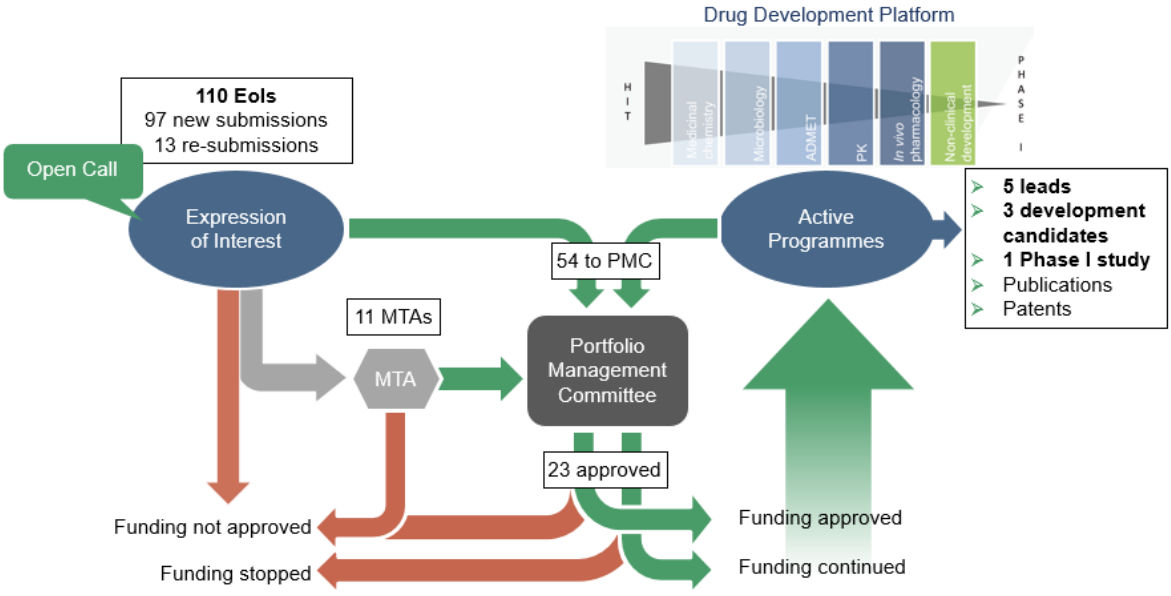
nature portfolio

https://doi.org/10.1038/d41573-021-00074-y

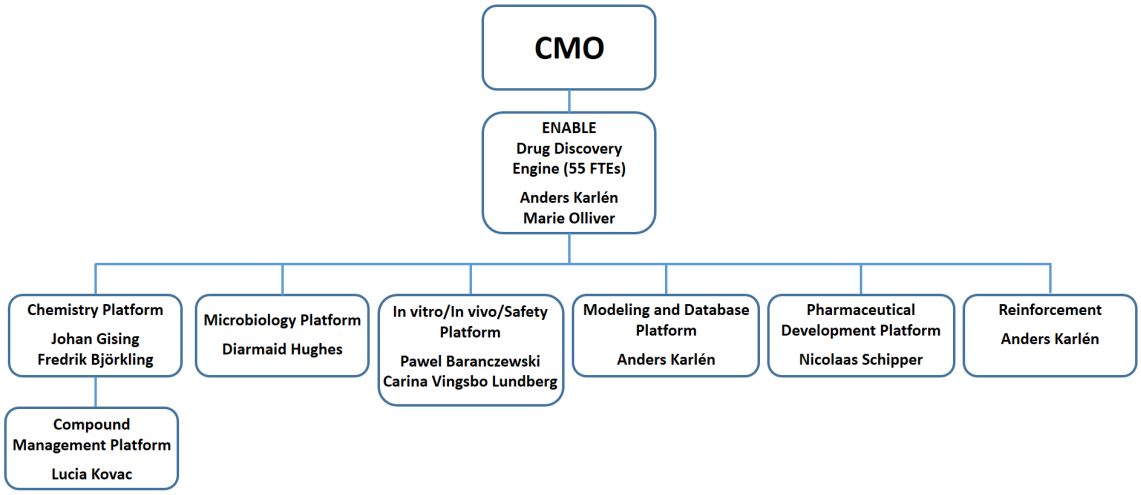
Supplementary information

ENABLE: an engine for European antibacterial drug discovery and development

In the format provided by the authors



Supplementary Figure 1 | The ENABLE model. The open call resulted in 110 expressions of interest (EoIs): 97 new submissions and 13 re-submissions. 54 EoIs met the entry criteria and were reviewed by the Portfolio Management Committee, and 23 of these were approved for funding. 11 programmes lacking key data were initially evaluated using a material transfer agreement (MTA) route prior to making a decision on entry. All active programmes in ENABLE are subject to quarterly reviews by the Portfolio Management Committee. In contrast to most other initiatives, ENABLE does not allocate a fixed sum to programmes, but instead provides funding, resources and expertise on need-based criteria.



Supplementary Figure 2 | ENABLE organizational chart.

Supplementary Table 1 | ENABLE platform partners

Partners	Type		Country	Platforms						
	Academic & research institute	SME		Modelling and Database	Chemistry	Microbiology	In vitro/in vivo/Safety	Pharmaceutical Development	Compound Management	Reinforcement
Uppsala University	■		Sweden	■	■	■	■			■
Cardiff University	■		UK			■				
Latvian Institute of Organic Synthesis	■		Latvia		■		■			
Molecular Discovery Ltd		■	UK	■						
National Medicines Institute	■		Poland			■				
Recipharm OnTarget Chemistry		■	Sweden		■				■	
Statens Serum Institut	■		Denmark				■			
Research Institutes of Sweden	■		Sweden				■	■		
Stichting VU/VUMC (Vrije University Amsterdam)	■		Netherlands		■		■			
University of Copenhagen	■		Denmark		■					
University of Helsinki	■		Finland		■					
Servicio Madrileno de Salud	■		Spain			■				
Fundación Medina	■		Spain				■			
Beactica AB		■	Sweden							■
Helmholtz Centre for Infection Research	■		Germany							■
Inspiralis Ltd		■	UK							■
John Innes Centre	■		UK							■
Region Hovedstaden	■		Denmark							■

Supplementary Table 2 | ENABLE management and platforms

Portfolio Management Committee (PMC)	
