(Basel)—have formed alliances with these smaller firms in the hopes of cutting years from the drug-development process.

This particular effort will aim to create lead compounds against unspecified molecular targets in the asthma and cancer areas. In addition, Pharmacopeia will provide Schering with combinatorial libraries of novel chemical structures for testing in Schering's in-house screening assays. "This is a real bonus for us," says Pickett. "We're free to develop any compound we find in these libraries in any application that we identify in our own drug-discovery work."

Pharmacopeia, in return, gets a huge potential outlet for its combinatorial-chemistry efforts. "Our focus is on using our expertise in combinatorial chemistry to create libraries of compounds that have activities against specific targets," says Joseph Mollica, Pharmacopeia's chairman and CEO. "We provide scientific expertise in one specific area."

For Pickett, that makes Pharmacopeia a perfect partner. "What I'm looking for is companies with outstanding science and outstanding people that can feed our in-house efforts," he explains.

—Joseph Alper

Ligand and Allergan form $100 million venture

NEW YORK—Over the past year or so, Ligand Pharmaceuticals (San Diego, CA) has bravely battled the storm that has battered the biotech sector. Its most recent effort is a joint venture with Allergan (Irvine, CA) to form Allergan Ligand Retinoid Therapeutics (ALRT), which will focus on the commercialization of small-molecule cancer drugs based on retinoids, synthetic versions of retinoic acid, a nonpeptide hormone that affects such cellular functions as growth and differentiation.

ALRT is potentially worth $100 million. A previous joint venture between Allergan and Ligand, formed in June 1992, has been dissolved, with the technology and assets from that venture going to ALRT, and with Allergan contributing $50 million and Ligand contributing $17.5 million to the new venture. Additionally, ALRT has filed a public offering of up to $32.5 million worth of units to stockholders of Ligand and Allergan. Rather than conduct research and development (R&D) on retinoid products itself, though, ALRT will fund R&D at Ligand and Allergan.

ALRT has inherited two retinoid products already in clinical trials, LGD1057 and LGD1069. Oral formulations of each product are currently in phase I/IIa trials for leukemias and Kaposi's sarcoma, while topical formulations of the products are in phase I/IIa trials for skin cancer.

ALRT's formation comes in the wake of the financially disappointing second anniversary of Ligand's intial public offering (IPO), which raised $43.2 million at $11 a share on November 24, 1992. At the time of its IPO, Ligand promised investors that, on the IPO's second anniversary, its stock price would have risen 31% to $15.88. If such a rise didn't occur, Ligand promised to issue additional shares to make up the difference between the company's actual stock price and the promised price.

Despite the numerous strategic alliances Ligand entered into following its IPO and the money raised through those alliances, the firm's stock didn't reach the promised price. This was due both to weak overall demand for biotech stocks, as well as to a deliberate desire by at least some investors for Ligand to fall short, as this would mean that Ligand would have to issue them additional stock. In fact, in the three days before the anniversary of Ligand's IPO, its stock dropped steadily, from $12 to $10.75. And last November 24, with the stock opening at $11, Ligand was forced to issue more than 2.5 million new shares of Class A common stock, increasing its shares outstanding by 16.6%. For every 100 shares of Class A common stock held, 33 new shares were issued. Class A common stock was then converted into Class B common stock, so that currently only one type of Ligand stock is traded. Without a doubt, Ligand's executives—who primarily held Class B common stock, which did not earn 33 new shares per 100 shares—were the clear losers, since their holdings were badly diluted.

Ligand's executives certainly tried, though. Last year alone, they inked three corporate alliances:

- an agreement worth up to $44 million with Wyeth-Ayerst Laboratories (Philadelphia, PA) to develop drugs that interact with estrogen or progesterone receptors for cancer, gynecological diseases, hormone-replacement therapy, and central nervous system disorders associated with menopause and contraception;
- a potential $26 million deal with Abbott Laboratories (Abbott Park, IL) to develop drugs for inflammatory diseases;
- and a marketing agreement with Chiron (Emeryville, CA), in which Ligand acquired exclusive Canadian rights to Chiron's Proleukin interleukin-2 for metastatic kidney cancer.

These deals came on top of Ligand's earlier-established alliances with Pfizer (New York), Glaxo (London), and E. Merck (Darmstadt, Germany). Almost all of Ligand's alliances are built around its intracellular receptor (IR) technology. IRs are proteins found inside cells that interact with extracellular hormones to control gene expression. A small-molecule hormone, or a synthetic analogue of that hormone, enters a cell and binds to an IR. The resulting hormone/IR complex then enters the nucleus of the cell, binding to its DNA and altering the transcription of RNA, and thus the protein produced from that RNA. The end result is that the cell behaves differently.

Together with its collaborators, Ligand has identified more than 40 IRs, half of which have not yet been "matched" to their appropriate extracellular hormones. Ligand has also developed automated assay systems to screen hormone libraries for activity against its IRs.

—Lesley Wright

Lesley Wright, who lives in New York, is a science writer specializing in biotechnology.

The joint venture will focus on the commercialization of small-molecule cancer drugs based on retinoids, synthetic versions of retinoic acid.