Cornell Equity Research

ArQule, Inc.
November 17, 1997
NASDAQ: ARQL
Rating: LONG TERM BUY

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Current Price	$22 1/8	1997E EPS	$0.06
52 Week high and low	$9 – 29 1/4	Price/earnings (1997E EPS)	353
Total Shares Outstanding	11.5 Million	1998E EPS	$0.51
Market Capitalization	$262.1M	Price Earnings (1998E EPS)	43
Book Value	$4.6	Dividend per Share	N/A
Price/Book	4.8	Dividend yield	N/A
Debt/Equity	0	Average Trading Volume	108,000

Analytic format

We have utilized three separate valuation models in an attempt to determine a fair stock price for this company: A discounted cash flow (DCF) analysis, an EBO (Edwards-Bell-Ohlson) valuation, and an industry multiples approach. Each method has its own strengths and weaknesses and we have provided justification and explanation where necessary. The price multiples approach is weakened somewhat by a lack of comparable companies. The EBO model is most valid when earnings can be predicted with some accuracy but is less useful when applied to a company such as ArQule which is experiencing rapid but potentially volatile earnings growth. A DCF analysis is the most valid for ArQule, particularly for the purposes of conducting sensitivity analyses on the impact of future milestone and royalty payments on share price. We have evaluated the share price both with and without estimated drug development and royalty revenues in order to determine a 'base' value for the stock and an estimate of its upside potential.

Background and Strategy

ArQule is a four-year-old combinatorial chemistry company headquartered in Medford Massachusetts. Producing vast 'libraries' of chemically pure compounds with commercial potential, ArQule scientists work with pharmaceutical/agri-chemical companies at each stage of the drug discovery process. From initial compound identification through the many steps of chemical 'editing' necessary to convert an identified compound into an optimized drug candidate, ArQule adds value to the process by dramatically shortening the time frame of discovery and improving the odds of producing an optimized drug candidate. An IPO and follow-on offering have left the company with ~12 million shares outstanding, $50,000,000 cash, no debt, and profitability projected by year-end 1997.

Investment Highlights

- Valuations generated by the models lead us to propose a target share price of $33.
- Less risky than typical biotechnology company due to solid revenue stream and multiple products and services.
- Impressive lead over nearest competitors.
- Perfect positioning to capitalize on pharmaceutical trends.
- Present share price does not fully reflect up-side potential.

Overview
The pharmaceutical industry offers significant growth opportunities for the coming decades. A demographic bulge in aging, affluent Americans will assure industry-wide growth of 10-15%/year and greater rewards to those companies that can effectively serve the geriatric market. New drug discovery will be a critical component of this process. A negative value-driver for individual companies comes from a drastically shortened time-to-competitive-entry reality that has had a major impact on drug development and product launch cycles. Instead of having as many as ten years of sole market ownership before competitive entry, pharmaceutical companies now have to be prepared for the possibility of nearly simultaneous market introduction of competing drug compounds. To confront this, drug discovery companies will need to push product candidates through the pipeline as rapidly as possible in order to derive the maximum benefit for their efforts. More than ever, time is of the essence. Because of this, drug companies have found that increasing spending to shorten the development process can pay handsome returns. Additionally, when consumers have had the choice between competing drugs they have demonstrated a clear preference for drugs with reduced side effects. ArQule is perfectly positioned to take advantage of these trends by offering a range of services that can both shorten the drug discovery process and increase the probability of developing a more highly optimized drug.

The drug discovery process
Historically, the discovery and development of drugs has been a costly, lengthy and often unsuccessful process. The time between identification of a biologically active compound and final FDA drug approval has averaged more than 10 years and has cost approximately $300 million. While it's true that we boast a particularly vigorous drug approval process in this country, a good portion of this extreme cost can be traced directly to the traditional drug discovery model.

