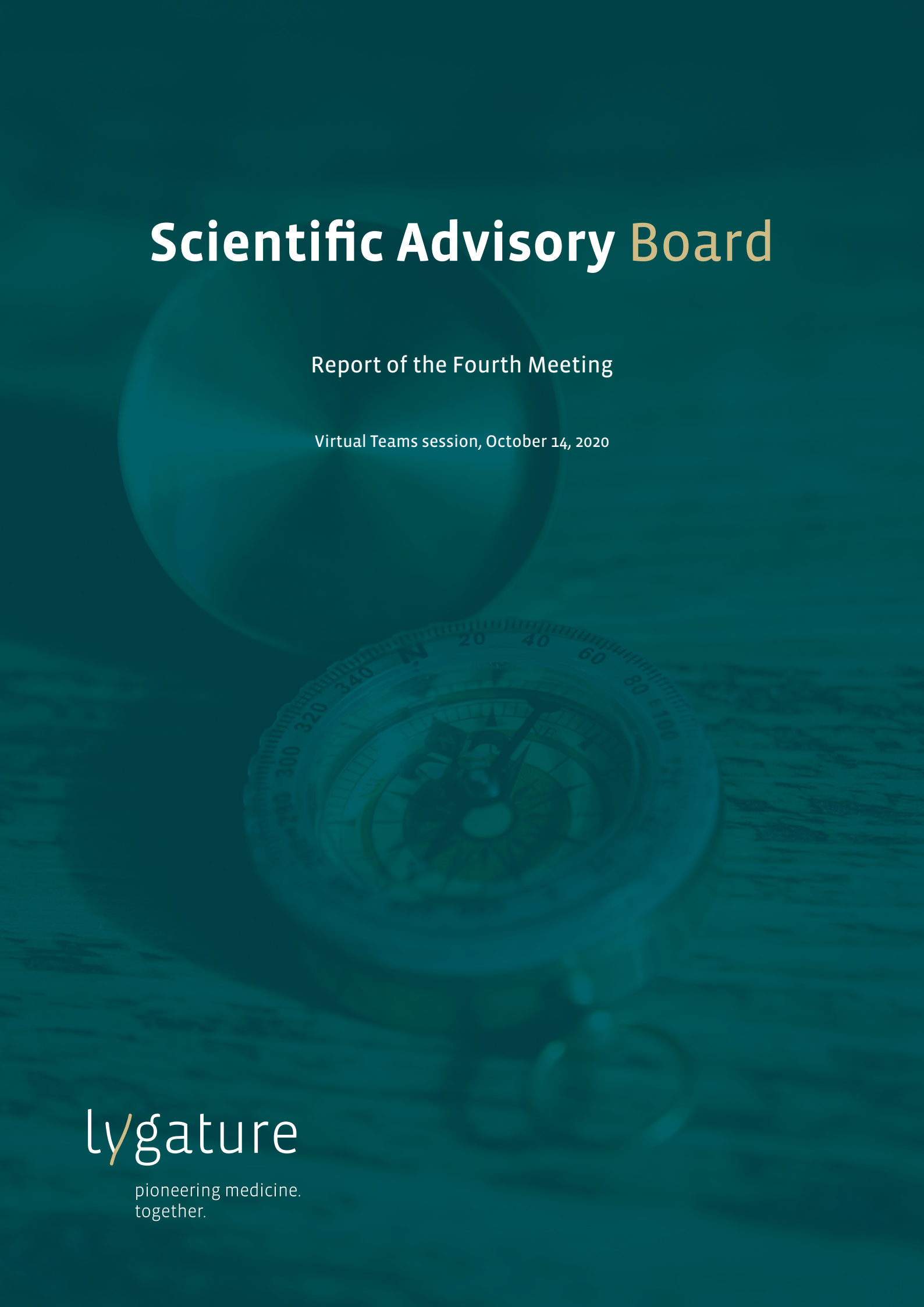
Scientific Advisory Board

Report of the Fourth Meeting

Virtual Teams session, October 14, 2020



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Approved by the SAB on November 24, 2020

1. Introduction

This report documents the Scientific Advisory Board's meeting on October 14, 2020. It details the tasks and composition of the Lygature Scientific Advisory Board (the SAB or 'the committee') and the agenda of the meeting, summarizes the main conclusions from the meeting, and provides a write-up of the discussion.
The report is publicly available on the Lygature website to inform Lygature stakeholders and other interested parties.

Tasks and composition

The fourth meeting of the Lygature Scientific Advisory Board was held on Wednesday, October 14, 2020. Due to the COVID-19 pandemic, the meeting was held virtually via Microsoft Teams.

The SAB is appointed by the Lygature Board of Directors. Its task is threefold:

1. On an annual basis, to advise on the coherence of Lygature's project portfolio, provide feedback, and identify opportunities for cross fertilization between projects in the various domains.
2. To provide input on the development of new public-private initiatives from an international perspective, building on the strengths of the Dutch Life Sciences & Health sector.
3. On an ad hoc basis, to review project proposals before submission by Lygature to various consortia funders (e.g. Bill & Melinda Gates Foundation, Japanese GHIT fund).

