

COMBACTE 6 years in

New projects, Updates on studies,
network and milestones

MARC BONTEN



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New Drugs for Bad Bugs (ND4BB)

Discovery

Clinical development

Commercialisation

Early discovery

Discovery & preclinical

Phase I

Phase II

Phase III

Regulatory review

Phase IV

Penetration barriers & efflux

ND/BB
TRANSLOCATION

ND/BB
ENABLE

Drug discovery engine

ND/BB
COMBACTE
NET

Observational and epidemiology studies in *S. aureus* and *Clostridium difficile* infections

Clinical management & outcomes of patients with CRE

ND/BB
COMBACTE
CARE

Epidemiology network and observational and epidemiology studies in *P. aeruginosa* and *E. coli*

ND/BB
COMBACTE
MAGNET

Inhaled Antibiotics in Bronchiectasis and Cystic Fibrosis Including Bronchiectasis patient registry (EMBARC)

iABC

Inhaled Antibiotics in Bronchiectasis and Cystic Fibrosis

DRIVE AB

New economic models

COMBACTE CDI

Epidemiology, best practices, burden of CDI

imi innovative medicines initiative

Total budget > € 650 million

COMBACTE: **C**ombating **B**acterial Resistance in **E**urope

Four consortia:



Create a self-sustaining antibacterial development network

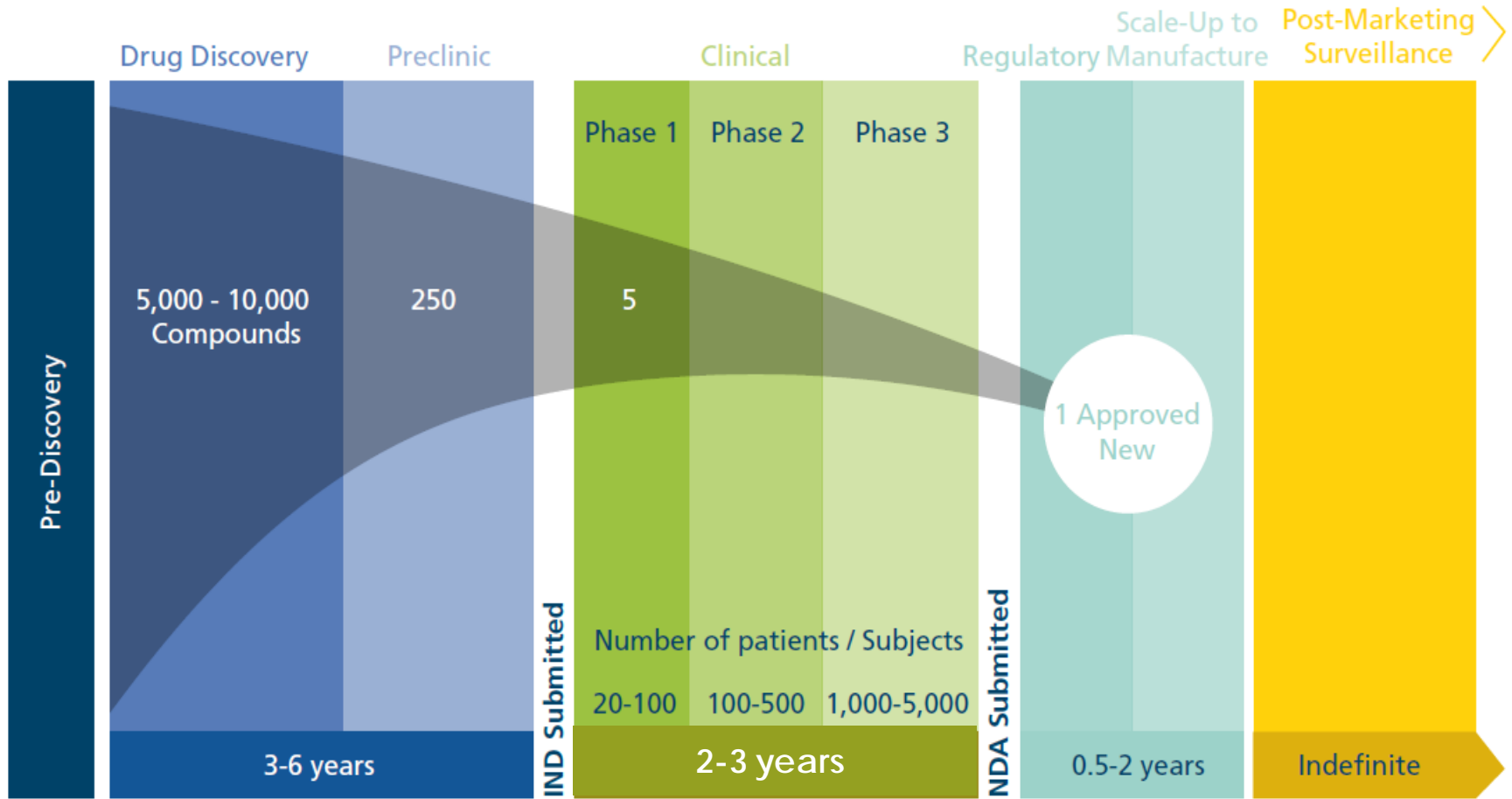
- Expanding research and laboratory networks
- Optimal alignment of clinical trials with investigator sites
- Obtain clinical and epidemiological data

