

WHITE PAPER

The Return on Investment for Ingenuity Pathways Analysis within the Pharmaceutical Value Chain

Sponsored by: Ingenuity

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IDC OPINION

Based on in-depth interviews with researchers and senior managers at pharmaceutical companies, Life Science Insights, an IDC company, concludes that there is a significant return on investment (ROI) from the use of pathways analysis applications within the context of traditional drug discovery and development. Our research on the Ingenuity Pathways Analysis application in particular, showed that companies can reap a significant ROI based on improvements in productivity, cost savings, and innovation across all phases of the drug development process from discovery through marketing.

Traditionally, many users of pathways analysis software limit usage to the early phases of drug discovery, such as target identification, target qualification, and target validation. However, our study uncovers many other compelling applications for pathways analysis within the pharmaceutical value chain including lead optimization, preclinical and clinical, life-cycle management, marketing, and sales. The benefits vary by the type of user and the specific application, but our market research demonstrates that pathways analysis software increases overall productivity by reducing failures and increasing successes, which reduces the cost and time of drug discovery and development.

At a fundamental level, pathways analysis provides a deeper understanding of the underlying biology. From this basis, Life Science Insights has uncovered other positive attributes of pathways analysis within the pharmaceutical value chain that are amenable to quantification, such as:

- ☒ **Target identification, qualification, and prioritization** — provide experimental focus and confidence
- ☒ **Target validation** — prioritizes projects within a portfolio
- ☒ **Lead optimization** — identifies potential toxicities and other therapeutic directions
- ☒ **Preclinical studies** — provides validated information for the selection of the right animal model
- ☒ **Clinical studies** — allow patient stratification during phase II and phase III clinical trials based on relevant biological data

- ☒ **FDA submission and approval** — demonstrates biological relevance of biomarkers and targets
- ☒ **Sales through market differentiation** — competitive advantage through greater understanding of the biology
- ☒ **Life-cycle management** — provides biological information for new indications and product distinction

METHODOLOGY

This white paper examines the ROI for broad deployment of the Ingenuity Pathways Analysis application within the pharmaceutical value chain (see Table 1).

TABLE 1

The Pharmaceutical Value Chain

Phase	Description
Target identification	Identify genomic targets for disease intervention
Target qualification	Predict relationship between target and disease
Target prioritization	Prioritize list of targets
Target validation	Prove that modulation of the target alters disease phenotype
Compound screening	Screening of compound libraries against targets and/or cell lines
Lead optimization	Addition of chemistries to lead compound to improve assay response
Preclinical studies	Testing of lead compounds in animal models
Clinical — phase I	Testing for adverse effects in 20–100 healthy volunteers
Clinical — phase II	Testing for efficacy and side effects in 100–500 patients
Clinical — phase III	Testing for efficacy, safety, dosage in as many as 1,000–5,000 patients treated with either drug or placebo
FDA review and approval	New drug application (NDA) submission and evaluation/approval by the FDA

Source: Life Science Insights, July 2004

The primary information source for this report is a series of in-depth interviews conducted by Life Science Insights analysts with researchers and senior

management at large pharmaceutical companies as well as interviews with small to mid-size specialty pharmaceutical companies (see Appendix). Over 20 interviews were conducted, with approximately one-half of the researchers being active users of the Ingenuity Pathways Analysis application. The researchers sampled in this study are engaged in all phases of the drug discovery and development process, while the sampling of senior management provides a broad perspective that covers all phases of the pharmaceutical value chain.

During these interviews we specifically inquired about the benefits of using the Ingenuity Pathways Analysis application and how the application's value could be demonstrated within all segments of the pharmaceutical process. ROI is particularly difficult to calculate within the many phases of drug discovery and development, thus a degree of extrapolation is required. Survey participants did, however, specify concrete examples and estimates of cost savings within numerous phases of the pharmaceutical value chain from which Life Science Insights analysts constructed an overall ROI model for Ingenuity Pathways Analysis.

Life Science Insights deliberately chose conservative estimates for the assumptions used in building the ROI model. In some cases, the interviewees' reported cost savings have been reduced by Life Science Insights to provide a more general estimate applicable to broader customer environments. The estimates included here are reflective of an overall conservative analysis, but it should be noted that some of the interviewees' uses of pathways analysis software reveal impressive returns and exciting new capabilities that point to direct economic benefits from a broad deployment of the Ingenuity Pathways Analysis application.

