

Notes for Superside:

- Need an eBook that we can use primarily as a download that we push on paid social
  - Image ad
  - Document ad
- Therefore needs to be visually engaging, particularly the first 4-5 pages
- And we need a front cover that pops and would work well as an image ad (12x12)
- Start on graphics and cover and then we will finalize text in the next week.

## eBook text:

Title

To reach scale, find what fits

Subtitle

How automation helps biotech startups scale

Brent - for this ebook, please add pictures of people working in labs - especially ones that look like startups - preferably with a Flex next to them (failing that, an OT-2, failing that, no robot).

Liquid Handling Value Throughout Startup Growth (make this into a pretty diagram):

- Research and Discovery
  - Accelerating workflows
  - Data quality
  - Cost efficiency
- Proof of Concept and Funding Rounds
  - Higher throughput
  - Investor confidence
  - Cost savings
- Scaling Operations
  - Scalability
  - Quality assurance and reproducibility
  - Resource optimization
- Commercialization
  - Speed to market
  - Production standardization
  - Resource optimization

## Introduction

The 21st century is becoming the Century of Biology, with breakthroughs now occurring at previously unimaginable speed. Cutting edge discoveries have paved the way for real world applications in fields from personalized medicine to environmental conservation. With technologies such as next-generation sequencing and CRISPR-Cas9 starting this revolution, the addition of artificial intelligence and a raft of high throughput methods are set to exponentially increase the pace of progress. As fast as scientific discoveries are made, scientists from companies small and large race to apply them. With this pressure sure to increase, successful innovators who achieve their visions to change the world will need not only an original idea, but perhaps also early adoption of technologies to develop and commercialize that idea. By wisely considering future needs, a company can raise its trajectory: forward-thinking adoption of technology early in a company's lifetime may be the route to continued funding and eventual commercialization before competitors.

In the world of these early stage biotech companies, securing the next round of funding is more than a milestone: in many cases it is a gateway to a new phase of research or growth. With every round of funding, a new clock starts with a fresh set of goals. Although this gives the appearance of a race, the reality is that quality and the ability to demonstrate readiness for the next phase are equally as important as meeting defined progress markers. Companies must therefore not only move quickly before funding runs out or a competitor outpaces them, but must do so in a credible and reproducible way to ensure investors have the confidence to finance their future growth.

*Quote: Retro Biosciences*

<https://opentrons.com/customer-stories/retro-biosciences-sc-rnaseq/>

*Machines are tireless, fast, and accurate. We are exploring unknown biology, and some of these explorations are across such a breadth of parameters, including combinations, that exploring them manually would be a waste of scientific minds.*

## Investors notice

While speed is undeniably paramount, investors look beyond this, scrutinizing results and demanding viable plans for the completion of future research and development phases. Completed work must demonstrable tangible science performed with discipline and care that reflects the scientific rigor necessary to eventually go to market. Plans for future phases must be scientifically, logistically, and financially realistic. Much of this can be distilled down to two seemingly competing imperatives: speed and scientific rigor. While these may at first glance seem mutually exclusive, in fact there are many companies that have achieved success in achieving both. Those that have done so have embraced a similar theme: embracing lab automation wherever possible.

Investors always consider market positioning when evaluating startups – a demonstrated commitment to cutting edge technology indicates a potential competitive edge, not only internally, but in attracting

collaborations or a future acquisition. By adapting advanced technologies such as automated liquid handling, startups signal their ability to compete and execute top tier science, aligning themselves with established pharma and biotech.

## Scalability

Successful biotech startups truly embrace a key concept: scalability. By thoughtfully considering likely future needs, scientists can implement the tools they will need to scale up later when they perform their earliest proof of concept studies. A prime example of this is liquid handling automation: while it might not appear worthwhile for initial experiments, establishing systems and protocols for experimentation in initial low throughput experiments means minimal revisions to experimental protocols once higher throughput is needed. Substantial savings in time and money can be realized by avoiding the need to redesign, implement, and validate new methods as throughput increases and research shifts from discovery to development.