Drug Discovery Process
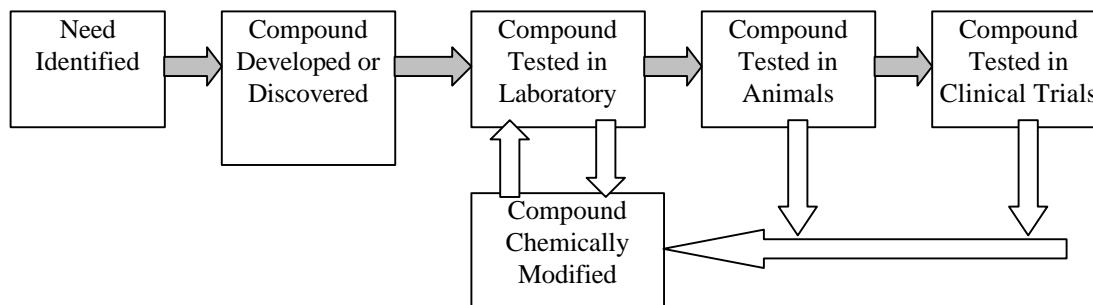
Under this model, once identified or developed, a single compound or class of compounds enters the development pipeline at the left and passes along the gray arrows until eventually (*if* successful) it passes out of clinical trials into the market place. However, at any stage of the development it may be determined that the compound needs chemical modification to overcome such deficiencies as poor absorbability, unacceptable toxicity, or poor stability. Under the traditional system, all such incremental chemical modifications of the original (or 'parent') compound are carried out by synthetic chemists at a cost of about $7500 per modification. Particularly efficient chemists might be able to accomplish 50-100 such modifications per year, provided that the compound is amenable to modification.

Depending on the degree of modification the 'new' compound might be placed back into the pipeline as far back as at the laboratory testing level to begin the entire process anew.

Flaw in the development system
This cycle repeats, chewing up time and money, until a compound is dropped or found to be 'acceptable'. While relatively inefficient, this drug discovery paradigm suffers from one additional and even more serious flaw: It depends on prior identification of a biologically active compound before it can even begin the optimization process described above. Modern scientific methods (and particularly genomics) have produced an unbelievably diverse array of intriguing biological targets for which no known drugs exist. In essence, the drug discovery process has been reversed. Now, instead of having a naturally occurring drug candidate in hand (whose target may or may not even be known) drug discovery scientists often find themselves with interesting targets but no known drugs. To discover a potential drug, a particular target is usually 'screened' against an array of drugs via a high-throughput assay methodology. However, screening against existing drugs can be a largely random and often ineffective process because the existing drug libraries are not logically arrayed and often take the equivalent of gigantic chemical 'steps' between individual compounds. By screening against a limited drug universe it is possible to miss finding an important interaction that might lead to a viable drug candidate.

Combinatorial chemistry to the rescue
Now, with the advent of combinatorial chemistry, an entirely new approach to the drug discovery process is available. Using what is essentially a statistical approach, combinatorial chemistry companies create enormous, diverse arrays chemical compounds that differ from each other in slight but critical ways and then screen targets *en masse* against these compounds utilizing recently developed high-throughput assay methodologies. Literally millions of compounds can be created and individually screened against a target of interest in the hopes that, randomly, one or more of them will interact with the target in a biologically relevant and exploitable manner.

Combinatorial Chemistry
The advent of combinatorial chemistry is a paradigm shift from the traditional process of drug development What a whole team of organic chemists could accomplish in a year, can now be achieved in less then a week of automated combinatorial chemistry synthesis. Combinatorial Chemistry allows scientists to synthesize vast numbers of diverse compounds, normally organized into libraries.

There are two distinct approaches used for synthesis of the combinatorial libraries. These are the Parallel Synthesis and the Pool-and-Split Methods. In Parallel Synthesis, all products are assembled individually in their own vessels, impurities are removed at every step and the exact identification of the molecule is precisely known. In the Pool-and-Split method, a mixture of related compounds are produced in the same vessel. Compared to Parallel synthesis, this approach significantly reduces the number of containers and has a multiplier effect on the number of different compounds generated at each step. Several major problems exist with this method. First, the exact identity of each compound has to be deconvoluted through a tedious computational method. Second, there is a higher probability of generating false positives when one screens mixtures of compounds rather than individual compounds because of multiple compound-target interactions. There may

also be a problem in false negatives given that compounds are typically present at very low concentrations in Pool-and-Split vessels. Third, the compounds are typically adhered to a substratum meaning that stereo-specific interactions between drug and target are hindered. The parallel synthesis method employed by ArQule avoids all of these problems and is therefore a much more powerful combinatorial chemistry methodology.   Furthermore, ArQule chemistry is performed in solution (vs. solid phase) taking advantage of reaction mechanisms developed over the last century allowing the design of libraries with tremendous chemical diversity.

Value of combinatorial chemistry
Irrespective of the type of approach used, combinatorial chemistry can add tremendous value to a drug company's discovery process. Using combinatorial chemistry methods, the cycle time for drug development can be drastically shortened both with respect to internal measures and, more importantly, to external competition. Shortening the process by even a few months can add value by saving R&D costs and by yielding a first-to-market position. In addition, combinatorial chemistry increases the chance of identifying potent lead compounds with reduced side effects, thereby increasing efficacy and minimizing side effects. This process also allows for a broader patent coverage where entire motifs of active compounds can be protected reducing potential future competition. The timing of this technology is perfectly suited to the large number of therapeutic targets being identified by the biotechnology industry.

