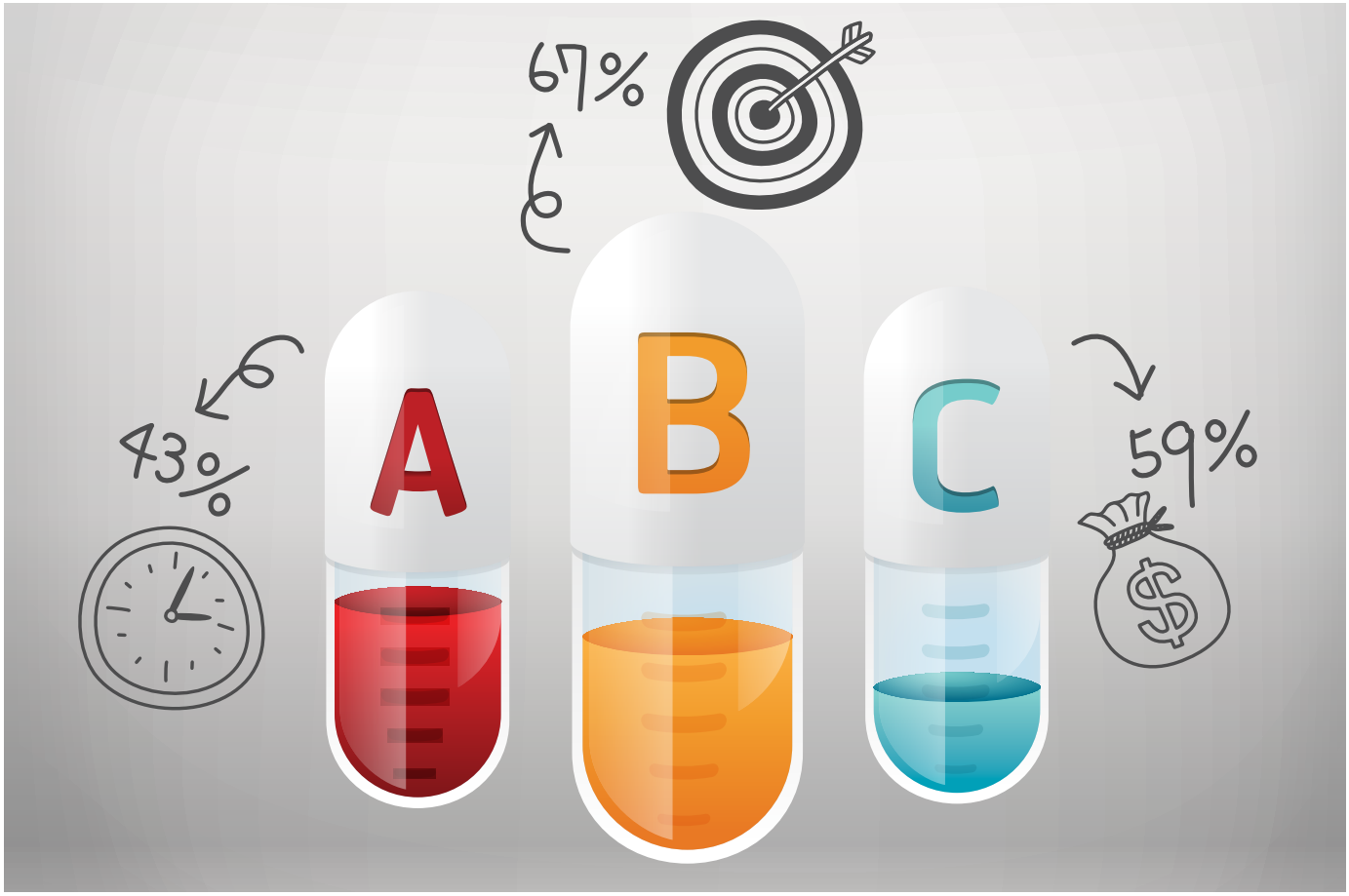

ILLUSTRATIONS: THINKSTOCK

A QUESTION OF VALUE

When assessing the value of breakthrough drugs, Health Economics & Outcomes Research can help generate the economic profile of a new therapy. **Mohan Bala** and **Meghan Gallagher** explain its use

In medical care decision-making, the definition of "value" is evolving. The value of new medicines used to be assessed solely on clinical benefit, but now the definition of value increasingly encompasses both clinical benefit and economic impact. What has long been business as usual in many countries is now trending in the United States, with payers demanding evidence that drug costs are commensurate with clinical benefit.

Globally, many payers have put in place formal Health Technology Assessment (HTA) systems to ensure that spending on new technologies (i.e. medicines) are justified by the benefits that they offer. HTA and other value-for-money driven systems assess (1) whether the new medicines bring meaningful added medical value, and (2) whether the incremental cost is justified by the added benefit. To be convinced of added value, payers usually require demonstration of improvement in patient-relevant endpoints such as survival or quality of life/functioning versus what they consider to be standard of care for the condition.

