Association of the British Pharmaceutical Industry (ABPI) – Written evidence (COV0046)

About the Association of the British Pharmaceutical Industry (ABPI)
The ABPI exists to make the UK the best place in the world to research, develop and use new medicines. We represent companies of all sizes who invest in discovering the medicines of the future. Our members supply cutting edge treatments that improve and save the lives of millions of people. We work in partnership with Government and the NHS so patients can get new treatments faster and the NHS can plan how much it spends on medicines. Every day, we partner with organisations in the life sciences community and beyond to transform lives across the UK.

The ABPI welcomes the opportunity to engage with the Lords Science and Technology Committee's inquiry on the "Science of COVID-19". The following response builds on ABPI's Oral Evidence at the Select Committee session on the 29th June 2020.

Overview of industry R&D to combat COVID-19

1.1. The global R&D effort in response to the COVID-19 pandemic is unprecedented in terms of scale and speed. There are multiple companies and partnerships globally looking at the development of a COVID vaccine, as detailed by the International Federation of Pharmaceutical Manufacturers and Associations[1]. Some examples are also outlined in Annex A.

1.2. According to the WHO, there are 17 candidate COVID-19 vaccines in clinical evaluation and a further 132 candidate vaccines in pre-clinical evaluation[2]. Analysis published in Nature in April outlined that 72% COVID-19 vaccines in development were being developed by private/ industry developers, with the remaining 28% being led by academic, public sector and other not for profit organisations[3].

1.3. For commercial R&D, as of 1st July, global industry had 444 potential therapies to treat and/or prevent COVID-19 in development, with 379 of those in Pre-clinical, 13 in Phase I, 38 in Phase II, 8 in Phase III and 1 in pre-registration. Across the 2,327 clinical trials being conducted globally, there were 532 trials in severe patients, as well as 60 in asymptomatic, 263 in mild, 531 in moderate, 194 in critical and 717 in COVID-associated pneumonia[4].

1.4. In the UK, the Government have set-up a process for nationally prioritising and approving Urgent Public Health studies for COVID-19 research, with 48 studies set-up to date and over 120,000 participants recruited[5]. This

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[1] International Federation of Pharmaceutical Manufacturers & Associations. COVID-19 Hub [Internet]. 2020 [cited 2020 Jul 2]. Available from: https://www.ifpma.org/covid19/

[2] World Health Organisation. Draft landscape of COVID-19 candidate vaccines [Internet]. [cited 2020 Jun 9]. Available from: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

[3] Le TT, Andreadakis Z, Kumar A, Román RG, Tollefsen S, Saville M, et al. The COVID-19 vaccine development landscape. Nat Rev Drug Discov. 2020 Apr 9;19(5):305–6.

[4] Pharma Intelligence. Coronavirus - COVID-19 Coverage [Internet]. [cited 2020 Jul 2]. Available from: http://pharmaintelligence.informa.com/resources/key-topics/coronavirus

includes 8 commercial studies, sponsored by companies Roche[6], Gilead[7,8], Novartis[9,10], GSK[11], Synairgen[12] and RevImmune[13], focused on developing treatments for COVID-19. These commercial studies are exploring the use of monoclonal antibodies in Phase II (Otilimab) and Phase III (Toclizumab and Canakinumab), broad-spectrum anti-virals (Remdesivir) in Phase III and immunological agents (including kinase inhibitor Ruxolitinib) in Phase II and III.

1.5. These studies are being conducted in patients with:

- COVID-19 pneumonia and pulmonary related disease (Roche, Novartis and GSK)
- moderate or severe COVID-19 (Gilead and RevImmune)
- COVID-19 associated cytokine storm (Lilly and Novartis)
- high-risk patients (incl. those with co-morbidities such as diabetes) (Synairgen)

Obstacles to be overcome in the development of COVID-19 vaccines and therapies

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[5] National Institute for Health Research. Urgent Public Health COVID-19 Studies | NIHR [Internet]. [cited 2020 Jun 10]. Available from: https://www.nihr.ac.uk/covid-studies/

[6] National Institute for Health Research. Roche Urgent Public Health Study - A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER STUDY TO EVALUATE THE SAFETY AND EFFICACY OF TOCILIZUMAB IN PATIENTS WITH SEVERE COVID-19 PNEUMONIA [Internet]. [cited 2020 Jun 10]. Available from: https://www.nihr.ac.uk/covid-studies/study-detail.htm?entryId=282099