ArQule mapping arrays
ArQule offers huge 'libraries' of mapped compounds to drug companies for screening against biological targets of interest. These 'mapping arrays', as they are called, simply exploit the power of numbers. Say that a drug discovery company has a single target identified. They can 'screen' this target against all known existing drugs in hopes of finding a 'hit'. But this method can be akin to finding the proverbial needle in the haystack. The currently existing drugs that they would use are limited in number and essentially random with respect to their shapes, sizes, and electrical charges. Furthermore, the company may or may not own the rights to these existing compounds. Thus the odds of discovering new therapeutic agents by this method are rather low. Instead, ArQule's mapping arrays consist of up to 1,000,000 logically ordered novel compounds that are delivered to the drug company allowing a tremendous number of combinations of chemical shapes and charges to be tested in a reproducible and deterministic manner. Given this, the chance of encountering a 'hit' increases with the number of compounds screened greatly decreases the chances of overlooking interesting molecular configurations.

ArQule business model
ArQule ships the mapping arrays to drug discovery companies but preserves the rights to those compounds. This means that similar arrays can be shipped to multiple companies thereby maximizing the number of targets against which their compounds are screened. This important fact greatly multiplies the probability that ArQule compounds will be commercialized and stands in stark contrast to the majority of biotechnology companies whose hopes are pinned on a single compound or treatment.

When a compound interacts with a target of interest this event is called a 'hit' and the compound will then usually enter a phase of directed development. Once a hit is identified ArQule may be called upon to develop a 'directed array' which is essentially a logical expansion of the chemical motif of the identified compound. As a lead compound moves through the pipeline ArQule receives milestone payments culminating, hopefully, in royalty payments when the compound is marketed as a drug. These payments are a source of significant potential future revenue and are an important component of ArQule's business plan. Given the sheer number of collaborative working agreements that ArQule has entered into, and the number of compounds and targets being tested, these payments could be significant. **With over 50 optimization programs underway it is reasonable to conclude that as many as 4-5 drugs could reach the NDA stage as a result of today's activities**. Our valuation model includes only the probability of 2 *or fewer* drugs reaching market over the next fifteen years - a very conservative estimate.

ArQule has also entered into agreements with over 12 biotechnology companies whereby the mapping arrays are shipped for free but retain 50% of all future revenues that might arise from the shipped compounds. Taken together, ArQule has an incredibly strong and viable business plan that generates significant revenues from ongoing activities but also retains the promise of significant up-side potential from future marketing of developed compounds.

Three and nine months ended September 30, 1997 and 1996
Revenue
The Company's revenue for the three months ended September 30, 1997 increased over $1.4 million from the same period in 1996 from $3.3 million to $4.7 million. Revenue was $11.2 million and $4.4 million for the nine months ended September 30, 1997 and 1996, respectively. The increases is primarily attributable to the addition of collaborative agreements with Roche BioScience, Monsanto Company and American Home Products in October 1996, December 1996 and July 1997, respectively.

Cost of revenue
The Company's cost of revenue for the three months ended September 30, 1997 increased $1.6 million to $3.0 million from $1.4 million for the same period in 1996. Cost of revenue was $7.3 million and $3.3 million for the nine months ended September 30, 1997 and 1996, respectively. These increases are primarily attributable to the costs associated with the hiring of additional personnel, addition of facilities, and general overhead and expenses associated with producing Mapping and Directed arrays as part of their ongoing agreements.

Net income (loss) The Company's net income for the three months ended September 30, 1997 was $0.3 million as compared to ($1.4 million) for the same period in 1996. The net loss was $0.4 million and $2.2 million for the nine months ended September 30, 1997 and 1996, respectively. The third quarter net income for 1997 results from an increase in revenues from the company's pharmaceutical partners and higher net interest income.

Competition
A number of companies are now offering custom approaches for lead-compound discovery

using combinatorial chemistry techniques. While there are several niche players in this rapidly growing industry, Pharmocopeia is by and large ArQule's main competitor. However, ArQule possesses what we see as a superior technological advantage over Pharmacopeia, which uses a Pool-and-Split methodology, as discussed above. Other imitators likely to duplicate ArQule's conceptual approach to lead-compound discovery have recently emerged. One such player is BioFocus, a Kent, UK based privately held company which offers an "integrated lead discovery and optimization service", conceptually quite similar to ArQule's. While ArQule has a time advantage over these companies, over time they may erode ArQule's profitability and market dominance. ArQule's other source of competition is from in-house development of this technology by big pharma. Merck recently spent over $100 million for internal development of this technology. On the positive side, this makes ArQule, and other companies in this niche attractive take-over candidates. Three such deals have taken place in recent years. These are: acquisition of Affymax by Glaxo for $540 million, Sphinx by Eli Lilly for $72 million and Selectide by Marion Merrell Dow for $60 million.