To meet these new payer demands, pharmaceutical companies need to organize themselves differently. It is critical that groups such as Health Economics & Outcomes Research (HE&OR) are fully integrated into development activities to ensure that the evidence generated will meet evolving payer demands. For HE&OR groups, foundational work begins in Phase I with generating insights from the publicly available data sources regarding disease characteristics and patient experience with currently available treatment options.

Such work continues as development programs evolve, and more

sophisticated HE&OR strategies are executed to quantify the economic and humanistic burden of disease through retrospective analyses and real-world observation. Once pivotal trial results are available, it is the role of the health economist to generate the economic profile of a new therapy based on clinical findings combined with additional evidence, including impact on healthcare resource utilization, impact on patient well-being, and wider societal benefits.

Core components of the HE&OR package include the health economic models (cost-effectiveness, or "value-for-money" assessment as well as budgetary impact calculations), and value dossiers, rich documents providing a summation of the evidence to support products through the reimbursement appraisal process.

HE&OR efforts do not end at product reimbursement and listing; rather, they go on to support the product in the transition from established clinical efficacy to real-world clinical effectiveness. Phase IV post-marketing studies, registry studies and other observational research are designed largely with health economic objectives and requirements in mind. It is imperative that a drug not only demonstrates value-for-money in the initial reimbursement review, but that the product continues to be recognized as an efficient and prudent use of healthcare resources over its lifecycle.

This framework for decision-making applies not only to medicines that are widely used, but now also to specialty and breakthrough medicines targeting smaller populations with substantial unmet medical need. For such targeted therapeutic development, there are often unique clinical and environmental factors at play.

Fundamentally, challenges present because the current framework for valuation of pharmaceuticals—comparative effectiveness and cost effectiveness—is designed with the traditional drug development pathway in mind. Biomarker-driven targeted therapeutics and specialty medicines intended for orphan-disease populations occupy an increasing share of pharmaceutical research. Such development also represents a progression toward smarter science, and arguably, a more responsible strategy, where therapies are developed with greater degrees of population specificity and in response to significant unmet medical needs that remain.

These development programs, however, are often fulfilled under shorter timelines, with smaller populations, and arguably weaker trial designs. They do not have the "luxury" of large cohorts that support greater statistical strength.

Healthcare regulatory authorities have been increasingly supportive of such programs to bring promising therapies to patients with high unmet needs. The manufacturers are then required to conduct more robust studies post regulatory approval to demonstrate that the product delivers meaningful incremental clinical benefit to patients over and above currently available treatment options.

Payer bodies, however, have not generally followed suit by modifying the assessment criteria for breakthrough products. They continue to demand robust evidence of benefit as compared to standard of care to demonstrate value with a high degree of certainty. If this persists it is likely that most breakthrough medicines will not have broad patient access, thereby undermining the intent of regulatory pathways such as accelerated or adaptive approval.

Improving access to breakthrough therapies will require changes on the payer and the manufacturer side. Payers have to be willing to accept indirect comparisons versus standard of care on surrogate endpoints to assess added value. Also, they have to be willing to accept greater uncertainty regarding comparative effectiveness and cost effectiveness for these types of treatments at the time of launch.

On the other hand, manufacturers have to conduct robust epidemiology studies and evidence synthesis to better understand the efficacy and safety of current standard of care to support indirect comparisons. Also, manufacturers will need to invest earlier on to generate evidence that links surrogate endpoints to payer relevant endpoints. Further, post approval studies should be designed so as to provide payers the robust evidence of added clinical benefit over current therapies on meaningful endpoints that they seek.

It has been said that drugs work only as well as they are taken. We may also say that drugs are only as good as they are available. As science advances and our understanding of disease and therapeutic options improve, we must find a better way to harmonize regulatory and reimbursement approval pathways and requirements.

Novel medicines have much to offer, but if payer expectations are not aligned with drug development requirements, we may increasingly be in the position where efficacious therapies fail to reach patients after their regulatory approval. ■

Mohan Bala, PhD, is VP, global health economics & outcomes research, Sanofi, and Meghan Gallagher, MSc, is director, global health economics & outcomes research, Sanofi Oncology.

Continuing to prove its worth

Health Economics & Outcomes Research (HE&OR) can help prove a drug is a prudent use of healthcare resources. Such evidence and insights are generated over a product lifecycle, from early clinical development to Phase IV post-marketing studies. With the payer's growing role in healthcare decision-making, HE&OR will maintain a big role in assessing new interventions. A look at how HE&OR helps satisfy evolving payer demands for evidence

Early development
- Foundational work to generate insights from the publicly available data sources

Late development/product launch
- Health economic models
- Value dossiers
- Summation of evidence to support products
- Impact on resource utilization and patient well-being

Post-marketing authorization/Phase IV
- Registry studies
- Retrospective analyses and real-world observation