at (M/D/YYY) 6/28/2020, 10:33:50 nachm.

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aths Global Recovered	3.168 deaths, 4.935 recovered ↓ US Deaths, Recovered ▷

5

125.74 57.070

Brazil 43.634 United

34,738

29,781 France

Italy



## Overview: Time-line of the pandemic & YUMAB activities



China: new pathogenic virus strain	human beta corona described	11. January first official d	2020: leath	09. April 2020 and >325,000	0: >3.2m cas 0 deaths	ses	28. June 20. and >500,00	20: >10m case )0 deaths	es	
	Dramatic incl infections fro ~10,000 offic	rease of m ~50 to ial cases	11. March 20 declares the (100,000 cas deaths in 11	020: WHO pandemic ses, 4,000 4 countries)					Future: n waves are ARE WE	ew infection e coming!!! PREPARED?
12/201	19	02/20	020	04/202	20	(	06/2020		12/2020	
	۲									
	01/20	20	03/2	2020	05/2	2020	С	7/2020		
		Yur		Technische Universität Braunschweig	B Ma No fu	ay 2020: public nding	CORAT THERAPEUTICS			
		Feb 20 YUMA progra	020: M AB starts C am for BI st	arch 2020: ORAT consortium arted		18. May 20 Corat The take over t	020: rapeutics found the CORAT prog	ed to proce	ug 2020: , cell line, ss	
		M 1 a	March 2020: <sup>st</sup> S1 blocking antibodies	April 2020: 1 <sup>st</sup> virus-neutra antibodies	07. lizing 1 <sup>st</sup> s adv	May 2020: scientific ice with PE	15. June 2 financing r	020: ound	Est. De IMPD /	cember 2020: start Phase1

Antibodies to Watch in a Pandemic, June 30, 2020

#### Target:

## Severe acute respiratory syndrome coronavirus 2



## Characteristics of SARS-CoV-2

- ✓ RNA virus
- ✓ Human-pathogenic beta corona virus: >99% identical to SARS (2002/2003)
- ✓ Spike (S) protein binds to host receptor ACE-2 like SARS, but with much higher affinity
- First transmitted from animals to humans (bats, pangolino, or unknown?), but then from human to human
- ✓ Low mutation rate



### Indication: Coronavirus disease 2019 (COVID-19)



✓ Infections typically start in the upper respiratory regions, later reach the lung

## Very high transmission rate human to human:

- Many asymptomatic cases
- ✓ Super-spreader events
- ✓ Aerosol transmission
- ✓ High stability

## Severe pathologies and complications:

- Endothelial dysfunction and blood clots
- Overshooting inflammation and cytokine storms
- ✓ Pneumonia, acute respiratory distress syndrome with severe lung condition (low O<sub>2</sub> blood transfer)
- ✓ Acute kidney injury and several organ failure, heart problems

Death

## No Fake but Bad News: SARS-CoV2 is a real "killer" in risk groups



#### **Risk groups in Germany**



statista

Ouelle: Statista-Recherche

FASCIA D'ETÀ	DECEDUTI	QUOTA %	LETALITÀ
0 - 9	3	0,0%	0,2%
10 - 19	0	0,0%	0,0%
20 - 29	9	0,0%	0,1%
30-39	58	0,2%	0,3%
40-49	252	0,9%	0,9%
50-59	1.027	3,6%	2,6%
60-69	3.043	10,5%	10,2%
70-79	8.058	27,9%	25,1%
80-89	11.797	40,8%	
>90	4.656	16,1%	26,6
Non noto	0	0,0%	0,0%
Totale	28.903	100,0%	13,2%

### Mortality vs. age in years (Italy, 11.03.2020 vs. Germany, April 2020)



🔵 Männer 🌘 Frauer

## The risk groups comprise 15-20 Mio people in Germany.

#### © YUMAB & Corat Therapeutics

## Antibodies to Watch in a Pandemic, June 30, 2020

## What can be done?

## The four (4) strategies against the pandemic

- 1. Lock-down & quarantine & social distancing & masks
  - Quarantines only for small outbreaks
  - Lock-down causes dramatic economic losses

## 2. Diagnostics

- ✓ Monitoring of the pandemic
- ✓ Asymptomatic cases not tested, no. of tests limited & repeated testing required

## 3. Vaccine

- ✓ No cure, but provides protection
- ✓ Herd immunity: vaccination of 60-70% of the population takes many years
- ✓ Not sure, if we ever get a safe, efficient and long protecting vaccine

## 4. Therapy & Drugs

- ✓ Sufficient intensive care units
- Life-saving treatment not available, but it is needed NOW
- ✓ Anti-viral treatment: RNA analogs, protease inhibitors, ANTIBODIES
- Drug reducing severe symptoms (e.g. anti-inflammatory drugs)



"Changes our life" >1 trillion of US\$

"High dark figure" >1 billion of US\$

Protection in years? >10 billion of US\$

Life saving cure!!! >1 billion of US\$

## The racing duel? Vaccines vs. drugs are both needed!



Features	Vaccine	Antiviral drug/Antibodies
Cure	No	Yes
Protection	Yes	IgG antibodies 2-4 weeks
Doses	50-70% of the healthy population? i.e. 100 millions to billions	Only patients with severe COVID-19!! i.e. hundred thousands
Total costs	>10 billion US\$	>1 billion US\$
Effect on this pandemic	Protection of the vaccinated only	Anyone, who gets severe COVID-19!!! immediate life-saving
Conclusion	Needed to protect lives	Needed to safe lives

