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Pursue regulatory innovation for outreach

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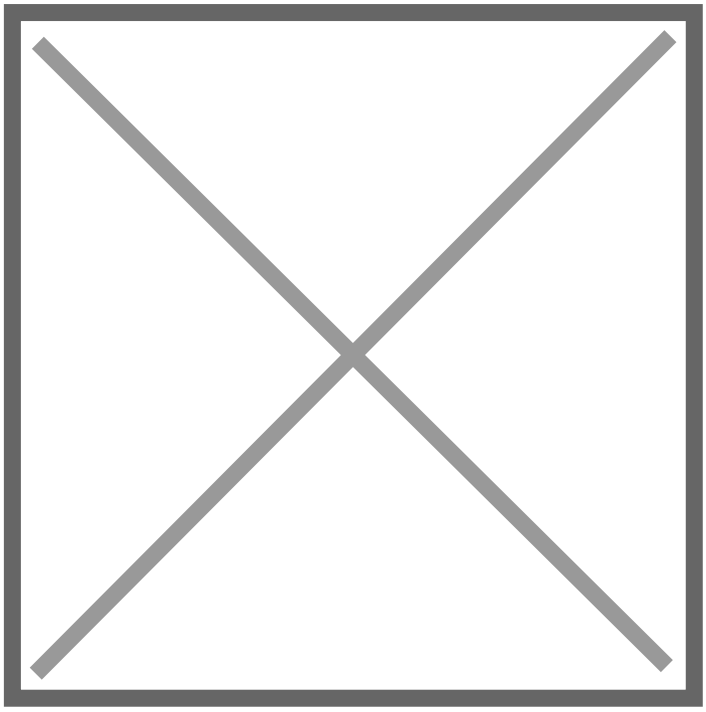

Dr Kiran Mazumdar-Shaw
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The author has been named among TIME magazine's 100 most influential people in the world. Under her stewardship, Biocon has evolved from its inception in 1978 as an industrial enzymes company to a fully integrated biopharmaceutical enterprise encompassing a portfolio of products and services with research focus on diabetes, oncology and auto-immune disease. During this transition, Biocon established two subsidiaries Syngene and Clinigene.

In recent times, regulators have adopted an inflexibly defensive mindset and seem to be looking for that perfect pill that scores a 100 on efficacy and a zero on side effects. As regulators keep raising the bar for approval, the drug pipeline is diminishing to a trickle, even while discovery research and drug development is gathering pace. On one hand, pharmaceutical companies are battling escalating costs, extended time to market, and a high failure rate in this risk-averse regulatory climate. On the other hand, the medical needs of millions across the world remain unmet.

Even when a drug is approved, healthcare systems do not support it unless pharma companies can rationalize the risk-benefit ratio to patients to an extent that justifies the drug's high cost. To get an idea of what it takes to develop a new drug, we need to consider the rocketing costs in terms of both time and money. A study by the Tufts Center on the study of drug development puts the average time and cost taken to develop a drug at eight years and anywhere between $1.2-2 billion.

If a new drug merely shows incremental benefits, as many drugs do, it fails the test of "acceptable risk-benefit profile" and healthcare systems may not reimburse insurers. Thus, patients who need the drug the most, do not get access. It is only when a drug fulfills a hitherto unmet need such as Yervoy (Ipilimumab), the first agent ever proven to improve survival in advanced metastatic melanoma, that the drug can end up on the right side of the risk-benefit ratio desired by regulators and command a premium price from healthcare systems and insurers.

In this risk-averse environment, we need to address the regulatory challenge in an innovative way. We need to pursue regulatory innovation that acts as the catalyst for ensuring that novel drugs, based on scientific advances, reach patients quickly. We need an approach that helps pharma companies reduce the cost of drug development and recover the cost of innovation, while providing access to patients who will benefit from such novel therapeutics at acceptable cost.

I believe that developing and incorporating biomarkers and companion diagnostics in the drug development process can help us attain these objectives. Companion diagnostics – the use of genetic, proteomic, or gene markers – can help pharma companies develop and deliver more effective and personalized medicines at a lower cost.

We can leverage bio-markers and companion diagnostics at the clinical trials stage, screening patients to guard against accepting subjects who may increase the drug's risk profile and selectively including those who can benefit. Selecting high responders in a drug trial can help reduce the trial size, enhance the trial outcome, contain costs, and, create a better reimbursement model. A pharma company can add clinical markers in the clinical design that address risks upfront – say microvascular or renal biomarkers in a diabetes drug trial – to admit or exclude certain patients. The patients enrolled in the trial are, therefore, likely to show better response with reduced side effects, and since the tailored treatment allows a better view of the outcome, fewer patients may need to be included for the trial.
When the safety risk is lowered in this manner and the efficacy profile enhanced, the outcome of the trial can be statistically significant through the extraction of augmented data. Given the reluctance of health systems in reimbursing high-priced drugs that provide only marginal benefit, such strong data can provide a much stronger risk-benefit rationale.

Combining drug development with a companion diagnostic, I believe, will help to lower regulatory hurdles and speed up the process. For instance, most recently, the USFDA gave a swift nod – in just over three months – to Roche's Zelboraf (vemurafenib), when it was presented for approval with its companion BRAF V600 mutation test. Compare this with approval challenges that many cancer drugs face from clinical data drawn from enrolling "all comers", something that most companies prefer to do to increase the market opportunity but fail in terms of statistical outcomes.

Not only does such an approach reduce the size and cost of regulatory clinical trials, it also enables insurers to reimburse healthcare providers for the treatment. Take Herceptin as a case in point. When it was proven through its companion diagnostic that HER2-positive breast cancer patients responded better to Herceptin, the drug was targeted at only such patients and won both regulatory approval and reimbursement support from healthcare systems.

With the deployment of companion diagnostics gaining traction, pharmaceutical companies need to develop their proprietary diagnostic tools in tandem with drug development. Such a strategy will allow the company to own the tool's intellectual property (IP) and will pay significant dividend in terms of speedier regulatory approval, increased market penetration and enhanced revenue whilst also protecting the IP of the drug itself.

When pharma companies are unable to stratify and select suitable patients, a drug under trial can show a risk profile that is unfairly attributable to it. Companion diagnostics can help pharma companies assess risk in a more meaningful way and ensure that drugs can be made speedily accessible and more affordable to patients.