External	Lynn L. Silver, LL Silver Consulting, United States
	Gerry Wright, McMaster University, Canada
	Malcolm G. P. Page, Malcolm Page GmbH, Switzerland
	David Pompliano, Lodo Therapeutics, United States
	Eva Bredberg, Bredberg&Bredberg Consulting, Sweden
Public	Diarmaid Hughes, Uppsala University, Sweden
	Frederik Deroose, Asclepia, Belgium
	Pawel Baranczewski, Uppsala University, Sweden
	Timothy Walsh, Cardiff University, United Kingdom
	Fernando Baquero, SERMAS, Spain
EFPIA	Michela Pecoraro, Evotec, France
	Eric Bacqué, Evotec, France
	Neil David Pearson, GSK, United States
	Helen Steel, GSK, United Kingdom
	Laurenz Kellenberger, Basilea, Switzerland
PMC Secretariat	Sally Miles, GSK, United States
Previous members	Balganesh Tanjore Soundararajan, External, CSIR Centre for Mathematical Modelling and Computer Simulation (C-MMACS), India
	Laurent Fraisse, Evotec, France
	Michel Doubovetzky, Sanofi, France
	Stephen Baker, GSK, United States
Consortium Management Office (CMO)	
Anders Karlén, Chair and Leader of the Managing Entity, Uppsala University, Sweden	
Neil David Pearson, Project Coordinator, GSK, United States	
Eric Bacqué, Project co-coordinator and Scientific Manager, Evotec, France	
Robert Neal, Alliance Manager, GSK, United Kingdom	
Anna Lobell, Finance Manager, Uppsala University, Sweden	
Marie Olliver, Programme Manager, Uppsala University, Sweden	
Frederik Deroose, Scientific Manager, Asclepia, Belgium	
Diarmaid Hughes, Scientific Manager, Uppsala University, Sweden	
Nathalia Murillo, Communication Manager, Evotec, France	
Clément Robijns, Communication Manager, Biocom, Germany	
Lilian Julia Löwenau, Communication Manager, Biocom, Germany	
Anna Karin Belfrage, Secretary, Uppsala University, Sweden	
Previous members	
Cecilia Nilsson, Secretary, Uppsala University, Sweden	
Anneli Hällgren, Programme Manager, Uppsala University, Sweden	
Laura Griestop, Communication Manager, Biocom, Germany	
Katja Bölcker, Communication Manager, Biocom, Germany	
George Stroup, Project Manager, GSK, United States	
Richard Grimes, Project Manager, GSK, United States	
Karen Philpott, Alliance Manager, GSK, United Kingdom	