IN THIS WHITE PAPER

In this white paper the reader will find a discussion of industry-accepted costs in dollars and time for drug discovery and development as well as the benefit of implementing Ingenuity's Pathways Analysis application. This paper then delineates and discusses the distinct phases of the drug discovery process where pathways analysis will increase productivity and add value. An ROI model is calculated for several phases of the pharmaceutical value chain and then summed *in toto*. Interwoven throughout the report are quotes from various researchers that help illustrate the various ROI scenarios. The following sections define three ROI scenarios, each of which is a combination of various steps in the value chain:

- ☒ Scenario 1 — ROI for Drug Discovery
- ☒ Scenario 2 – ROI for Preclinical and Clinical Testing
- ☒ Scenario 3 – ROI Beyond R&D, including FDA Review and Approval, Sales and Marketing, and Life-Cycle Management

Overwhelmingly, we discovered that pathways analysis provides researchers an increased level of experimental confidence and a greater ability to prioritize their work. Most important, we found that Ingenuity Pathways Analysis helped researchers identify biologically validated targets, choose the proper animal model, and segment clinical trial cohorts. Additionally, we found that researchers and managers credited

the application with helping them innovate (through identification of new targets and pathways), communicate (by having a common reference source in the application), and differentiate (by enabling the articulation of product capability and function). In summary, we discovered that users feel Ingenuity Pathways Analysis will lead to increased efficiency, greater success rates, and fewer late-stage failures.

SITUATION OVERVIEW

ROI is an underlying concern for all forms of business. This paper focuses on the ROI that is realized in the pharmaceutical value chain through the broad deployment and use of the Ingenuity Pathways Analysis application. Specific examples demonstrate how savings can be realized during target identification, target qualification, target validation, lead optimization, preclinical development, clinical studies, the FDA submission and approval processes, sales and marketing, postmarketing, and life-cycle management. The phases of the pharmaceutical value chain are listed below, including the industry-accepted time and cost per phase (see Table 2). The data is collected from various industry reports, internal sources, and validated by the opinions of the interviewees.

TABLE 2

Cost and Time Breakdown of The Pharmaceutical Value Chain

Phase	Time (Years)	Cost (\$M)
Target identification, qualification, and prioritization	1	165
Target validation	2	205
Compound screening	0.5	40
Lead optimization	2–3	120
Preclinical studies	3	90
Clinical — phase I	1	45
Clinical — phase II	2	65
Clinical — phase III	3	205
FDA review and approval	1–2	N/A
Post-marketing testing	1	N/A
Total	17–18	935

Source: Life Science Insights, Ernst & Young, Tufts CSDD, and Boston Consulting Group, July 2004

The cost and time of developing and bringing a drug to market is over \$900 million and often takes as long as 15 years, if not longer. A key cost driver is the large

number of failures during the expensive clinical trial phases. Research illustrates that over 80% of the drugs that enter clinical trials eventually fail to get approved by the FDA. A recent study from the Tufts Center for Drug Development concluded that 75% of the drugs that enter phase I move forward to phase II, however, only 42% of those progress to phase III. Of those phase III drugs, only 64% successfully make it through to FDA approval. Crucial to reducing this key cost driver of drug development is the ability to "fail early and fail often."

A different though related metric of a company's productivity is the output of new molecular entities (NMEs). Ironically, even though pharmaceutical investments in R&D programs are consistently increasing, the number of NMEs continues to stagnate.

One challenge faced by the industry is achieving productivity gains by increasing the number of NMEs per year and by increasing the failure rate early in the development process. Many product teams are focused on identifying new, broadly applicable technology solutions that are capable of advancing productivity on both fronts.

Pathways analysis is a method of visualizing biological pathways and for providing a greater understanding of diseases. Increased knowledge through pathways analysis allows decisions to be formulated early in the pharmaceutical process, thereby decreasing later stage failures. All of the pharmaceutical researchers and executives we talked with agree that a greater understanding of biological pathways is a more intelligent and efficient method of pharmaceutical development than the traditional reductionist approach that focuses on a single gene or an individual protein.

"Ingenuity brings the data back into the biology...the gene, the cell, the tissue, the function of an organ, the behavior of all these parts of the body in a disease setting. Ingenuity reassembles the puzzle. And that is, of course, a great value."