*Quote: Cytera*

<https://opentrons.com/customer-stories/opentrons-user-interview-with-dr-xian-weng-jiang-of-cytera-cell-works/>

*When we started at Cytera, we had to run all these same assays by hand. It was a waste of time to run them over and over and over again that way. We're a startup, so it made no sense to do that when we could have the OT-2 robot handle all of the repetitive work.*

## Reproducibility

Researchers often describe the best technicians as “like a machine”, citing the qualities of focus and lack of errors as particularly admirable. Even the best technicians will at times be distracted and make mistakes, particularly in the most repetitive tasks such as pipetting into 96 or 384-well plates. The cost of these errors may be high, especially if they go unnoticed or are part of a lengthy or expensive protocol, but can be cheaply mitigated with the addition of an automated pipetting solution. Doing so not only frees up technicians to prepare for subsequent experimental steps, but eliminates the all-too-common mistake of aspirating from or dispensing into an incorrect well. By incorporating automated liquid handling, biotech companies can turn questions of precision and reproducibility into talking points for investors, demonstrating their capabilities as an advantage over competitors also seeking funding. In particular, investors appreciate proactive efforts taken to minimize experimental variation and increase efficiency.

## Costs

Liquid handling has historically been defined by either manual processes necessitating hiring additional operators, or automated systems that themselves were more expensive than an additional employee. In the last few years, however, systems have become available that not only cost little enough not to qualify

as a capital expense, but enable labs to realize cost savings that return the cost of the robot in several months.

One of the most important cost savings caused by automation is the often-overlooked increased value achieved by technicians. By freeing technicians from highly repetitive pipetting, several benefits can be realized. The first of these, and most obvious, is that personnel are freed up to complete other tasks, for example preparation steps for the next stage of an experiment, thereby speeding up the time to result. Secondly though, the technician is able to devote their time to something that better utilizes their skills and knowledge, thereby returning a higher value return on their time. Lastly, and seldom considered, is the reduced strain on technicians themselves. While physical injuries such as those caused by repetitive strain are well-recognized, the sustained concentration necessary for pipetting using plate formats should not be dismissed. By automating this mentally taxing aspect of lab work, lab personnel are less mentally drained, reducing errors and increasing productivity throughout the day.

**Quote: MilliporeSigma**

**<https://opentrons.com/customer-stories/opentrons-user-interview-with-milliporesigmars-d-r-annabel-shang/>**

*These assays require a lot of physical arm movement and finger pressing, which can easily cause neck and back pain as we keep one posture for a long time. They also require high-attention and focus, which makes people feel exhausted afterwards. But with the [Opentrons robot], minimal physical or mental effort is needed, which is good for operators who have bad neck and back issues, and for maintaining our focus and energy levels.*

Additional value can be realized through automation by miniaturizing experiment volumes. For example, by reducing 25  $\mu\text{L}$  reactions in a 96-well plate to 12.5  $\mu\text{L}$  reactions in a 384-well plate, not only is the cost of reagents halved, but also the volumes of precious samples needed. The number of plates is also reduced by 75%; a cost reduction realized not only in purchasing, but also in waste disposal, with complimentary environmental benefits. By miniaturizing using liquid handling robotics in this way, the need for controls and standards is also reduced, as is inter-plate variation in data.

*Quote: Animal Health Lab Prairie Diagnostic Services Inc.*

**<https://opentrons.com/customer-stories/opentrons-user-interview-with-anatoliy-trokhymchuk-and-mengying-liu-of-animal-health-lab-prairie-diagnostic-services-inc/>**

*But the benefit is not needing a highly skilled tech—and freeing that tech’s time to do something else. We are working to standardize this throughout the lab.*

## Speed

While increased speed is often touted as a primary benefit of introducing lab automation, this is often secondary to an even more important benefit: reductions achieved in hands-on time. A robot will generally pipette faster than even a focused human operator, but far more importantly will work without

tiring or need for breaks. Moreover, with lab automation capable of incorporating thermal cyclers, shakers, and magnetic bead protocols, robots equipped with a gripper to move labware and tips from one deck location or instrument to another are capable of running entire protocols without human intervention. This is especially valuable overnight as liquid handling robots can take on an additional role as a second shift, working through the night in order that researchers arrive the next morning to be greeted with prepared samples or completed experiments. While in the short term this accelerates research, in the long term this is also a route to higher throughput and scalability without increasing costs.

