Repurposed Drugs in the Fight Against COVID-19

July 7, 2020

By Patricia Folkins, Melanie Szweras and Nicole LaBerge

Repurposing existing or abandoned drugs is an attractive route to finding a treatment and cure for COVID-19 quickly. To initiate such efforts, the World Health Organization (WHO) has set up a research network with the aim of identifying drug therapies and combinations that could be used to treat COVID-19.[1] Such drugs have already undergone safety, efficacy, and toxicity studies for treatment of a different disease. Repurposing drugs presents pharmaceutical companies with new sales and marketing opportunities, is budget conscious, and faster than developing a drug from scratch. Past examples include minoxidil, sildenafil (Viagra™), and thalidomide.

Within the last few years, roughly one third of drug approvals have been based on repurposed compounds. Annually, repurposed drugs are estimated to comprise one quarter of pharmaceutical revenues.[2] Several open-source platforms have been set-up to support initiatives dedicated to repurposing drugs to treat and cure COVID-19. For instance, the National Center for Advancing Translational Sciences (NCAT) has launched an OpenDataPortal designed to assist scientists with sharing COVID-19-related drug repurposing data and experiments for all approved drugs[3] Excelra has launched a COVID-19 Drug Repurposing Database, and the Chemical Abstracts Service (CAS) has released information relating to effective agents against RNA viruses including SARS-CoV and MERS-CoV.[4] Such venues provide great opportunity for sharing and identifying potential candidates for drug repurposing.

Repurposing drugs is further incentivized through the granting of intellectual property (IP) rights, such as patents. Patents are a form of IP in which an Applicant is granted an exclusive right to a new, useful, and non-obvious invention for 20 years. The rights granted by a patent allow the owner to, subject to regulatory approval and freedom to operate clearance, exclusively sell their invention for the set period of time. Patents covering drugs are pivotal to business strategy, as they can be used to attract investors and be used in marketing. They also foster cross-licensing opportunities and further collaboration.

Drugs can be protected by different types of patent claims, including composition of matter and use claims. To obtain a patent for the drug's repositioning, a new and non-obvious innovation for that drug must be identified. For example, this could include alternative crystal forms, salt forms, formulations, alternative delivery methods, stereoisomers, or deuterated analogues. Further examples of possible patent claims for existing drugs that are relevant to the present COVID-19 pandemic, are claims to new uses of the drug to treat a specific disease or diseases and claims to new combination therapies. Such innovations may be patentable if the discovery is novel, unexpected, and potentially beneficial. This means the new use or combination must not have been disclosed or suggested prior to filing a patent application for the new innovation and there must be some evidence to support that the drug or combination has potential as a therapeutic to treat the new indication (i.e. COVID-19).

Regulatory matters are another legal aspect that must be considered when repurposing a drug. In Canada, a repurposed drug must be filed as a New Drug Submission (NDS) with Health Canada.[5] The NDS filing requires information regarding the drug's safety, efficacy, quality, and results from preclinical and clinical trials whether completed in Canada or elsewhere. The applicant must also disclose information relating to the drug's production, packaging and labelling details, along with information on therapeutic claims and side effects. Health Canada then evaluates the data along with information the sponsor provides to health care practitioners and consumers such as label and product brochures. A Notice of Compliance (NOC), along with a Drug Identification Number (DIN), is issued provided the drug's benefits outweigh its risks and Health Canada is satisfied that patent(s) that may be listed on the Patent Register for the repurposed drug's original patent holder (if any) have been addressed (i.e. are either not valid or not infringed).[6] Once an NOC is issued, the sponsor can then market the drug in Canada. In response to COVID-19, the Minister of Health has issued an *Interim Order Respecting Clinical Trials for Medical Devices and Drugs Relating to COVID-19*. Under this order, marketed drugs may be subjected to an accelerated approval process if they have already been granted an NOC or DIN for a previous indication.[7]

In the United States, the *Food, Drug, and Cosmetics Act* outlines three regulatory approval pathways allowing approval of distinct classifications of drugs. Of these three, section 505(b)(2) is relevant to drug repurposing.[8] This provision allows the applicant to rely upon studies the Federal Drug Administration (FDA) previously considered in evaluating the drug's safety, saving both time and money[9] Further, to receive a full 505(b)(2) approval, the applicant must identify what is new about the drug, for example, a new administration route or disease target.[10]

In Europe, a similar approval pathway is available through the European Medicines Agency (EMA) under Article 10a of Directive 2001/83/EC.[11] If there have been no changes to the reference drug and it has been in well-established medicinal use within the Union for at least 10 years with recognized efficacy and an acceptable level of safety, the applicant may rely on published scientific literature to replace results of some pre-clinical and clinical trials. If there have been changes to the reference drug, then an Applicant cannot rely on Article 10a for expedited approval. In this case, studies supporting the repurposed drug must be tailored to the differences from reference drugs. Currently, the EMA is actively engaged with 144 potential COVID-19 treatments. [12]

Of the many therapeutics being investigated for treatment of COVID-19, several are already on the market for the treatment of other indications. Potential candidates range from small-molecules to biologics such as antibodies. Protease inhibitors, Lopinavir-Ritonavir (Kaletra™ or Aluvia™) used to treat human immunodefiency viruses (HIV) are being considered.[13] Small molecule combination therapies are also being investigated, for example, Danoprevir (Ganovo™), co-administered with Ritonavir.[14] Dexamethasone, a steroid-based medication used to treat asthma and rheumatoid arthritis is also being evaluated.[15] Research efforts to pursue Hydroxycholoroquine suflate (HCQ) used to treat malaria and autoimmune diseases have been halted due to results indicating the drug does not benefit patients with COVID-19.[16] Biologics being examined include monoclonal antibodies such as, Tocilizumab (Actemra™) that is used to treat rheumatoid arthritis, alone and in combination with Favipiravir (Avigan™) that is used to treat influenza.[17]

Repurposing drugs in the fight against COVID-19 is an attractive option for researchers and pharmaceutical companies. Entities pursuing such efforts should be aware of existing intellectual property rights and regulatory aspects to ensure treatments can transition from bench to bedside as quickly as possible.

---

1 https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments

2 Naylor S, Kauppi DM, Schonfeld JP. Therapeutic drug repurposing, repositioning and rescue part II: business review. Drug Discovery World. 2015;16(2):57–72.

3 https://ncats.nih.gov/preclinical/repurpose

4 https://www.excelra.com/covid-19-drug-repurposing-database/

https://www.cas.org/covid19

5 https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/fact-sheets/drugs-reviewed-canada.html

6 *Patented Medicines (Notice of Compliance Regulations)*, SOR/93-133.

7 https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/interim-order-respecting-clinical-trials-medical-devices-drugs.html

[8] 21 USC § 355 (2012).

[9] 21 USC § 355(b)(2) (2012).

[10] https://www.fda.gov/media/72419/download

[11] https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/european-medicines-agency-pre-authorisation-procedural-advice-users-centralised-procedure_en-0.pdf

[12] https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines-covid-19

[13] https://covid19-evidence.paho.org/handle/20.500.12663/1087

[14] https://clinicaltrials.gov/ct2/show/NCT04291729

[15] https://www.bbc.com/news/health-53096736

[16] https://www.who.int/news-room/detail/04-07-2020-who-discontinues-hydroxychloroquine-and-lopinavir-ritonavir-treatment-arms-for-covid-19

[17] https://www.genengnews.com/a-lists/vanquishing-the-virus-160-covid-19-drug-and-vaccine-candidates-in-development/2/