IN brief

NCI revamps trials

The National Cancer Institute (NCI) is restructuring its long-established clinical trials program to take advantage of new understanding in molecular oncology and improvements in clinical trial design. The NCI's clinical trial Cooperative Group program's nine groups will be consolidated into four entities. "As we start defining illness based on molecular or genetic signatures, we start homing into more specific patient populations, which require screening for larger populations," says Jan Buckner, professor of oncology at Mayo Clinic in Rochester, Minnesota, and the chair of the North Central Cancer Treatment Group. The NCI's Cooperative Group program was founded over 50 years ago and involves more than 3,100 institutions. The organizational changes follow a NCI-requested report released last April by the Institute of Medicine (IOM), of Washington, DC. Efficiency will be boosted by revamping informational technology infrastructure, outfitting all groups with a uniform information system and seamless sharing of information, sample banks and databases. One of the major goals is to speed up the time taken to approve and initiate phase 2 and phase 3 clinical trials. "We desperately want to get new treatments out to cancer patients, and do this in the most expeditious and safe way possible," says James Doroshow, director of the Division of Cancer Treatment and Diagnosis at NCI in Bethesda, Maryland. *Nidhi Subbaraman*

Yardsticks for R&D

Two nonprofits—the Critical Path Institute (C-Path), based in Tucson, and the Clinical Data Interchange Standards Consortium (C-DISC) of Round Rock, Texas—are teaming up to set common standards for companies to report clinical data on diseases considered major public health challenges. The aim is to quicken R&D efforts and potentially facilitate the evaluation of new therapies at the US Food and Drug Administration (FDA). "Most companies are recognizing greater efficiency when we all call an apple an apple," says Raymond Woosley, C-Path's president and CEO. The data standards are intended as useful guidelines rather than mandates. C-Path and C-DISC built a database for Alzheimer's disease, launched in June 2010, as part of C-Path's Coalition Against Major Diseases project, and data from 4,000 patients have now been mapped to the standard. The joint effort will now be expanded to include data on amyotrophic lateral sclerosis, Huntington's disease, multiple sclerosis, lung cancer and diabetes. Standardized data would allow regulators to compare clinical data results across trials and across companies. ShaAvhree Buckman, Director of the Office of Translational Sciences at the FDA's Center for Drug Evaluation and Research (CDER) welcomes these data standards, as they capitalize on work already set in motion by existing groups. *Nidhi Subbaraman*

approve biosimilars, but states that a developer must wait 4 years after a brand product is approved before filing an application. It also says a developer of a follow-on biologic must wait 12 years before it can receive approval for a drug made relying on innovator data. Also, an innovator can receive an additional 12 years of exclusivity for a modified product that produces changes in safety, purity or potency.

That has sparked a debate over the meaning of exclusivity and has cornered FDA Commissioner Margaret Hamburg. Senators Kay Hagan (D-NC), Orrin Hatch (R-UT), Michael Enzi (R-WY) and John Kerry (D-MA) sent her a letter on January 7 saying the law provides for data exclusivity. This means that a biosimilar developer that relies on its own data need not wait 12 years to file a biologics license application.

Thirteen follow-on biologic supporters, including the American Association of Retired Persons of Washington, DC, health insurance company Aetna of Hartford, Connecticut, specialty pharma Hospira of Lake Forest, Illinois, and Teva, also wrote to Hamburg in a January 20 letter suggesting that if data exclusivity expires after 4 years, it clears the way for developers to file applications relying on innovator data, even though the approval cannot come until the marketing exclusivity (the full 12 years) ends.

Clarification finally came from sponsors of the law, Representatives Anna G. Eshoo (D-CA), Jan Inslee (D-WA) and Joe Barton (R-TX). The intent is to give companies 12 years of data exclusivity—not market exclusivity. That means biosimilar companies may not rely on innovator data but could still develop their own data for a similar product that could be marketed alongside the original. The bill does prohibit evergreening (a process whereby innovator companies make trivial or minor improvements to a drug in an effort to extend patent life), although brand manufacturers that launch next-generation products could gain their own exclusivity period, if they can be sufficiently differentiated from the originator molecule.

The money at stake is staggering. New York–based consultants IMS Health's most recent data show that biologic drugs generated $130 billion worldwide in 2009. If the US follow-on biologic pathway were in place, several large biotechs would be facing a patent cliff similar to what big pharma is currently facing. For instance, 74% of Thousand Oaks, California–based Amgen's 2010 revenue (~$11 billion) and 57% of Boston-based Genzyme's 2010 revenue (~$2.3 billion) would be exposed through patent expiry by 2015.

With Rituxan's patents facing expiration, the drug has become a prime target for biosimilar makers. Teva has launched clinical trials in both rheumatoid arthritis and non-Hodgkin's lymphoma with its biosimilar, TL011. The rheumatoid arthritis trial is enrolling 60 patients and will be completed by August. Two Irvine, California–based companies, Spectrum and Viropro, are collaborating to produce another version of Rituxan. Dr. Reddy's Laboratories, of Hyderabad, India, already launched its own copy, Reditux, in India in 2007.

How much it costs to develop a biosimilar is hard to pin down. Estimates range from $40 million on up to $250 million and far beyond, depending on the complexity of the molecule, and the premarket work can take up to seven years. Still, if a biosimilar steals a conservative 20% share of a $1 billion product, at the 20% price discount that some analysts predict, it reaps $160 million in annual revenue.

But despite the rewards, the business of developing new versions of brand biologics still has much higher barriers to entry than chemical generics, even assuming that the EU pathway works smoothly and the FDA finally hammers out a guidance. Companies hoping to get into the follow-on biologic game will need ample resources to comply with manufacturing requirements, run clinical trials and go to court over biotech patents. Even cleared drugs may bump against patient prejudice and physicians reluctant to replace a proven therapy with a cheaper one.

Sandoz's copy of Rituxan was developed at its facilities in Schaftenau, Austria. The company spent years using different combinations of manufacturing processes and media components with the same gene sequence to identify its biosimilar. Intensive characterization followed using different methods to ensure its version fit within the normal variability of the original product. "It's really, really tough to do this," Sandoz's global head of biopharmaceuticals, Ameet Mallik, says. "You basically need innovator capabilities."

Yet the list of interested parties grows. Teva signed a deal two years ago with Basel's Lonza Group to develop biosimilars, and Whitehouse Station, New Jersey–based Merck BioVentures spent $130 million setting up its biosimilar capabilities through a buyout of Richmond, Virginia–based Insmed (*Nat. Biotechnol.* **27**, 299–301, 2009). Even those at risk of losing share to biosimilars are looking to get into the game: Amgen and Biogen Idec both expressed interest in the space at the recent JP Morgan healthcare conference.

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