

The real value driver

PATRICK LUCY explains the benefits of protein expression and opportunity cost.

At the heart of most, if not all, biologic drug development programs is the ability to express human proteins in their proper three-dimensional state. Whether the protein is required for structural studies, analytical assessment, or per se is the therapeutic/vaccine candidate, it is imperative to rapidly produce high quality protein of interest in sufficient quantities for evaluation. The cost of delayed drug development is estimated at \$1 million per day and the cost of each day of delay is the same, regardless of the source of the delay (due to inability to synthesize protein) during the drug development lifecycle.

“The cost of delayed drug development is estimated at \$1 million per day”

The traditional approach to protein expression is to seek a host perceived to be inexpensive, facile to use and accessible. Recent research suggests that this type of approach results in a 75 percent failure rate, with success being defined as high titers of soluble, active, high quality protein. Once the initial failure has occurred, most efforts will involve seeking alternative hosts in a linear, iterative and extremely costly process, until finding a solution, or in some cases, altogether abandoning efforts for expression and product development. Experience from a myriad of biotechnology companies suggests a recombinant protein host strain requires typically between six to 18 months of development time, to ultimately ar-

rive at a host that will meet near and long term needs. This development effort typically does not occur in one continuous effort, but rather during periods of increased and intense product demand during the development process. While this type of approach is extremely common, it results in significant opportunity cost and manifests in delayed programs, inefficient use of resources, and overall pipeline stagnation.

What if there was a single platform in which one could screen hundreds to thousands of unique host strains using a high throughput, parallel approach, which demonstrated a success rate of greater than 95 percent, and routinely delivered a robust production strain capable of producing high titers of soluble, active protein within eight weeks? This performance would enable the drug developer to express approximately three-to-four-fold more proteins, and arrive at a production strain in one-seventh the time. The Pfēnex Expression Technology platform provides this type of success and speed to drug developers. The platform consists of a vast library of expression components including novel proprietary plasmids and host strains. These components combined with *Pseudomonas fluorescens*' obligate aerobic nature and a robotic, parallel screening process results in unprecedented protein expression speed and success rate.

As an example, consider a vaccine development program for which the innovator company has identified 10 putative antigens for a vaccine formulation. The ideal approach to

down selection is to test each antigen in vivo to measure immunogenic performance. If a development team approached this program in the traditional linear and iterative fashion, it would initially attempt the expression of each antigen in *E.coli*. On average only two to three of the 10 candidate antigens will be produced in soluble active form. The remaining antigens require screening in additional expression strains, at larger scale, in alternative hosts or refolded,

which presents significant product quality/reproducibility risks in addition to long-term cost of goods challenges. Alternatively, if the researcher expressed the same set of 10 antigens in the Pfēnex Expression Technology, eight to 10 soluble, active antigens would be available for evaluation within five to eight weeks. Hence, as opposed to using the most efficient technology, the traditional *E. coli* approach to protein expression would incur significant opportunity cost, at an extreme competitive disadvantage.

Protein expression is at the core of every pharmaceutical development effort, with the challenges experienced by protein expression scientists significant. Antiquated technologies with limited tools

simply cannot meet the challenges posed by today's next generation drug development programs. The Pfēnex Expression Technology platform provides a robust solution to the challenge of efficient, high quality protein expression, and enables drug development with the avoidance of millions of dollars in opportunity cost. ■



Patrick Lucy is the Vice President of Business Development of Pfēnex Inc. He played a leadership role on the original team that developed Pfēnex Expression Technology and subsequently led the successful commercial launch of the platform. Lucy is experienced in the areas of alliance management, licensing, intellectual property, biopharmaceutical operations and biopharmaceutical facility design, construction and validation.