Claire Skentelbery, Open Call Manager, European Biotechnology Network, Belgium		
Robert Stavenger, Project Coordinator and Scientific Manager, GSK, United States		
Anders Alderborn, Finance Advisor, Uppsala University, Sweden		
David Holmes, Project Coordinator and Scientific Manager, GSK, United States		
Platform and hub		
Chemistry Platform	**Uppsala University** Sweden *Medicinal Chemistry Hub (H2L)*	Johan Gising
		Anna Karin Belfrage
		Dmitry Antonov
		Stefan Lindström
		Charles Hedgecock
	University of Copenhagen Denmark *Medicinal Chemistry Hub (H2L)*	Fredrik Björkling
		Niranjan Thota
		Jolanta Ludvigsen
		Anna Mette Hansen
		Yuri Ermolovich
		Henrik Franzyk
		Peter E. Nielsen
		John Nielsen
		Wouter Hogendorf
		Niloofar Yavari
		Huizhen Liu
		Chirag Mudaliar
	University of Helsinki Finland *Medicinal Chemistry Hub (H2L)*	Jari Yli-Kauhaluoma
		Paula Kiuru
		Andrew Neal
		Piyush A. Patel
		Raisa Haavikko
	Vrije Universiteit The Netherlands *Medicinal Chemistry Hub (H2L)*	Rob Leurs
		Geert Jan Sterk
		Guido Janssen
		Rick Riemens
		Mounir Andaloussi
		George Johannes Josephina Panis
		Maikel Wijtmans
	Latvian Institute of Organic Synthesis Latvia *Medicinal Chemistry and Process Chemistry Hub (L2CD)*	Edgars Suna
		Martins Ikaunieks
		Einars Loza
		Dmitrijs Lubriks
		Igors Sokolovs
		Kaspars Leduskrasts
		Victoria Ryabova
		Tatjana Kukosha
		Nadezhda Trufilkina
		Marina Martjuga
		Galina Shuleva
		Kirill Shubin

		Anna Nikitjuka
		Martins Priede
		Pavel A. Donets
		Daina Lola
		Aiva Plotniece
		Viktors Andrianovs
		Irena Leite
		Konstantins Kalinins
		Andrejs Krasikovs
		Vita Ozola
		Ilga Mutule
		Martins Katkevics
		Jana Spura
		Linda Supe
		Martins Rucins
		Irena Piskunova
		Andrejs Pelss
		Laura Krasnova
		Ilze Kaula
		Olga Bobileva
		Andrei Baran
		Maija Kurtenoka
		Jevgenijs Kuzmins
		Jevgenijs Kuznecovs
		Andrejs Petuskovs
	Recipharm OnTarget Chemistry Sweden *Compound handling*	Lucia Kovac
		Mohamed Haj Bakour
		Thomas Damberg
		Alf Eriksson
		Åse Ekdahl
		Santosh Raman Acharya
Microbiology Platform	**Uppsala University** Sweden *Microbiology Hub*	Diarmaid Hughes
		Douglas L. Huseby
		Sha Cao
		Karin Hjort
		Onur Ercan
		Anna Petersson
		Kavita Yadav
		Rachel Hickman
		Linnéa Garoff
		Lisa Crone
		Paraskevi Giachou
		Talía Berruga-Fernández
		Daniel John
		Anna Tamara Leber
	Cardiff University	Timothy Walsh

