

Pharm Exec's Pipeline Report is packed with 25 of the year's most eye-catching experimental drugs. What's their secret? No smoke or mirrors—just innovative science, therapeutic value, and good business sense.

Science fiction writer **Arthur C. Clarke's** Third Law states: "Any sufficiently advanced technology is indistinguishable from magic." Paul Ehrlich, the Nobel Prize-winning pharmaceutical pioneer, used to say, "We must learn to shoot microbes with magic bullets." This year's 25 Most Attention-Getting Investigational Compounds (MAGIC), are all products of advanced technology—"bullets" that may well appear magical some day. But there are no tricks involved. Chosen by pharmaceutical analysts and consultants asked to name the late-stage products that caught their notice (candidates had to be beyond Phase II but not yet launched, and new uses for known products were counted as new), they embody the hopes and hard work of countless people.

Keeping in mind the effort, the uncertainty, the inevitable twists and turns and ups and downs, it might be said that every molecule tells a story. Here then, out of hundreds swimming upstream through the pipeline against all odds, are 25.

BLOCKBUSTER

All drugs in this section are projected to have peak sales of at least \$1 billion worldwide.

BLOCKBUSTER

\$ Acomplia [rimonabant]
from Sanofi-Aventis

TARGET INDICATION

Obesity

EST. GLOBAL PEAK SALES

\$1,700MIL

LIKELY LAUNCH

2006

PROBABILITY OF SUCCESS

60%

The most popular selection in the MAGIC 25, Acomplia (rimonabant) has been dubbed the antimunchie drug because, as a cannabinoid CB1 receptor antagonist, it blocks sites "believed to mediate hunger responses when individuals smoke marijuana," says 2Value analyst Marc Samet, PhD. This mechanism has produced "promising clinical data for two indications—obesity and smoking—both large consumer-friendly spaces," says Mara Goldstein, pharmaceutical analyst for CIBC World Markets. What's more, subjects in a recently reported two-year trial not only lost an average of 19 pounds, their cardiovascular profiles improved. And patients who stayed on the drug tended to maintain their weight loss, while those who went off it gained theirs back. Says David Moskowitz, an analyst with Friedman, Billings, Ramsey: "There may be some nervousness in the wake of fen-phen, but there is clearly a need for a way to reduce weight safely, especially since abdominal fat is an important indicator of cardiovascular risk."

Acomplia is "not an extraordinary breakthrough," in the view of David Goldstein, MD, PhD, formerly with Eli Lilly and now a consultant and a member of the board of the American Society for Clinical Pharmacology and Therapeutics. But it is "a novel mechanism that will add to physicians' arsenals and allow them to try multiple treatments for obesity." Although, he adds, the efficacy of these combinations "has not been tested." He expects "marginally better results from Acomplia compared with other recent products," and thinks it will "probably get off to a hot start—people are hungry for something new." But then "reality will set in: It won't