## Life-saving drugs are needed more urgently!

## The racing duel? 100+ drug programs against COVID-19



## Why do we so many programs?

- ✓ Success rate from phase 1 to market <90% (i.e. >10 phase-1 programs only one successful drug)
- ✓ Different modes of action
- Mutation of the virus and new strains
- ✓ Different clinical stages, different symptoms
- Combinatory therapy
- ✓ What is the market of COVID-19 in 2 or 3 years?
  - ✓ No-one can predict a pandemic market
  - ✓ Profit is uncertain

## Many programs to get one drug or vaccine! Financial support of governments required!

**Collaboration** between <u>academic science</u> **AND** <u>industry</u> is needed!

#### **Overview:**

## Drug development is not ready for pandemics



Drug discovery and development timeline.

- High risks and accelerated development to be addressed with:
  - 1. Discovery robust platforms, clear MoA
  - 2. Developability many hits, fast assessment
  - 3. Safety! safety measures, fast assessment
  - 4. Efficacy clear MoA, fast assessment
  - 5. Market uncertain!

YUMAB

## **Overview:** Novel concepts for accelerated vaccine development





Difference between Traditional Vaccine Development and Development Using a Pandemic Paradigm.

✓ In the past, new vaccines for SARS (2002/3) or Ebola (2014-16) were too late

### ✓ Novel concepts:

- Preparedness (costs, infrastructure, logistics, decision process, raw materials)
- ✓ Nested and parallelized development
- Early manufacturing
- Support by public funding required

Drug development needs the same extreme acceleration to save lives without risking safety and achieving clinical efficacy!

Lurie et al: http://www.nejm.org/doi/10.1056/NEJMp2005630

## Goal: How to accelerate drug development >10x





Drug discovery and development timeline.

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## How to accelerate drug development?

- 1. All expertise you can get: Academia+Industry
- 2. Pragmatism: Safety vs Efficacy >> perfection
- 3. Early discussion with regulatory authorities
- 4. Use standardized processes and parallelized workflows

## Costs: ???

#### Location @

## **Germany's Center of Infectious Disease Research**





## The approach: CORAT fast track approach





### Mechanism of Action: SARS-CoV-2 infects human cells expressing ACE-2





## Mechanism of Action: SARS-CoV-2 neutralizing antibodies block infection



Virus-neutralizing antibody block virus infection



## **References for the MoA: Antibodies can efficiently fight pathogens**







Schütte et al. (2009)

**HIV** 



Zhou et al. (2013), Trott *et al.* (2014)





Meyer et al. (2012)

Influenza

WO 2012072788 A1,

EP2646050A1

## **Alphavirus (VEEV, WEEV)**

Clostridium botulinum

(toxin)



Kirsch et al., (2008) Rülker et al. (2012) Hülseweh et al. (2014)

### Sudan virus (Ebola)

**Bacillus anthracis** 

(toxin)



Pelat et al., (2007)

Froude et al. 2018







Dübel



Technische Universität Braunschweig

### **Marburg Virus**



Froude et al. (2017)

## Safety: Antibody dependent Enhancement (ADE)



- Unsufficiently neutralizing SARS-CoV-2 antibodies may enhance infection (in ACE2-, FcγR+ cells)
- Inflammatory symptomatic of severe COVID-19 could be associated with such antibodies



Virus

FcγR

### Safety: ADE needs to be avoided!



- Unsufficiently neutralizing SARS-CoV-2 antibodies may enhance infection (in ACE2-, FcγR+ cells)
- Inflammatory symptomatic of severe COVID-19 could be associated with such antibodies
- ✓ We need safety measures implemented into the antibody drug design!!!

#### Data:

## Fast track development of anti-SARS-CoV-2 antibodies





## Data: Cluster analysis from the immune libraries



- ✓ 67 Clusters detected
- ✓ 48 clusters with functional active (blocking) antibodies



Please note:  $\geq$  5 AA differences in HCDR and LCDR = different cluster Graphs include more antibodies (all clones from the immune library + Fab library from this track + 5 unique antibodies from track 3)

### Data: CORAT-antibodies neutralizing SARS-CoV-2 (MoA)





Data: Prof. Dr. Luka Cicin-Sain, Helmholtz Centre for infectious research (HZI), Braunschweig

### Data: Virus neutralization is diverse





## Outlook: Next steps



- ✓ DP01: One Lead to go!
  - ✓ Subnanomolar virus neutralization (life virus)
  - ✓ No developability issues
  - ✓ Safe format
- ✓ Cell pool/Cell line
- Parallelized development steps and standard processes
- Accelerated preclinical studies and ongoing stability study
- ✓ IMPD planned for Dec 2020
- ✓ Clinical testing (phase 1/1b)

## Fast track against COVID-19

- Excellent expertise of team & partners  $\checkmark$
- Efficient & safe SARS-CoV-2 neutralizing antibody therapy
- From target to lead in <4 months</p>
- ✓ From lead to IMPD in <6 months
- ✓ FIH est, end of 2020

## More financial support required!

Many thanks to the support by our





Inauguration of YUMAB at our new head guarter (2018)



many partners! YUMAB & Corat Therapeutics GmbH

> Inhoffenstr. 7, Building A 38124 Braunschweig, DE



+49 531 481170-0



info@yumab.com



www.yumab.com

www.corat-therapeutics.com