	United Kingdom *Microbiology Hub*	Jonathan M. Tyrrell
		Ali Aboklaish
		Laura Espina
	SERMAS-IRYCIS Spain *Microbiology Hub*	Fernando Baquero
		Rafael Canton
		Maria Garcia-Castillo
		María-Carmen Turrientes
	National Medicines Institute Warsaw Poland *Microbiology Hub*	Dorota Żabicka
		Małgorzata Urbaś
		Marek Gniadkowski
		Katarzyna Bojarska
		Magdalena Tomczak
In vitro/In vivo/Safety Platform	**Uppsala University** Sweden *In vitro ADMET*	Pawel Baranczewski
		Maria Backlund
		Ivailo Simoff
		Anders Eneroth
		Richard Svensson
		Maria Mastej
		Bryndis Birnir
		Sergiy V. Korol
		Rolf Larsson
		Lena Lenhammar
		Zhe Jin
		Per Artursson
		Björn Hellman
		Lena Friberg
		Elisabet I Nielsen
		Tomás Sou
		Niklas Tyrefors
	Latvian Institute of Organic Synthesis Latvia *In vivo ADMET*	Edgars Liepins
		Solveiga Grinberga
		Dace Hartmane
		Baiba Gukalova
		Eduards Sevostjanovs
		Helena Cirule
		Janis Kuka
		Maija Dambrova
	Statens Serum Institut Denmark *In vivo efficacy*	Carina Vingsbo Lundberg
		Jon Hansen
		Niels Frimodt-Møller
	Fundación Medina Spain	Olga Genilloud
		Francisca Vicente
		Maria C. Ramos
		Mercedes de la Cruz Moreno
	Vrije Universiteit, The Netherlands	Wilbert Bitter
		Gunny van Stempvoort

	Zebra fish assay	Theo Verboom
		Eva Habjan
Modeling and Database Platform	*Computational Medicinal Chemistry*	Anders Karlén, Uppsala University, Sweden
		Peter Brandt, Uppsala University, Sweden
		Christian Sköld, Uppsala University, Sweden
		Simon Cross, Molecular Discovery, United Kingdom
Pharmaceutical Development Platform	**Research Institute of Sweden** Sweden *CMC*	Nicolaas Schipper
		Ulf Tedebark
		Bo Lassen
		Vahak Abedi
		Fredrik Lake
		Martin Bollmark
		Ulf Larsson
		Pia Appelqvist
		Ylva Rosell
		Göran Lundin
		Neeraj Garg
		Anne-Charlotte Hällgren
		Fernando Fernandez Huerta
		Anna Winqvist
		Sofie Alvér
		Ronja Widenbring
		Anders Bøgevig
	Research Institute of Sweden Sweden *Preclinical toxicology*	Björn Platzack
		Ian Cotgreave
		Johan Lindberg
		Karin Cederbrant
		Jenny Lindahl
		Susanne von Mentzer-Andersson
		Marcus O.D. Sjödin
		Fredrik Andersson
		Maritha Marcusson-Ståhl
		Björn Glinghammar
		Anna-Karin Sternbeck
		Rodrigo Palma Villar
		Susanna Nevala
		Benita Hyllbrant

Supplementary Box 1 | Details of expressions of interest

- 110 expressions of interest (EoIs) were received. 50% of the EoIs met the entry criteria and were reviewed by the Portfolio Management Committee, and 43% of these were approved for funding (21% funding rate).
- 95% of the EoIs were in Hit to Lead phase and the rest were in Lead to Candidate phase.
- 62% of the EoIs were submitted by SMEs, 34% by academia and 4% by EFPIA companies.
- The EoIs came from 20 European countries, most from the UK (24%), followed by Spain (12%), the Netherlands and France (both 8%).
- EoIs included small molecules and peptides (majority), as well as a few sugars and natural products.

Supplementary Box 2 | ENABLE entry criteria

Hit to Lead programmes:

- MIC ≤32 μg/ml vs a key Gram-negative pathogen (*E. coli*, *K. pneumoniae*, *P. aeruginosa* and/or *A. baumannii*), with activity against resistant strains, if targeting a known mechanism
- Activity not due to non-specific activity (detergent-like)
- Proven chemical structure, preliminary SAR
- Favourable chemical properties and reasonable route of synthesis (or availability of product if natural-product derived)
- Promising phys-chem parameters (e.g. clogP<4)

Lead to Candidate programmes:

- MIC90 ≤16μg/ml vs a key Gram-negative pathogen, with activity against resistant strains, if targeting a known mechanism
- MICs ≤64μg/ml vs other key Gram-negative pathogens
- Experimentally determined target (or pathway) activity
- Acceptable frequency of resistance
- Time kill analysis
- Sustainable antibacterial SAR
- Preliminary understanding of DMPK/in vitro pharmacology
- Tractable synthetic route with 2 modifiable positions