[7] National Institute for Health Research. Gilead Urgent Public Health Study - A Phase 3 Randomized Study to Evaluate the Safety and Antiviral Activity of Remdesivir in Participants with Moderate COVID-19 Compared to Standard of Care Treatment [Internet]. [cited 2020 Jun 10]. Available from: https://www.nihr.ac.uk/covid-studies/study-detail.htm?entryId=282026

[8] National Institute for Health Research. Gilead Urgent Public Health Study - A Phase 3 Randomized Study to Evaluate the Safety and Antiviral Activity of Remdesivir in Participants with Severe COVID-19 [Internet]. [cited 2020 Jun 10]. Available from: https://www.nihr.ac.uk/covid-studies/study-detail.htm?entryId=282007

[9] National Institute for Health Research. Novartis Urgent Public Health Study - Phase 3 randomised, double-blind, placebo-controlled multi-center study to assess the efficacy and safety of ruxolitinib in patients with COVID-19 associated cytokine storm. [Internet]. [cited 2020 Jun 10]. Available from: https://www.nihr.ac.uk/covid-studies/study-detail.htm?entryId=282417

[10] National Institute for Health Research. Novartis Urgent Public Health Study - Phase 3 multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of canakinumab on cytokine release syndrome in patients with COVID-19-induced pneumonia (CAN-COVID) [Internet]. [cited 2020 Jun 10]. Available from: https://www.nihr.ac.uk/covid-studies/study-detail.htm?entryId=282416

[11] National Institute for Health Research. GSK Urgent Public Health Study - A randomised, double-blind, placebo-controlled, study evaluating the efficacy and safety of otilimab IV in patients with severe pulmonary COVID-19 related disease. [Internet]. [cited 2020 Jun 10]. Available from: https://www.nihr.ac.uk/covid-studies/study-detail.htm?entryId=283089

[12] National Institute for Health Research. Synairgen Urgent Public Health Study - A randomised double-blind placebo-controlled trial to determine the safety and efficacy of inhaled SNG001 (IFN-β1a for nebulisation) for the treatment of patients with confirmed SARS-CoV-2 infection [Internet]. [cited 2020 Jun 10]. Available from: https://www.nihr.ac.uk/covid-studies/study-detail.htm?entryId=281317

[13] National Institute for Health Research. RevImmune Urgent Public Health Study - Recombinant InterLeukin-7 (CYT107) to Improve clinical outcomes in lymphopenic pAtients with COVID-19 infection 'ILIAD 7 trial' [Internet]. [cited 2020 Jun 10]. Available from: https://www.nihr.ac.uk/covid-studies/study-detail.htm?entryId=283184

2.1 The development of vaccines and therapies is a lengthy and expensive process, typically taking 10 years to produce a licensed vaccine[14]. During this period, multiple candidates are tested, with high failure rates. Many of the vaccine candidates which are currently being explored for COVID-19, are being developed at unprecedented speed. Vastly condensed timelines have been enabled by cross sector collaboration, and close working with regulatory agencies, and governments around the world. Obstacles however remain which will need to be overcome.

2.2 For any new vaccine or treatment, there are some common obstacles and challenges:

- For vaccines and agents being developed in early and pre-clinical stages, it will be essential to ensure that the highest patient safety standards are maintained whilst accelerating the transition to clinical trials.
- COVID-19 clinical trials need to be optimised in terms of trial design, data collection and sharing and patient recruitment, to ensure they are adequately powered to generate the evidence needed.
- Funding and resources need to be available and prioritised to support COVID-19 research efforts alongside research into other diseases – COVID-19 R&D potentially comes at the expense of research into other disease areas.
- In order to identify gaps in R&D and prioritise funding and resource, national decision-makers need a thorough understanding of current COVID-19 R&D efforts. Research findings need to be accessible and available rapidly, to ensure decision-making is supported by a robust evidence-base. This approach will also help avoid duplicative R&D efforts.
- Patient and public involvement and engagement needs to be embedded in COVID-19 R&D to ensure the development of vaccines and treatments has real-world relevance and truly addresses unmet needs across society, especially in BAME communities who are disproportionately impacted by COVID-19.
- The need for healthcare delivery to continue addressing ongoing COVID-19 burden, which may detract resources and research staff away from R&D.

Obstacles for vaccine development and uptake

2.3 Conventional vaccine development typically follows a linear sequence of steps, with multiple pauses for data analysis or manufacturing-process checks, however in order to rapidly develop a vaccine for COVID-19, new processes and efficiencies will be required[15]. Research and development of multiple vaccines will be needed as many will fail during the development process and multiple vaccines may be needed clinically for different populations.