Overall, we expect the market for combinatorial chemistry to grow. As the technology evolves and is further refined, there will be opportunities for the major players in this niche market to become further specialized, deliver service and develop a loyal customer base. The trend is definitely there for a number of players to participate in this market and achieve profitability.

Arris Pharmaceutical develops synthetic small-molecule therapeutics. Their business model is quite different from ArQule's. They use a broad, integrated approach to structure-based drug design, combining X-ray crystallography with genomics with subsequent lead compounds developed using combinatorial chemistry and high throughput screening. The company's primary focus is on protease-based therapeutics to treat asthma, cytomegalovirus, herpes, anemia-related kidney failure, cancer, and osteoporosis. Most of the company's pharmaceuticals are in the research and preclinical-testing stages of development, with an asthma drug at the clinical-testing stage. Arris Pharmaceutical has entered into collaborative research agreements with Merck, SmithKline Beecham, Bayer, Pharmacia & Upjohn, and Amgen. At present it doesn't represent an immediate threat to ArQule's business model.

BioFocus is a new European based company which has business and technological model quite similar to ArQule. It was launched in 1997 by leading drug-discovery scientists from the pharmaceutical industry. It offers a lead identification process conceptually similar to ArQule's Mapping and Directed Arrays. They offer a number of monomer choices as the building blocks that are used to construct compound arrays for lead expansion and optimization. BioFocus combines the power of combinatorial chemistry with QSAR analysis, molecular modeling and computational analysis to provide the best possible chance of identifying a lead compound. BioFocus received its first contract in September this year from Roche Discovery Welwyn, a vote of confidence in its technology and management. Over time, we expect BioFocus to become a viable competitor to ArQule.

Pharmacopeia develops technologies that accelerate the drug-discovery process. Its Pool-and-Split process creates chemical compound mixtures in hetergenous batches that are then used t screen against the targets of choice. Pharmacopeia's technology uses tiny plastic

beads that record each step in the chemical-synthesis process which simplifies, but does not eliminate, the subsequent problem of identifying which compound in a mixture is responsible for the detected activity. It licenses its library of compounds principally to biotechnology and pharmaceutical companies. While Pharmaceopiea is perhaps ArQule's biggest competitor, its approach to lead compound identification using the split pool method is not as attractive as ArQule's. To date, Pharmacopeia has developed partnership arrangements with a number of prominent pharmaceutical companies such as Bayer, Berliex, Diachi, Schering, Sandoz and Zeneca.

Trega Biosciences is a drug discovery company, which utilizes combinatorial chemistry and other technologies to create novel small-molecule drug candidates. The company has leveraged its technology platform by entering into pharmaceutical alliances, enabling partners to access Trega's technologies in exchange for licensing fees, potential milestone payments and royalties, and by establishing joint-discovery alliances with biotechnology companies. Trega also uses its drug discovery technologies in its internal development programs.

Tripos traditionally has been the leader in providing software for lead compound discovery, such as Sybyl, Alchemy, Unity, Triad and ChemSpace. Recently, it has also started offering certain web based products such as GASP and a joint collaboration with MDL Information Systems, Inc., a chemical database company. Tripos's software allow scientists to model molecular processes, access and analyze chemical and biological data, construct working models of systems to guide the experimental process and build virtual libraries of chemicals for lead compound discovery In 1995, Tripos, in alliance with Panlabs, Inc. added a combinatorial chemistry arm to identify lead compounds. By end of 1996, it had 85,000 compounds in its Optiverse screening library. Tripos has received research contracts from Bristol-Myers Squibb, Menarini, Union Chemie Belge, Hoechst and Pfizer.