– Principal research scientist, genomics department

"I think there are a lot of uses for Ingenuity — transcript profiling, target discovery, toxicogenomics, preclinical, clinical, as well as identifying and monitoring biomarkers. Basically, in every phase where you can use genomics or genetics, Ingenuity is doing what I always felt our software should do."

– Head of genomic solutions

Ingenuity and the Pharmaceutical Value Chain

Scenario 1 — ROI For Drug Discovery

Target Identification

The target identification, qualification, and prioritization process takes approximately one year and costs as much as \$165 million. This process includes the identification of putative drug targets, linking those targets to a specific disease, and selecting the targets with the highest potential for interrupting the course of its related disease. The sequence of the human genome provides a laundry list of potential targets and the underlying challenge is the isolation of the most promising disease-related genes and resulting proteins. Much of this data is captured from gene expression analysis and single nucleotide polymorphism (SNP) evaluation.

Many gene expression experiments analyze 15,000 to 30,000 genes, and the output is stored in databases that may house thousands of individual experiments. For instance, one group at a large pharmaceutical company may run "a couple of thousand gene chip experiments in a month." This level of scale requires support from applications and tools that can help researchers interpret the complex biological networks.

Ingenuity's Pathways Analysis application is often implemented during gene expression analysis. A user can investigate the biological function of a list of genes through pathways analysis formed via data compiled from millions of curated scientific findings. Comments from end users include:

"Using Ingenuity shortened our target identification phase by a couple of months and provided us biologically validated targets."

— Principal research scientist, genomics department

"It definitely gets you to target identification faster. It helps you make the right decision first. "

— Group leader, gene expression analysis

"Ingenuity analyzes a list of 500 genes, focuses the list to 50, and then prioritizes it to 15 genes of high biological relevance."

— Principal investigator, gene discovery

A potential drawback of expression profiling experiments is they may miss biologically relevant genes that are not differentially expressed. Through pathway analysis, Ingenuity can help identify potential drug targets that are not differentially expressed in some gene expression experiments.

"Ingenuity has helped us identify new drug targets that were not picked up by differential gene expression experiments. For example, we identified five differentially expressed genes, however,

Ingenuity identified another five targets in the analysis of the biological pathway. Only through using Ingenuity did we identify the other genes, and now one of them is our target."

— Principal scientist, genetic technologies

Target Qualification and Prioritization

Target qualification and prioritization begin to shorten the list of targets produced from the identification phase by establishing a causative relationship between target and disease. Much of this work is performed using cell-based assays characterizing functional relationships. Additional data is gathered from protein-protein interaction and subcellular localization studies.

The cost and time for target qualification and prioritization are integrated into the industry estimates for target identification. Many of the users feel that the Ingenuity Pathways Analysis application provides the biological information needed for efficient target qualification and prioritization.

"We were working on a data set for over a year trying to prioritize the targets, but we had no good way to analyze it. We ran it through the [Ingenuity] application and immediately identified the pathways. If we would have had that information a year ago, it would have saved us considerable time and provided the right place to start."

— Scientist, investigative pathology

"We have an expert here who looks at the long list of identified genes for target qualification. Using the pathways information, I don't have to give him a list of hundreds of genes. Ingenuity allows us to prioritize the list of targets."

— Group leader, gene expression analysis

"It definitely helps you strengthen and define your next round of studies. Ingenuity helps you validate or 'disvalidate' your hypothesis."

— Principal research scientist, genomics department

Target Validation

Target validation can take two years and cost \$205 million. The goal is to perturb the target and demonstrate that modulating the behavior inhibits the function, reverses the disease phenotype, and/or produces a desired physiological effect. Experimentation includes study of disease models, cellular and biochemical assays, evaluation of target polymorphisms to identify genetic risk factors that may affect specific segments of a population, and modulation of gene expression studies. Further validation investigations include toxicity and efficacy profiling of a particular class of targets and a gene's or protein's druggability (oral availability, chemical structure for affinity binding, etc.).

"By running Ingenuity Pathways Analysis and noting that the target is located in the middle of a pathway provide validation that this is real, and it is supported by all of this evidence. It definitely increases the level of confidence."

