YUMAB’s approaches to anti-SARS-CoV-2 antibody therapeutics

Corat Therapeutics – Fast track against COVID-19

Dr. Thomas Schirrmann, CEO/Managing Director
Facts:

About YUMAB

- Founded 2012/13, Braunschweig, DE
- Founders from University of Braunschweig
- Privately owned CRO & biotech
- Antibody discovery & development
- 25 FTEs, 850 m² (2021: >1200 m²)
- Globally active (>100 clients)
- Since 2018 @ Science Campus BS-South

André Frenzel
Thomas Schirrmann
Michael Hust
Overview:

YUMAB® platform – Fast track from target to lead

Target Discovery Development Preclinical Clinical

- Target
- Hits
- Lead
- Final lead

Selection/Screening Lead development

Biology

- Antigen Libraries
- Selection Sequencing
- Antibody format Bioinformatics
- In silico optimization

Market

- IND
- Drug
- CMC
- Patient

- Production Analytics
- Humanization Assays
- In vitro evolution

- Fully human
- Natural sequence
- Closed to germ-line
- Ultra-fast discovery
- All target types
- All antibody formats

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Antibodies to Watch in a Pandemic, June 30, 2020
Case study:
YUMAB contract research supported client’s $1Billion deal

Boehringer Ingelheim, Enleofen Ink $1B-Per-Product Anti-IL-11 Partnership Focused on NASH, Lung Disorders

January 9, 2020 0

No vaccine and no curative medicine/treatment are available!
Overview:

Time-line of the pandemic & YUMAB activities

- **11. January 2020:** first official death
- **09. April 2020:** >3.2m cases and >325,000 deaths
- **28. June 2020:** >10m cases and >500,000 deaths

Dramatic increase of infections from ~50 to ~10,000 official cases

- **11. March 2020:** WHO declares the pandemic (100,000 cases, 4,000 deaths in 114 countries)

Future: new infection waves are coming!!! ARE WE PREPARED?

- **Feb 2020:** YUMAB starts program for BI
- **March 2020:** CORAT consortium started
- **March 2020:** 1st S1 blocking antibodies
- **April 2020:** 1st virus-neutralizing antibodies
- **09. April 2020:** >3.2m cases and >325,000 deaths
- **18. May 2020:** Corat Therapeutics founded to take over the CORAT program
- **07. May 2020:** 1st scientific advice with PEI
- **15. June 2020:** financing round
- **Est. December 2020:** IMPD / start Phase1

**China:** new human pathogenic beta corona virus strain described

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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 O₂ blood transfer)
  ✓ Acute kidney injury and several organ failure, heart problems
  ✓ Death
The risk groups comprise 15-20 Mio people in Germany.
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!

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

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 academic science AND industry is needed!
Overview:
Drug development is not ready for pandemics

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!

Typical drug development takes 10-15 years and costs 1-3 billion US$

Drug discovery and development timeline.
Overview:
Novel concepts for accelerated vaccine development

✓ 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!

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

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1. Discovery – robust platforms, clear MoA
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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: ???
Germany’s Center of Infectious Disease Research

- Fast track anti-COVID-19 antibody therapy
- One of largest biological resource centers worldwide
- Fast track antibody discovery and development
- BSL3 facilities
- Animal Facilities
- German Center of Infectious Disease Research
- Cell line development GMP, Fill in Finish
The approach: CORAT fast track approach

Healthy donors → Infection → Convalescent patient

Selection & Screening → Virus neutralization!

Accelerated development → Process development & Manufacturing

Early clinical testing → Safety Efficacy

Status:

1-1.5 months → > 750 human antibody

~2.5 months → 1 Lead

4-5 months

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Mechanism of Action:

SARS-CoV-2 infects human cells expressing ACE-2

SARS-CoV-2 binds via S-protein to ACE-2

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

**Aspergillus fumigatus**
- Schütte et al. (2009)

**Salmonella T.**
- Meyer et al. (2012)

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

**Influenza**
- WO 2012072788 A1, EP2646050A1

**Clostridium botulinum (toxin)**
- Pelat et al., (2007)

**Bacillus anthracis (toxin)**
- Froude et al., (2018)

**Alphavirus (VEEV, WEEV)**
- Kirsch et al., (2008)
- Rülker et al. (2012)
- Hülswehe et al. (2014)

**Sudan virus (Ebola)**
- Froude et al. 2018

**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
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!!!
Fast track development of anti-SARS-CoV-2 antibodies

Libraries
Screening
Unique
RBD:ACE2
inhibition
Life virus neutral.
Lead selection
tissue
neutralization +
bioinformatics +
CMC assessment-1
Top3 for TC &
CMC-2
Final lead
TC: tissue
crossreactivity,
CMC-2

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Data:
Cluster analysis from the immune libraries

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

Please note: ≥ 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)

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CORAT-antibodies neutralizing SARS-CoV-2 (MoA)

Data: Prof. Dr. Luka Cicin-Sain, Helmholtz Centre for infectious research (HZI), Braunschweig
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
✓ Efficient & safe SARS-CoV-2 neutralizing antibody therapy
✓ From target to lead in <4 months
✓ From lead to IMPD in <6 months
✓ FIH est. end of 2020

More financial support required!

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