Collectively, the members of the SAB span three dimensions of Lygature's activity: scientific discipline (medtech, pharma, regulatory), geographic scope (national, international), and organizational structure (public, private).

Attendees

SAB members present in the meeting were:

- Daan Crommelin (Chair), Professor Emeritus of Biopharmaceutics at Utrecht University
- Rob Williams PhD, Chief Drug Development Scientist at the Centre for Drug Development, Cancer Research UK
- Matthias Gottwald PhD, former Head of R&D Policy and Networking at Bayer AG Pharmaceuticals Division
- Laurent Degos MD PhD, Professor Emeritus of Hematology at the University of Paris Diderot Hospital Saint Louis Paris, founder and first President of Haute Autorité de Santé, and past Vice President of the Pasteur Institute and Curie Institute
- Sjaak Deckers PhD, Venture Partner at NLC Health and CEO of Microsure
- Tomas Salmonson PhD, partner at Consilium Salmonson & Hemmings, former chair of the Committee for Human Medicinal Products at the European Medicines Agency

The meeting was also attended by Ton Rijnders, former General Director of Oncode Institute (among other appointments), who was appointed by the Lygature Board of Directors as the new SAB chair to replace Daan Crommelin, who is stepping down due to retirement.

From Lygature, Jon de Vlieger, Alexander Duyndam and Jorg Janssen joined the meeting. Bert Leufkens was unable to attend due to a planned holiday.

At the end of the meeting, Daan Crommelin and Matthias Gottwald, both of whom are stepping down from the SAB due to retirement, said their goodbyes. In the coming year, the SAB will be expanded, with a special focus on enhancing its diversity and inclusiveness.

Agenda

Due to the virtual nature of the meeting, the agenda was shortened and divided into two sessions:

1. Update on progress since last year's SAB meeting and the impact of COVID-19 on Lygature.
2. Discussion session on trends and developments in the European Life Sciences & Health sector.

2. Update on progress since last year's SAB meeting

The committee was updated on progress made by Lygature since the previous SAB meeting in September 2019.

Steady growth in 2019 continued into 2020, as seen for example by the number of full-time employees (FTEs) active in Lygature's portfolios and strategic alliances. In line with the strategic plan, dynamics in its portfolios and alliances were clearly visible – for example, the merging of various data infrastructure projects into the strategic alliance with Health-RI.

When the COVID-19 pandemic hit in March 2020, a comprehensive scenario analysis was executed to assess the impact on Lygature's various projects and alliances, as well as the impact on Lygature itself. This analysis not only helped to cope with the challenges faced by the projects, the approach used was also adopted by projects outside the Lygature portfolio. Overall, the negative impact of the pandemic was greatest for clinical trials. At the same time, in the data domain the urgency for sharing data and samples became even more evident and gained further traction. Six months into the pandemic, the impact is less severe than anticipated in the Spring, partly thanks to risk mitigation measures put in place as a result of the early analysis. Overall, the impact on Lygature's operations has been manageable, and the pandemic has even had some positive effects (see discussion session). Observational trials have already picked up better than previously expected.

An update was also provided on the steps taken in organizational development requested during last year's SAB meeting. The committee applauded the approach to people development and expressed its appreciation that this has been continued, especially during these challenging times.

3. Trends and developments

The discussion on trends and developments resulted in the following observations and advice in five areas:

a) The impact of the COVID-19 pandemic is huge, but it has positively affected public-private collaboration in Europe – ways will be found to collaborate with the UK after Brexit
b) People with personal experience in health challenges are increasingly included in setting research priorities – this can be taken to a next level
c) Innovation in the regulatory system is needed to adapt to developments in advanced therapy areas as well as in the use of artificial intelligence (AI)
d) The inter-institutional sharing of data, for example, in multicenter trials, has become more important than ever – data sharing in Europe can be improved
e) The positive learnings from the pandemic, including the adaptability of organizations and the lowered bar to reaching out to each other, should be nurtured for the future

These five areas are discussed in the sections below.

a) The impact of the COVID-19 pandemic is huge, but it has positively affected public-private collaboration in Europe – ways will be found to collaborate with the UK after Brexit