— Biomarker development and validation group leader

"Ingenuity provides confidence, time savings, and cost savings. It helps us nail down pathways that we are interested in."

— Principal Investigator, gene discovery

The validation process is ongoing, continuing through late-stage clinical trials. Many targets within a discovery portfolio are incompletely validated, despite screening and optimization of directed compounds and ongoing research by discovery scientists. Incomplete validation is often due to a lack of understanding of the underlying biology and presents managers with a project portfolio consisting of varying levels of "quality." Discovery managers have a demonstrable need for applications that aid their portfolio management efforts by enabling them to cut less preferable projects as early as possible.

"Ingenuity is a portfolio management application for discovery managers. The molecule identification and optimization phase is cheaper than the target validation phase, and the pressures to manage a target portfolio will only increase over the next 2–3 years. Ingenuity provides a higher quality information base to deprioritize projects."

— Chairman of research and development

Compound Screening

The compound screening process averages 4 to 6 months and costs \$40 million. Ingenuity Pathways Analysis can be utilized to improve compound selection efficiency and early toxicity analysis.

"We were using Ingenuity to look at some genetic markers in response to a specific compound and we saw something new that we haven't seen before. Now, we can use this compound for a different use, and we have taken it down another road."

- Group leader, gene expression analysis

Lead Optimization/Prioritization

Lead optimization averages 2 to 3 years and costs approximately \$120 million. This stage of drug development focuses on identifying the best small-molecule entity for interrupting a disease pathway. During lead optimization, potential drug compounds are further analyzed to identify their mechanism of action and optimal chemical formulation.

Many users commented that the Ingenuity pathways application can be used during compound prioritization.

"Ingenuity has potential to direct a whole program. For example, we had five compounds that were effective and not toxic. Next, we wanted to ask if the compounds were acting through the same pathways or different pathways. Ingenuity identified that three of them were involved in off-target pathways so they were dropped before the expensive animal experiments."

— Group leader, gene expression analysis

"Ingenuity Pathways Analysis can be used to help kill a compound and increase our success rate. We use it to prioritize compounds and plan more efficient experiments."

- Biomarker development and validation group leader

Summary of Scenario 1 – Ingenuity Pathways Analysis ROI for Drug Discovery

Based upon the data and examples described above, our analysis shows that Ingenuity Pathways Analysis can reduce the costs of discovery by as much as 10% when applied to target discovery, target validation, and lead compound optimization. These reasonably conservative estimates relating to increased productivity and cost savings result in a \$50 million plus per drug benefit for this entire stage of the value chain (see Table 3):

TABLE 3				
Ingenuity Pathways Analysis ROI for Drug Discovery				
Phase	Average Estimated Cost (\$M)	Percentage of Savings	Cost Benefit (\$M)	New Estimated Cost (\$M)
Target identification, qualification and prioritization	165	10	16.50	148.50
Target validation	205	10	20.50	184.50
Compound screening	40	10	4	36
Lead optimization	120	10	12	108
Total	530		53	477

Source: Life Science Insights, July 2004

Scenario 2 — ROI for Preclinical and Clinical Testing

Preclinical Studies

Preclinical studies aim to interpret the drug response and can take 2 to 4 years and cost \$90 million. The goal of a preclinical study is the early detection and understanding of toxicity in animal models as well as the discovery, validation, and monitoring of biomarkers that may be indicators of drug response and disease progression. Pharmacogenomic data gathered during preclinical studies may be able to identify a specific population cohort that demonstrates an optimal response to a drug, thus enabling patient stratification during subsequent clinical trials. Preclinical studies may also lead to the identification of potential new indications.

Some of the researchers we interviewed felt that Ingenuity Pathways Analysis demonstrates its greatest utility and benefit within preclinical studies, in particular, by providing biologically relevant data indicating which animal model is best for study. Other approaches of gene expression analysis may miss key relevant biological information. Gene expression data analyzed through Ingenuity can confirm the function of a target within a disease pathway, and provide the essential information needed to determine which knockout model to use during the preclinical analysis. Without pathways analysis, the wrong model organism may be chosen leading to improper or failed studies. Choosing the wrong animal model is a significant contributor to productivity loss through increased late-stage failure rates. Better preclinical results will directly impact phase II clinical trials and influence the successful passage to phase III.