Increase efficiency of antimicrobial drug development

- Align clinical trials with cutting edge molecular methodologies and trial design
- Deliver clinical trials with various candidate compounds from pharmaceutical companies



COMBACTE's ambition



The four pillars of COMBACTE



CLIN-Net
Clinical investigator network
Improve the efficiency of clinical study execution



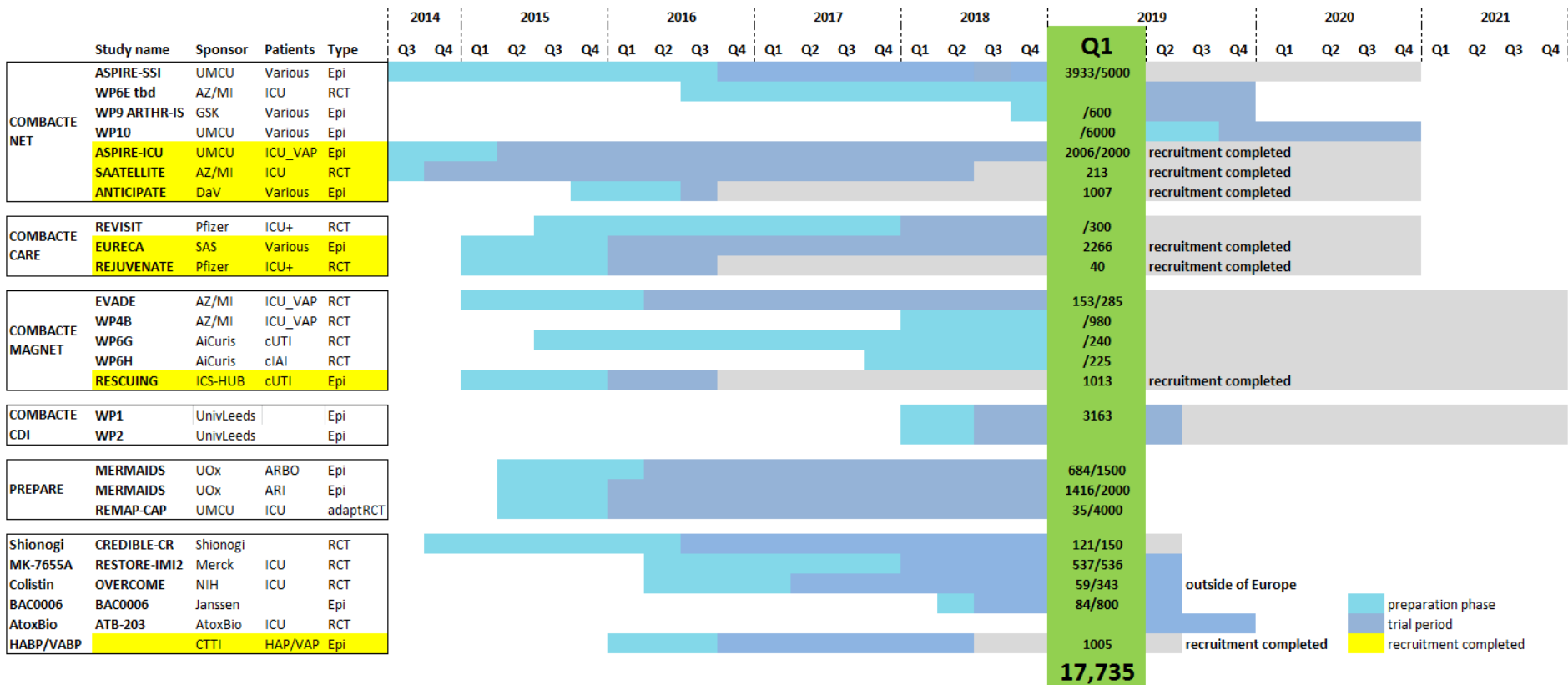
LAB-Net
Laboratory surveillance network
Optimize diagnostics in clinical studies

