COVID-19 presents a clear and present danger to millions of lives. Healthcare systems around the world are not scaled for the vast influx of patients. Thousands have died; the lives of millions are threatened. We need COVID-19 treatments and vaccines, now.

Fortunately, multiple investigational treatments for COVID-19 are available. But we are concerned that patients will not receive them in time due to the traditional, slow process of developing and authorizing new medicines.

Traditionally, highly selected patients are randomized in clinical studies to receive either the investigational therapy or placebo, withholding a promising therapy from half of study patients while all are in need. It can take years to yield results, regulatory approval and broad patient access. During this time, patients outside studies do not have access to a potentially life-saving new treatment. They are literally left behind.

We believe that in the current crisis, this traditional approach is inadequate – if not unethical – as countless lives are at stake, now.

We request a dramatically accelerated approach of patient access, development, and approval of investigational therapies in a pandemic emergency. Patients—the ultimate stakeholders in healthcare—must get access early on. Our proposed approach—APANDEMIC—is fast, pragmatic, and feasible through digital technology. Importantly, it must be benchmarked against the cost of “doing the same thing over and over again” and accepting that thousands will die that our approach could save.

Our proposal can be implemented in five steps.

**Step 1 – Identify Suitable Investigational Therapies**
Investigational therapies with a strong rationale of efficacy against COVID-19 should be considered suitable for APANDEMIC, as long as there is no evidence predicting major safety issues. Suitability depends on the strength of the biological rationale and existing knowledge about the compound’s efficacy and safety.

Repurposing therapies that already are in development or approved for another disease presents particularly compelling opportunities to rapidly advance with an established safety database.

**Step 2 – Enable Immediate Patient Access**
To seize the prospective upside of saving those patients whose lives are at an immediate risk, every physician at the frontlines should be provided with the suitable therapies. They should be entrusted to make appropriate real-world decisions focused on their patients’ need and based on our quickly evolving knowledge about COVID-19.

**Step 3 – Minimize Safety Risk for Patients**
To minimize the risk of unpredicted adverse events, the data of every patient receiving investigational therapies must be monitored constantly and in real time, using digital technology. This technology already exists and can be adopted to this effort quickly. A virtual command center can flag safety signals the moment they occur.

An independent safety monitoring board would have the ability to quickly redefine the target patient population or discontinue access to a therapy should the evolving data on benefits and risk warrant such action.

**Step 4 – Assess Efficacy Continuously and On Time**
Efficacy measures should also be tracked continuously, using the same technology applied for safety recording. This way, our knowledge and confidence in the efficacy and safety gradually increases, day by day.

To know whether and in which patients an investigational therapy is effective, multiple indicators of efficacy will be combined and evaluated. They include patient outcomes after early vs. late start of treatment, high vs. low dosing, short vs. long therapy duration as well as in patients who were not able to get an investigational therapy.

We have to get away from establishing efficacy only through traditional thinking – efficacy that is determined on one single day and far in the future once the trial database has been locked. We never do this to evaluate safety. Central committees continuously monitor all safety data from day 1 and can change the design of or halt a study –
because patient lives are at stake. This is exactly why also, we must rethink how to establish efficacy in this emergency situation. Because right now, thousands of lives are at stake!

Statistical methods for evaluating real-world data in real time exist, including so-called time-series and Bayesian inference. Traditional thinking, however, considers these mathematical and statistical analyses merely exploratory and hypothesis-generating.

We do not agree and believe that the continuous analysis of compounded efficacy parameters from big data sets of increasing patient numbers and follow-up, will eventually increase confidence to a point where this confidence equals or is similar to traditional standards. At that point, we will not only have reached the comfort many associate with traditional methods but also, will have protected the lives at stake now, our primary goal.

**Step 5 – Authorize Upfront and Adjust Real-Time**

We believe that the regulatory system for global emergencies must enable, encourage and incentivize promising investigational therapies to be immediately and broadly provided to patients in need. Regulatory authorities (and/or trusted proxies like WHO or CDC) must get the same real-time access to the evolving data that is collected by the non-profit or for-profit sponsor of the APANDEMIC approach.

This way, authorities can conditionally approve an investigational therapy upfront. They have the authority and ability to immediately redefine the suitable patient population or even halt patient access on the basis of incoming real-time, real-world evidence. Monitoring of all treated patients must continue after the crisis.

A precedent of this patient access approach has already been implemented during an epidemic crisis in Germany. In 2011, a toxic *E. coli* bacteria infected thousands of people, overwhelming hospitals, ICUs and staff. Addressing the urgent need of patients and the medical community, Alexion Pharmaceuticals started an access program for an investigational therapy that had promising clinical data for this medical application and a safe track record in another disease for which the therapy was already approved. Patient access was initiated within 48 hours, a formal clinical program in 6 weeks, and efficacy and safety were monitored and reviewed real-time and from the start – all contributing to end the 2011 crisis.

We call upon leaders across medicine, life sciences, technology and government to focus on how to maximize the number of lives saved through an APANDEMIC or similar approach. We ask proponents of traditional methods to join thinking outside the box and advance together with the speed of viral replication.

Because one traditional wisdom always applies, “*We are not only responsible for what we do, but also for what we do not do.*”

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We speak as concerned citizens, scientists and physicians and do not represent the opinion of any organization we are member of.

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