2.4 These are some of the obstacles and challenges that need to be overcome:

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[14] Association of the British Pharmaceutical Industry. How are vaccines researched and developed? [Internet]. 2020 [cited 2020 Jun 18]. Available from: https://www.abpi.org.uk/new-medicines/vaccines/how-are-vaccines-researched-and-developed/

[15] Le TT, Andreadakis Z, Kumar A, Román RG, Tollefsen S, Saville M, et al. The COVID-19 vaccine development landscape. Nat Rev Drug Discov. 2020 Apr 9;19(5):305–6.

- Information is limited on the specific SARS-CoV-2 antigen(s) used in vaccine development and specific animal models need to be developed to understand the virus and disease.
- Protection induced by vaccination will be dependent on different factors such as the selected vaccination platform and technology and routes of vaccination. Further research is needed to understand how these factors can affect the efficacy of potential vaccines.
- Attrition rates for vaccine development are high, so careful evaluation of effectiveness and safety will be needed to ensure potential COVID-19 vaccines have the greatest chance of successful development and licensing.
- It will be important to ensure coordination of vaccine manufacturing and supply capability and capacity to meet demand.
- Strong national and international coordination and cooperation between Governments and industry will be needed to ensure that promising late-stage vaccine candidates can be manufactured in sufficient quantities and equitably supplied to all affected areas. Industry has significant 'know how' of manufacturing and supplying vaccines at enormous scale.
- For future COVID-19 vaccination programmes to be effective, public trust and confidence will be essential. Public engagement and transparency across R&D efforts is required to earn this trust.

Obstacles for therapy development

2.5 Similarly to vaccine development, it can take 10-12 years to develop a new medicine, with many candidates failing during clinical development[16]. There are two categories of therapies being investigated: repurposed existing medicines and novel COVID-19 medicines. These are some of the obstacles and challenges that need to be overcome:

- The research needs to answer the 4Rs (right patient, right medicine, right dosage, right time).
- It is possible that none of the current therapeutic interventions being trialled or recommended will prove beneficial, hence innovation cannot be stifled. With a wealth of avenues being explored nationally and internationally, duplication of efforts and limitations on funding and resources available will be a challenge.
- Repurposing existing medicines for COVID-19, such as Remdesivir (a broad-spectrum anti-viral agent), may offer a de-risked and shorter development pipeline, however the safety and effectiveness for treatment of COVID-19 still needs to be explored. Furthermore, the lack of specificity of broad-spectrum anti-viral agents can contribute to the emergence of more virulent strains.
- Novel and innovative COVID-19 therapies will take longer to develop than repurposed existing medicines due to the need to advance through the R&D pipeline vigilantly and establishing safety profile. Whilst novel COVID-19 therapies are at higher risk of failing in R&D and will take longer, targeted treatments potentially offer greater benefit as towards treating patients with COVID-19.

[16] Association of the British Pharmaceutical Industry. How are new medicines developed? | ABPI [Internet]. 2019 [cited 2020 Jun 10]. Available from: https://www.abpi.org.uk/new-medicines/medicine-pricing-in-the-uk/how-are-new-medicines-developed/

Key considerations for overcoming these obstacles

2.6 In order to support the rapid and robust development of COVID-19 vaccines and therapies and overcome the obstacles outlined – the following considerations are key.

- UK Urgent Public Health studies must have robust peer-review of findings and rapid publication of results. This will add to the growing evidence-base.
- Any learnings from Urgent Public Health studies must be shared with the rest of the R&D community to enable other research (COVID or otherwise) to benefit.
- COVID-19 is a global problem which requires a global solution. The UK government must have a strategic and coordinated approach, that harnesses the expertise of industry, academia and the public sector, and takes advantage of the UKs strengths to ensure we make an effective and complementary contribution to the global effort.
- The effects of COVID will be here for a number of years, it's critical that the UK learns from the successes and challenges of the initial COVID research effort to ensure the UK restarts non-COVID-19 research, recovers from the pandemic and remains a leader in research.
- Industry has decades of experience of research, development, manufacturing and supply of medicines. Finding a potential medicine is just one step in the getting a reliable medicine to patients and the UK must link in with industry and integrate this broad expertise on an ongoing basis.

3 July 2020

Annex A: Case studies of industry R&D efforts to combat COVID-19

Case study 1: AstraZeneca supports the development of a novel COVID-19 vaccine

In the UK, AstraZeneca has partnered with the Government to support the development and distribution of Oxford University's vaccine (formerly ChAdOx1 nCoV-19 and now known as AZD1222). This vaccine uses a viral recombinant adenovirus vector, containing the genetic material of SARS-CoV-2 protein. This was chosen to generate a strong immune response from a single dose, without causing an ongoing infection in the vaccinated individual. AstraZeneca is working on a number of global agreements, to ensure equitable supply of the potential vaccine. Current sourced capacity totals one billion doses through 2020 and into 2021, with agreements to supply 400 million doses[17].