"Analyzing gene expression data through Ingenuity indicated the best animal model to go after. Before Ingenuity, we chose the animal model based on limited data and a few papers in the literature. Ingenuity provides the totality of information so we can link the gene to its pathways and then to the correct animal model."

— Head of healthcare and CEO of Worldwide Pharmaceuticals

Clinical Testing

Time and cost estimates in the clinical testing phase range between 5 to 7 years and \$260 million to \$320 million. A breakdown of clinical testing is listed below:

- ☒ **Phase I** — 1 year and \$45 million, designed to determine the pharmacokinetic and pharmacologic actions of the drug, adverse effects, and side effects associated with increasing doses in 20–100 healthy volunteers.
- ☒ **Phase II** — 2 years and \$65 million, testing for efficacy, side effects, and risks in 100–500 patients.
- ☒ **Phase III** — 3 years and \$205 million, testing for efficacy, safety, dosage in as many as 1,000–5,000 patients treated with drug or placebo.

Ingenuity's application can improve the efficiency of phase II through the information garnered in the preclinical studies using the proper animal model. Furthermore, the application may impact phase III by providing information on genetic differences

between responder and nonresponder populations. This information is then used to stratify the patient population into different subgroups, possibly improving clinical success. More efficient clinical screening in turn leads to enhanced justification for premium pricing on population-targeted therapeutics.

"Ingenuity Pathways Analysis helps us understand the gene expression data and why exposure to a particular drug causes gene expression events. These gene expression events can be used as biomarkers in our animal experiments. Next, using Ingenuity, we can determine if the biomarker is found in blood, synovial fluid, or a skin biopsy, and then we can take the data to the clinic and eventually use the biomarker during human trials."

- Biomarker development and validation group leader

"In the clinic, you can monitor a patient's blood for biomarkers to see what is going on. Using Ingenuity, the biomarker discovery is faster and easier."

- Head of genomic solutions

Pharmacogenomic data from gene expression analysis and SNP evaluation analyzed with Ingenuity translates into:

- Enhanced efficiency of drug development through better prediction of treatment outcomes
- Targeted patient population based on optimal drug response
- Repositioned compounds that have failed in Phase II or Phase III
- Approved products with additional applications for indications other than their current use
- Niche products for the development of targeted medicines

Summary of Scenario 2 – Ingenuity Pathways Analysis ROI for Preclinical and Clinical Testing

The value of pathways analysis in preclinical and clinical testing is best summed up by one of the researchers we interviewed:

"Ingenuity can potentially reduce preclinical costs by 20% and increase the success rate of phase II from 50% to 60% and probably reduce the cost of phase II to \$50 million."

- Chairman of research and development

Our data gathered on preclinical and clinical testing is incorporated into Table 4. Note that despite some of the anecdotal evidence provided on efficiency increases during phase I and phase III, we have not attributed direct economic value to these stages for the Pathways Analysis application because the more direct impact occurs during preclinical animal studies and the subsequent correlation to safety and efficacy analysis during phase II. Some of the quotes below speak to the additional late-stage clinical benefits experienced using pathways analysis.

TABLE 4				
Ingenuity Pathways Analysis ROI for Preclinical and Clinical Testing				
Phase	Average Estimated Cost (\$M)	Percentage of Savings	Cost Benefit (\$M)	New Estimated Cost (\$M)
Preclinical studies	90	20	18	72
Phase I	45	N/A	N/A	45
Phase II	65	20–25	15	50
Phase III	205	N/A	N/A	205
Total	405		33	372

Source: Life Science Insights, July 2004

ROI for Ingenuity Pathways Analysis in Discovery and Development

It is widely agreed that the majority of drug development costs are due to accumulated late-stage drug failures.

"The global cost of drug development for a successful drug is between \$1 billion and \$1.25 billion, and 70% to 80% represents the cost of failures along the route."

- Head of research and development

Ingenuity Pathways Analysis may help save an estimated 8–10% of the total costs associated with drug discovery and development by eliminating factors that accumulate and contribute to late-stage drug failures. Table 5 below summarizes the data gathered for Scenario 1 — ROI for Drug Discovery, and Scenario 2 — ROI for Preclinical and Clinical Testing.