STAT-Net
Improvements in trial design
Develop more efficient study designs & better methods for data analysis

EPI-NET
Epidemiology support for ND4BB & beyond
Improve information on AMR in Europe from existing surveillance systems



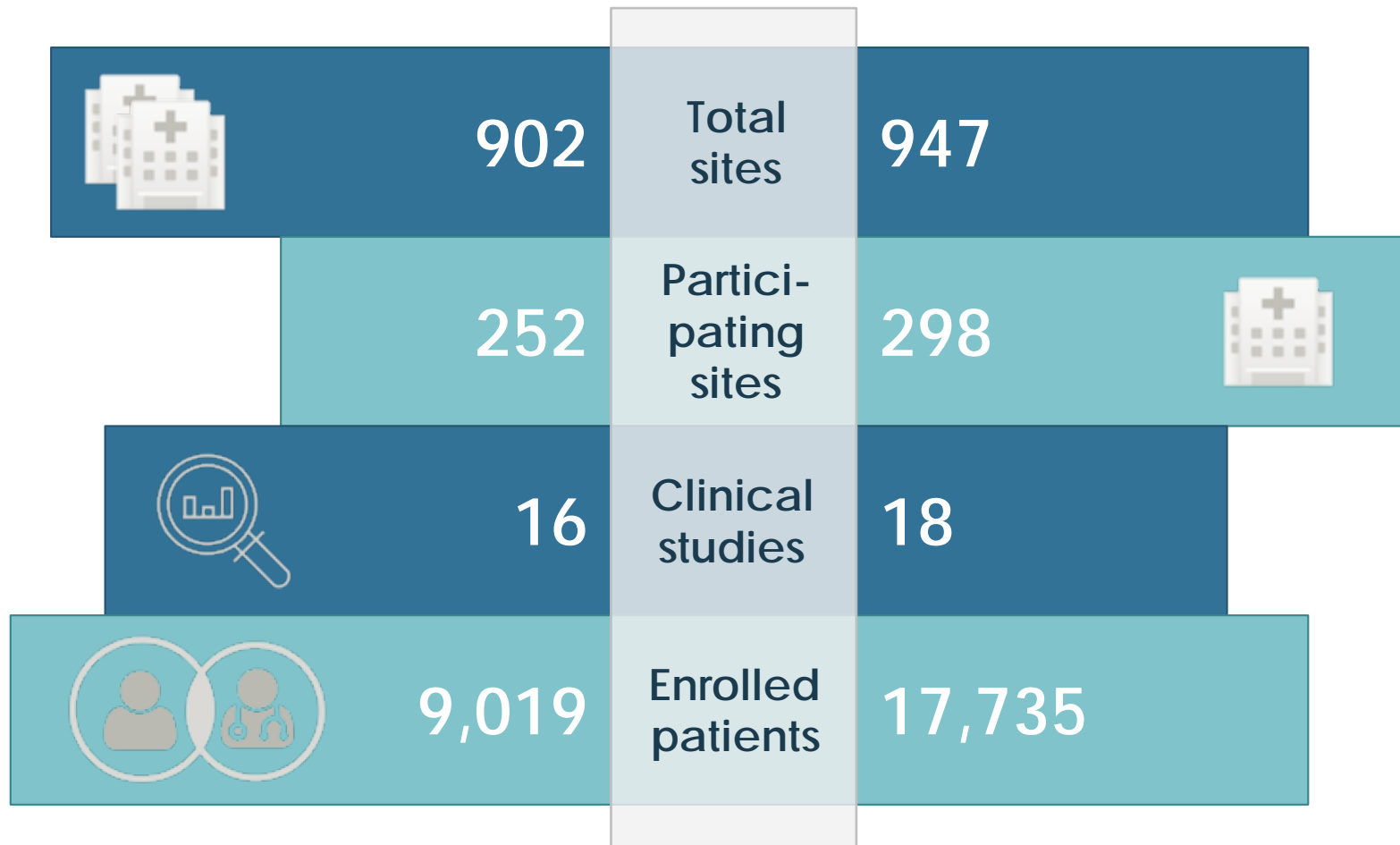
COMBACTE Clinical studies



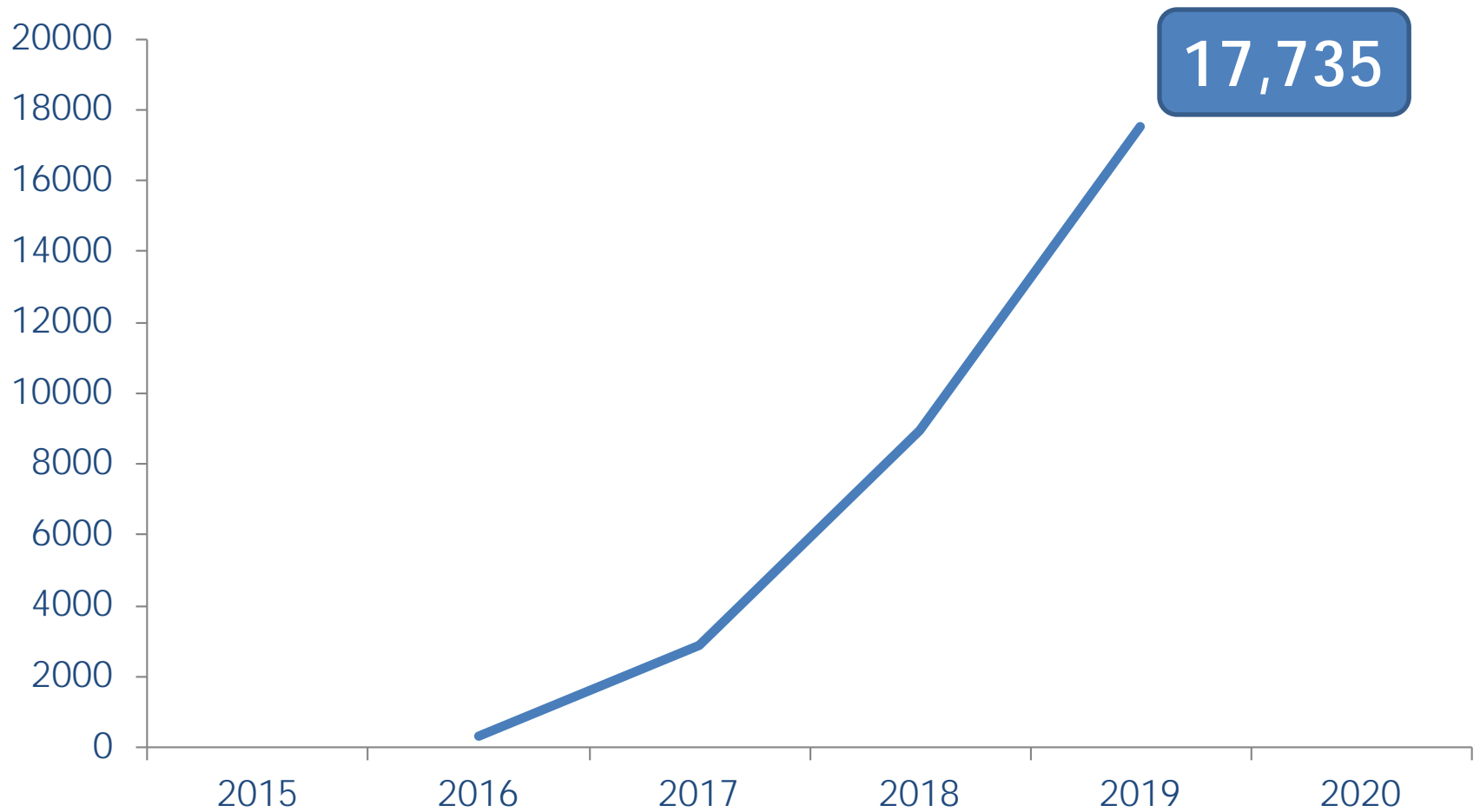
17,735 patients enrolled



March 2018 vs April 2019



Cumulative enrollment of patients in COMBACTE studies



Site Selection

Distinct Selected Sites by Country for COMBACTE + non-COMBACTE studies



27
countries

298
hospitals



COMBACTE

Public Private Partnership in Practice

True collaboration and Complementary relationship between key stakeholders

Academic Partners

- Scientific leaders in their respective fields
 - *Clinical researchers with intimate understanding of disease area and unmet medical need*
 - *Preclinical and translational scientists*
 - *Epidemiologists*
- Scientific alignment and shared vision among consortium members

EFPIA

- Drug discovery, development & manufacturing
- Large scale, global clinical trials
- Regulatory expertise

Shared leadership and accountability, with mutually agreed roles and responsibilities



Midterm review NET, CARE, MAGNET

WP2: Very good progress has been made in enhancing and building the clinical network and the GCP training of investigators (using online and face-to-face meetings), especially in Eastern Europe. The extent of the network is clearer and there is good performance reporting. Also there have been external collaborations with PREPARE, several US studies, and non-EFPIA pharmaceutical companies. The practical experience, capacity and credentials of some of the participating sites in the network should be strengthened, documented and widely presented to support sustainability. National coordinators have been selected for 28 countries and a site certification system is being built to include several performance indicators and to categorize sites by level of involvement. Site selection has been performed for several

3. MAJOR ACHIEVEMENTS AND DISSEMINATION

a. Impact: Comment on the major achievements at this stage of the project.