Case study 2: Pfizer working in partnership to develop potential therapy and vaccine for COVID-19

Pfizer are applying their drug development expertise at a global scale, to search for potential vaccines and therapeutics for COVID-19. In terms of vaccines, Pfizer are working in partnership with BioNTech, to develop an mRNA vaccine

[17] AstraZeneca advances response to global COVID-19 challenge as it receives first commitments for Oxford's potential new vaccine [Internet]. [cited 2020 Jun 10]. Available from: https://www.astrazeneca.com/media-centre/press-releases/2020/astrazeneca-advances-response-to-global-covid-19-challenge-as-it-receives-first-commitments-for-oxfords-potential-new-vaccine.html

candidate, BNT162, which is now being tested in clinical trials[18]. Pfizer are also actively scaling up their manufacturing capacity and distribution infrastructure in order to ensure the potential global supply of millions of vaccines by the end of 2020 and into 2021.

Building on their research efforts against the SARS in 2003, Pfizer has also been able to identify a lead protease inhibitor[19], which has shown antiviral activity against SARS-CoV-2. Subject to positive completion of further pre-clinical testing, Pfizer are looking to start a clinical trial of this lead molecule in Q3 in 2020.

Case study 3: MSD are building on expertise in responding to public health outbreaks to help combat COVID-19

MSD are applying their expertise in both vaccine and anti-viral development, alongside their experience gained in responding to the Ebola outbreak, to the current pandemic. They are pursuing multiple efforts, including research across basic science, treatment, and prevention to help combat COVID-19. They have announced three significant initiatives to help combat COVID-19[20]. These include two agreements to develop vaccines and a collaboration to advance the development of an oral antiviral candidate. In the UK, MSD are also supporting Genomics England through their industry consortium to help understand the role of the genome in the response to COVID-19. They are also supporting the Vaccines Manufacturing and Innovation Centre (VMIC) in Oxford to develop the UK's manufacturing capacity and ability to respond to pandemics[21].

Case study 4: Lilly collaborates to accelerate research of existing therapies for use against COVID-19

Lilly's Baricitnib is an immune modulating therapy which is being tested in Phase III clinical trials for hospitalized COVID-19 patients[22]. The potential application of baricitinib in the context of COVID-19 was first identified by a UK start-up, BenevolentAI, who utilised their AI and machine learning platform to trawl libraries of existing medicines for prospective therapies. In addition to its own research efforts, Lilly is also supporting the University of Cambridge with their TACTIC-R trial[23], with is one of the UK's Urgent Public Health studies. This study is one of those given priority urgent public health status by the UK Government.

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[18] Pfizer. Pfizer and BioNTech Start Human Trials as Part of Global COVID-19 Vaccine Development Programme [Internet]. pfizer.co.uk. 2020 [cited 2020 Jul 2]. Available from: https://www.pfizer.co.uk/pfizer-and-biontech-start-human-trials-part-global-covid-19-vaccine-development-programme

[19] Pfizer. Pfizer Advances Battle Against COVID-19 on Multiple Fronts [Internet]. pfizer.co.uk. 2020 [cited 2020 Jul 2]. Available from: https://www.pfizer.co.uk/pfizer-advances-battle-against-covid-19

[20] MSD. MSD Announces Multiple Scientific Efforts to Combat COVID- 19 [Internet]. 2020 [cited 2020 Jul 2]. Available from: https://www.msd-uk.com/news-room/index.xhtml

[21] The Vaccines Manufacturing and Innovation Centre [Internet]. VMIC UK. 2020 [cited 2020 Jul 2]. Available from: https://www.vmicuk.com

[22] Eli Lilly and Company. Lilly Begins a Phase 3 Clinical Trial with Baricitinib for Hospitalized COVID-19 Patients [Internet]. Eli Lilly and Company. 2020 [cited 2020 Jul 2]. Available from: https://investor.lilly.com/news-releases/news-release-details/lilly-begins-phase-3-clinical-trial-baricitinib-hospitalized

[23] National Institute for Health Research. Multiarm Therapeutic study in pre-ICU patients admitted with COVID-19 - Repurposed Drugs [Internet]. 2020 [cited 2020 Jul 2]. Available from: https://www.nihr.ac.uk/covid-studies/study-detail.htm?entryId=282213