TABLE 5				
Ingenuity Pathways Analysis ROI in Discovery and Development				
Phase	Average Estimated Cost (\$M)	Percentage of Savings	Cost Benefit (\$M)	New Estimated Cost (\$M)
Target identification, qualification and prioritization	165	10	16.50	148.50
Target validation	205	10	20.50	184.50
Compound screening	40	10	4	36
Lead optimization	120	10	12	108
Preclinical studies	90	20	18	72
Phase I	45	N/A	N/A	45
Phase II	65	20–25	15	50
Phase III	205	N/A	N/A	205
Total	935		86	849

Source: Life Science Insights, July 2004

In addition to not considering cost savings during phases I and III clinical trials, we feel that this overall estimate is relatively conservative. Some participants in our panel thought that the savings could be much more dramatic:

"The Ingenuity application could reduce the cost of failures by 50% and reduce the global cost of drug development by 50%. Which is truly phenomenal and possible."

- Head of Research and Development

Scenario 3 – Beyond R&D: Implications for Pathways Analysis in FDA Review and Approval, Sales and Marketing, and Life-Cycle Management

FDA Review and Approval

Following the phase III trial, an NDA is filed with the FDA for review and approval. The FDA has recently begun to focus on optimizing the review and approval process to reduce the time that it takes to approve a drug. Many of the researchers that we interviewed are currently engaged with the FDA in improving the NDA review and approval process by incorporating new types of data, such as gene expression analysis for biomarker identification and patient stratification, and SNP analysis for pharmacogenomics and toxicogenomics. Pathways analysis is used to emphasize the clinical relevance of genomic biomarkers within a disease pathway.

"We are working with the FDA trying to explain how to use gene expression data. The FDA really doesn't understand. They basically have come to us and asked how do we interpret all of this stuff. And actually, Ingenuity is a part of the presentation that we present to them."

- Scientist, investigative biology

We have not attempted to quantify the value that this application brings to new FDA initiatives, but it clearly may help expedite the review and approval process.

Increased Sales Through Market Differentiation

Market differentiation may increase drug sales if that drug is linked to additional information, such as pharmacogenomic data, that might enable patient population stratification. Pathways analysis may help identify markers that can be used to determine which segments of a patient population are ideal for the drug. One of our interviewees commented that "a 60% drug response rate can be improved to 90% using pharmacogenomic data." Post-approval, revenue might be increased by clearly differentiating the product from the competition through more targeted marketing. Pharmacogenomic data can also be used to rescue drugs with excessive adverse events that occur during and post phase III trials.

Rescuing failed drugs, increasing the odds of successful clinical trials, and enabling focused marketing are additional facets of the Ingenuity Pathways Analysis application that add value. For purposes of this study we did not calculate an actual dollar figure; however, we expect these areas to promise dramatic productivity gains.

"We are putting together a story in a mouse model comparing two drugs, ours and a competitor's. I looked at the data for two years trying to figure out the best way to tell the story — until we started

using Ingenuity, and the top network that differentiated the drugs appeared. The competitor's drug induced the apoptosis pathways and the story was finally written for us. Now our sales rep can say to a doctor, 'Our drug does this, but the competitor's turns on other pathways, and here is a publication in a major journal to prove it.'

- Scientist, investigative pathologist

"Ingenuity helps establish a relationship between the mechanism of action and the pathophysiology. This information provides market differentiation that can potentially increase sales 50% and dramatically increase its NPV (net present value)."

- Chairman of research and development

Life-Cycle Management

Ingenuity Pathways Analysis aids in the life-cycle management of a drug by identifying alternative clinical scenarios and providing an extended window of time under patent protection. First, pathways analysis could be used to identify alternative biological pathways that contain the target, thus allowing a well validated and clinically approved drug to be used for more than one disease or therapeutic area. Clearly, this is highly dependent upon the drug in question and so cannot be generalized to all therapeutic products. However, most companies should find products in their portfolio for which these types of additional market opportunities can be uncovered.

"By looking at a couple of markers with Ingenuity, we were able to see pathways that we were unable to see by looking at the cells. They found a novel use for the compound."

- Group leader gene expression analysis

"Ingenuity can demonstrate other clinical capabilities by showing the significance of a drug that acts upon a target involved in multiple pathways. This may lead to different clinical disease scenarios and increase the overall NPV of that drug."

- Chairman research and development

In addition, product life cycles may be enhanced through the extension of the commercial availability period under patent coverage if Ingenuity Pathways Analysis contributes to a shorter drug development period, as indicated in the scenarios above.