The COVID-19 pandemic has had a huge impact on innovation in the European Life Sciences & Health sector. Firstly, in terms of how quickly people and organizations were able to adapt to the changes and start developing solutions, from vaccines to medical devices. As a result of the need for cooperation to curb the pandemic, public-private collaboration in Europe is now seen in a much more positive light.
However, the pandemic's long-term impact on the funding landscape is still unclear. The immediate impact on charities has been massive, with a 30-50% drop in income in some cases. In addition, scientific societies face enormous challenges, because their business models have been turned upside down. The international congresses they normally organize are not bringing in the finances needed to run these societies. As a result, new interaction models between scientific disciplines and industry have to be found.
General preparedness for infectious diseases is top of the worldwide agenda, although it is too early to judge whether reprioritization of funding to therapeutic areas will happen. Post COVID, it is likely that challenges in global health, such as antimicrobial resistance (AMR) and neglected diseases, will be higher on the agenda, although extra funding for COVID-19 research might exhaust R&D budgets.
Brexit is also posing challenges to UK-European collaboration, but within the research community there is optimism about finding ways to collaborate after Brexit. These collaborations are considered too important to stop. Ideally, an agreed post-Brexit deal should include associate partnership for the UK in Horizon Europe.
In addition, regulators want to stay as aligned as possible on both sides. In the UK, several charities and the Association of British Pharmaceutical Industries (ABPI) have collectively called on the UK government to invest hundreds of millions of pounds to relieve the pressure on research funding budgets.
Given the current geopolitical situation, a case can be made for a strong European Life Sciences & Health sector in the post-Brexit era.

b) People with experience in health challenges are increasingly included in setting research priorities – this can be taken to a next level

People with direct experience in health challenges are increasingly being involved in the research and development process. Examples include patient advisory boards in consortia, and companies including patients in Target Product Profile (TPP) definition teams. The fact that education and training is offered to people with health challenges, for example, via the European EUPATI initiative, is of great help and adds to the effectiveness of their input. Additionally, the IMI PARADIGM project has provided a toolbox that combines recommendations, tools and background information to make patient engagement in medicine development easier for all parties involved.
Nevertheless, there is still room for improvement by taking patient engagement to the next level. Some companies do not take the patient perspective seriously in, for example, defining clinical endpoints to prove the value of an innovation. Also, on the regulatory side, further steps need to be taken to ensure that patient voices become a natural and essential part of medical innovation. It is good to see that Lygature has a proactive policy for meaningful involvement of people with direct experience in health challenges.

c) Innovation in the regulatory system is needed to adapt to developments in advanced therapy areas as well as in the use of artificial intelligence (AI)

The discussion on regulatory innovation included two important examples: ATMPs and AI.
Firstly, there is a clear need to adapt and create new approaches and regulatory pathways to prove, in a more sophisticated way, the effectiveness of regenerative medicine solutions, including advanced therapy medicinal products (ATMPs). While this area is growing, the (small) registration data packages, as well as regulations around manufacturing and quality control, are not well enough advanced. As stated in the meeting, 'the honeymoon with ATMPs is over'. An innovating regulatory environment, including adaptive pathways concepts, will be crucial in judging and regulating these innovations in the future.
The second area is the use of artificial intelligence in developing therapeutic interventions and solutions for patients. New techniques and algorithms used to analyze data, especially the large data sets generated by apps and gadgets, should not become 'black boxes' in registration procedures. The regulatory system needs an active strategy to keep pace with developments and ensure the ethical application of these technologies.
The Netherlands has historically held a strong position in regulatory science, further strengthened by the arrival of the European Medicines Agency in Amsterdam. This provides an ideal breeding ground for collaboration on regulatory innovation and is an opportunity that should not be missed.

d) The inter-institutional sharing of data, for example in multicenter trials, has become more important than ever – data sharing in Europe can be improved

COVID-19 has had a positive impact on the urgency and willingness to share data, creating a lot of traction in this area. At the same time, the pandemic and its impact on clinical trials was an eye opener, proving that data sharing on a European level needs to be better organized. Going beyond inter-institutional sharing of data, better sharing of data between countries is the next challenge.
The EMA's updated ICH-E9 guidance[1] on statistical principles in clinical trials and how to deal with unexpected events was very timely given the current circumstances and led to valuable discussions. There are big challenges in combining heterogenous sources and making effective use of the data sets generated. Consortia are needed here, and to be effective they should start locally by bridging the gap between the lab and the real world.
In addition, COVID-19 provided an enormous boost for trials@home concepts. The question here is: how can we learn from the generated data in ways other than those employed in classical clinical trials? Remote monitoring with devices such as Fitbits is promising, yet it remains a fact that real-world data concepts do not get the traction they deserve. The discussions on privacy, open access and the right to exploit results should focus on giving patients a key role in decision-making.
The Netherlands is a large and important player in the data infrastructure domain. Through Health-RI it can further extend this position and connect with similar initiatives in other countries.

e) The positive learnings from the pandemic, including the adaptability of organizations and the lowered bar to reaching out to each other, should be nurtured for the future

One of the positive aspects of the COVID-19 pandemic - increased adaptability - has already been highlighted above. Visible across many different sectors, it is proof that in times of real need, working towards solutions together is possible.
The use of videocalls made it much easier to connect with others and lowered the bar to quickly reaching out to various levels in organizations, something that was much more difficult in pre-COVID times. For example, finding matches in technology transfer discussions has improved significantly. While virtual meetings cannot replace true face-to-face meetings, they certainly are efficient in some ways.
These and other positive learnings from the pandemic should definitely be nurtured for the future.

[1] See https://www.ema.europa.eu/en/ich-e9-statistical-principles-clinical-trials

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