Company	Focus	Ticker	Stock Price	Shares Outstanding	Market Value MM ($)
Arris	Protease based Therapeutics	ARRS	10 5/8	15.07	173.5
BioFoucs	Combinatorial Chemistry	-	-	-	2.5
Trega	Combinatorial Chemistry	TRGA	4 1/16	13.49	56.8
Pharmacopeia	Combinatorial Chemistry	PCOP	18 3/8	11.56	213.6
Tripos	Software & Combinatorial Chemistry	TRPS	15 1/4	3.55	54.2

Valuation methods and models

Discounted Cash Flow
Assumptions for Income Statement are indicated in footnotes at bottom of model. The P/E valuation at the bottom of the page uses a multiple of 45 and is based on 1998E

earnings. The discount rate of 15% is low for a biotechnology company but we argue that ArQule, with its multiple products and signed revenue agreements should be discounted at a lower rate than the 20%-25% that is typically applied to biotechnology companies. The ArQule business model, with its emphasis on diversifying its risk across multiple product lines and drug development companies, is considerably safer than the typical biotechnology company whose fortunes may rest on a single product (and may not receive any revenues unless successful). Note that no 'risky' revenue such as drug development or royalty revenue is included in this model as these revenue sources are dealt with in the Monte-Carlo simulation. The company was forecast out for a period of fifteen years reflecting the longer product development and life cycle of pharmaceutical agents.

Balance sheet items were forecast off of sales or assets where appropriate and based on historical data when available. Significantly, this company reports no inventories and no debt. None were projected as a component of our analysis and so assets and liabilities increased primarily as a result of an increase in cash and deferred revenue, respectively. While a different proportional distribution of assets is expected, the underlying working capital ratio will not change and so we are comfortable with this approach.

Edwards-Bell-Ohlson (EBO) Model
The discount rate is again set at 15% and the model excludes any and all potential revenue from drug development and royalties. Stock valuations for these revenue streams are dealt with under the Monte-Carlo simulation DCF model. The long-term growth rate of 25% yields a slightly lower near term estimate of EPS but is on target with our 13-year estimate and slightly over estimates our 15-year target derived from the DCF model. No dividends are forecast for this company.

Monte Carlo Simulation DCF Model
Monte Carlo simulation method allows one to deal with the inherent uncertainties in the drug development process and the fact that a substantial portion of the drug development and milestone revenues are back loaded. Given that the odds of getting a drug in the market may be somewhat of a random event, we can use this approach to estimate the likelihood of a successful event. The output from this model was used to evaluate the impact on the revenues, costs, net income and ultimately the stock price through year 2012. We used a cost of equity of 15 % to discount the cash flows back to present. We believe that given ArQule's existing revenue stream and the diversified nature of its biotech and pharmaceutical collaborations, it merits a discount rate later lower than most one or two product biotech companies (~20-25 %) but higher than pharmaceutical companies (~11-12 %). Using a set of conservative estimates and this simulation approach, we estimate that there is a 60 % chance that the present value of the stock is at least $33.

Summary

- ArQule is one of the few combinatorial chemistry companies that can deliver value to both its drug discovery collaborators and shareholders.
- ArQule's approach provides the most rapid and effective means for discovering and optimizing small molecule drugs.
- ArQule is perfectly positioned to capitalize on the pharmaceutical industry trends

- ArQule is unlikely to receive any significant near-term competition either from other combinatorial chemistry companies or from big pharma in-house development.
- On a long-term basis we view ArQule as possessing a supremely talented management team that will successfully negotiate the transition from being service provider to being a more fully integrated drug discovery company.
- Our very conservative estimates of future royalty and drug development income indicate that a stock price significantly higher than the current price of $22 is justified.
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ArQule Pharmaceutical and Selected Biotechnology Partnerships

Pharmaceutical partners

Date	Company	Value and Structure	Targets
June 95	Abbott Labs	$35 MM Mapping and Directed Array Program	neurological, metabolic, immunological & infectious diseases
November 95	Solyay Duphar B.V.	$50 MM Mapping and Directed Array Program	Multiple Targets
September 96	Roche Bioscience	$60 MM Directed Array Program	Multiple Targets
January 97	Monsanto	5 year collaboration, $12 MM for delivery + milestones, royalties	crop protection products herbicides, pesticides
July 97	Wyeth Ayerst	Royalty and milestones ~ $26 MM in 1998 + $2 MM in equity. Minimum of 15 compounds over 5 years $100 MM excluding royalties	Multiple Targets
July 97	Pharmacia Biotech AB	Third extension since 1995	Multiple Targets
November 97	Sankyo Pharmaceuticals	Collabortaion	Multiple Targets

Sample Biotechnology Partners

January 97	Signal Pharmaceuticals	Joint Venture	Gene Expression
April 97	Genzyme	Option, joint or exclusive Licensing	Cancer, infectious diseases, autoimmune
June 97	FibroGen	Joint	Surgical scarring, Fibrosis
July 97	UCSF	ArQule retains exclusive licensing rights	Protease inhibitors
July 97	GenQuest	joint	Melanoma, Prostate, Breast cancer

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