Collaboration

The Ingenuity application enables insight and intelligence by providing a well laid-out picture of biological pathways. By presenting biological pathways that are comprehensive, yet easy to view, the application enhances collaboration among different types of researchers. Improved collaboration should result in improved

productivity with better results, but again, it is hard to quantify direct bottom-line benefits.

"The value for a company is created when a number of individuals, such as the genomics experts and the *in vivo* biology expert, can sit together, maybe at different sites, and analyze the data together. It brings the genomic groups together with the therapeutic area. It helps bridge the gap."

- Head of research and development

"We actually just presented Ingenuity analysis data at a worldwide conference. And, we are going to publish a paper using Ingenuity as one of the figures because it really explains the data in a way that you can't see in any other way."

- Scientist, investigative biology

Time Savings

The interviewees enthusiastically agree that Ingenuity Pathways Analysis will increase their productivity, though many were not willing to extrapolate an estimate of overall time savings. Most researchers felt more comfortable affirming the statement that the cost of drug development will dramatically decrease due to a reduction in failure rates, however, the impact on the time involved to develop any individual drug is unknown. We believe that broad deployment and sustained use of pathways analysis can shorten the time of drug development by increasing efficiency and reducing the number of failures, while enhancing collaboration in the process. As researchers and management gain more experience with this technology, we expect that time savings benefits will become more evident and we will have more quantitative data.

CONCLUSION

Overall, we conclude that the Ingenuity Pathways Analysis application is a valuable asset to be deployed throughout the entire pharmaceutical value chain. Although the ROI is difficult to measure, we feel that we have accurately approximated a conservative estimate for the Ingenuity application's impact on productivity throughout the various phases of drug development:

- ☒ The Ingenuity Pathways Analysis application, when broadly deployed, may help increase a large pharmaceutical firm's overall product development productivity by approximately 10%. This is a conservative estimate in light of the fact that some felt that a global cost reduction of 30–35% could be achieved using the Ingenuity Pathway Analysis application.
- ☒ Alternatively, ROI may be calculated as saving roughly \$90 million per drug over the entire development process, reducing the cost of drug development from \$935 million to \$850 million.
- ☒ The current cost of successful drug development is due to the high number of failed drugs. Ingenuity can dramatically increase the efficiency of drug development by reducing failures by a predicted one-third.
- ☒ Choosing the right animal model is critical for preclinical studies and the follow-on phase II studies in humans. Ingenuity Pathways Analysis provides an improved platform on which to base animal model decisions.
- ☒ Ingenuity Pathways Analysis may help increase revenue by extending the period of time a drug is under patent protection through speeding time to market. In addition, sales may increase through improved life-cycle management via competitive differentiation and reaching additional target patient populations. Depending on the type of drug, some experts foresee that Ingenuity may lead to a 50% increase in sales of a particular drug.
- ☒ More intangible areas where the Ingenuity Pathways Analysis application adds value include collaboration and communication, both internally within a company and externally with key partners or constituencies, such as the FDA during the submission process.
- ☒ The value and return on investment of the Ingenuity Pathways Analysis application will only increase as the application of genomics and proteomics continues to expand across the entire drug-to-market process.

Appendix

Pharmaceutical and biotechnology companies interviewed for this report:

- ☒ Amgen
- ☒ Biogen
- ☒ Centocor
- ☒ Genomics Institute of the Novartis Research Foundation
- ☒ GlaxoSmithKline
- ☒ Helicon Therapeutics
- ☒ Johnson & Johnson
- ☒ KAI Pharmaceuticals
- ☒ Novartis
- ☒ Pfizer
- ☒ Roche
- ☒ Tularik
- ☒ Vanda Pharmaceuticals
- ☒ Wyeth

Titles of interviewees include:

- ☒ CEO of worldwide pharmaceuticals
- ☒ Chairman of research and development
- ☒ Head of healthcare
- ☒ Head of genomic solutions
- ☒ Manager of preclinical science
- ☒ Biomarker development and validation group leader
- ☒ Group leader, RNA dynamics
- ☒ Bioinformatics scientist
- ☒ Principal research scientist, genomics department
- ☒ Preclinical and clinical development scientist

- Principal scientist, genetic technologies
- Investigative pathology and toxicology scientist

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