Is there evidence that the project has/will have the potential to be rapidly and broadly spread and taken up within the scientific/industrial community?

Comments

A very definitive “Yes.” A major achievement has been the establishment of the infrastructure in CLIN-NET, LAB-NET and STAT-NET, with the potential for self-sustainability (assuming proper future investment). In particular, other programs are already

New studies

- COMBACTE-NET
 - WP6E
 - WP7B
 - WP2-4
 - WP9
 - WP10



COMBACTE-NET

- WP6B SAATELLITE (Phase 2): study has been completed and will be presented at ECCMID (Tuesday late-breaker clinical trials)
- WP6E: Phase 3 study is planned
 - Design; double-blind placebo-controlled RCT, pts colonized with *S. aureus* and at risk for HAP/VAP in ICU
 - Status: CRO has been selected (Covance), awaiting results phase 2 study
 - Lead: AZ/MedImmune and Limoges



COMBACTE-NET

- WP7 ANTICIPATE: study has been completed and is analyzed
- WP7B: Phase 3 study is planned
 - Design; double-blind placebo-controlled RCT, hospitalized pts receiving antibiotics and at risk for developing *Clostridium difficile* infection
 - Status: Amendment (including funding for WP7B) has been approved. Protocol development has been started.
 - Lead: DaVoltera and UMCU



COMBACTE-NET

- WP4 STAT-NET activities have been completed.
- WP2 CLIN-NET is building network based on national coordinators
- New combined WP2/4 activity: Platform trial in 10-15 hospitals, with funding for local study activities
 - Design; To be determined (observational study for HAP/VAP)
 - Status: Amendment (including funding for WP2/4) has been approved. Protocol development has been started.
 - Lead: UMCU (CLIN-Net) and Uni Geneva (STAT-Net)



COMBACTE-NET

- New WP9
- Design: Retrospective study to quantify costs of prosthetic joint infections caused by *S. aureus*.
 - EU countries: tbd (20 sites in 5 EU countries)
 - Status: Site selection to start
 - Lead: GSK and Sevilla



COMBACTE-NET

- New WP WP10
- Design: Observational study to prepare a large RCT evaluating the effectiveness of a new *E. coli* conjugate vaccine.
 - EU countries: UK, France, Italy, Germany, Spain
 - Protocol in development phase
- Lead: Janssen Vaccines and UMCU (CLIN-Net)



Acknowledgements!



Testimonials from our network

— the drive within —



*"I found the COMBACTE project very attractive because of the unique and novel collaboration between independent academia and the pharma. **Uniting academic investigators with the pharma to develop new antibiotics is a right way forward**"*

- Prof. Dr. Mical Paul, Rambam Medical Center, Israel



*"I hope COMBACTE will succeed and bring a lot of papers which will be quoted for years. **Once I retire I will be proud to know that I had a small contribution**, while reading and recognizing footprints of project results in papers available on a tablet"*

- Prof. Dr. Bruno Barsic, University Hospital of Infectious Diseases, Zagreb



*"**COMBACTE is an engine that is developing a sense of global responsibility and commitment** not only around Europe, but also the entire world. No doubt COMBACTE is doing more than science"*

- Dr. Jose Bravo-Ferrer, Hospital Universitario Virgen Macarena, Seville



Testimonials from our network

— the drive within —

“Without the collaboration and dedication of the study team, it would be impossible to maintain this rate of patient inclusion.

Team work is very important”

- Dr. Miquel Pujol, Hospital Universitari de Bellvitge



“It's very important to have a dedicated team and be very involved as Principal Investigator.

We made a good division of tasks, and we solve the challenges together. Daily communication ensures we don't miss any potential subjects”

- Dr. Biljana Carevic, Clinical Center of Serbia



*“This is a European project in which renowned academia are taking part. The scientific, development, and research part are very well represented. **We liked the multilevel, international side of it”***

- Prof. Dr. Simin Florescu, Clinical Hospital of Infectious & Tropical Diseases ' Dr. Victor Babeş', Bucharest