**Quote: MilliporeSigma**

**<https://opentrons.com/customer-stories/opentrons-user-interview-with-milliporesigmast-d-r-annabel-shang/>**

*While the robot is running by itself, I can save two hours per assay in tedious sample dilution and liquid transfer.*

## Drug Discovery and AI

The use of AI in biotechnology is reshaping drug discovery, predicting drug candidates and enhancing the ability to find new treatments. With this promise of progress, however, comes the need to screen these candidates faster and more efficiently. Traditional methods for doing so are limited by their manual aspects, even when additional labor can be made available. Automation provides the only real viable pathway to scale up the screening of identified candidates, as the sheer number of experiments needed becomes immediately overwhelming for manual methods. Incorporation of automated liquid handling in drug discovery has become not simply an advantage, but a strategic imperative, providing a model for a plethora of other biotechnology endeavors.

## Important considerations for startups considering automated liquid handling

The startup environment is a unique blend of demands and constraints, chief among these the needs to move quickly and efficiently in order to secure continued funding. Startups must be careful not to overcommit, but also must make intelligent investment decisions that serve not only immediate, but also future needs.

A prudent early investment should be made in automated liquid handling. Doing so means that as many protocols as possible are first established using a liquid handling robot. In this way, savings in time and money can be immediately realized, and the need to subsequently convert and validate manual protocols to automated ones is negated.

**Quote: AIM Biotech**

**<https://opentrons.com/customer-stories/aim-biotech-organ-on-chip/>**

*“We knew compatibility with automated fluid handling was going to be a critical useability factor. We wanted to validate our idenTx Handling Protocols on a capable, affordable and easy to use automation system and the Opentrons [robot] proved to be an ideal platform for this,” says Sei Hien Lim, AIM Biotech Applications Development Manager.*

Although it is a strongly defining feature of biotech startup companies that the future is harder to predict than that of more established companies, efforts should be made to anticipate both future workflows and workloads. Consider not only increased speed and cost savings that can be achieved by automating current or short-term future processes, but whether a system that fits a current budget will be suitable for future work. Typically, the most important considerations are scaling to higher throughput, in which case a liquid handling robot capable of pipetting 96 channels simultaneously may be essential, and also the full walk-away automation of more complicated workflows, for which a gripper is necessary in order to move plates and replace empty tip boxes.

An open-source and easy to use liquid handling solution is key. While most vendors offer expensive protocol programming services, it is important to have a range of methods available to match your needs as they evolve. For example, existing protocols for a wide variety of kits from various manufacturers can be downloaded for free from the Opentrons website. For new kits or protocols, a simple and free drag and drop interface is available, and for users who are comfortable using python and wish to explore advanced settings, an API is also available without charge. This has the added benefit of enabling integration with other systems and equipment, further increasing the value of adding automation.

## Summary

Early stage biotechnology companies are faced with a unique and challenging existence. While on the surface it appears that producing scientific results in a limited timeframe is central to survival, successful, experienced entrepreneurs know that this superficial summation will lead to bewilderment when milestones are met but additional funding does not materialize. As investors are faced with a seemingly endless menu of companies, it becomes incumbent on those companies to proactively demonstrate that they are more than their recent scientific results. By demonstrating not only speed, but scientific rigor, efficiency, and preparedness for the future, startup companies distinguish themselves from the field and position for success.

This quote below is a spare for now - after we're in layout, let's see if there's somewhere we want to use it.

*Quote: Fidabio*

*<https://opentrons.com/customer-stories/opentrons-user-interview-with-brian-sorensen-and-henrik-jensen-of-instrument-developer-fidabio/>*

*Our customers, however, run larger experiments where it doesn't make sense to have technicians pipette faster to complete them; a robot can pipette and the scientist can carry out analysis. As soon as the experiment involves a larger dilution series, or more samples need to be aliquoted, you should consider automation.*

*Also:*

*With a liquid handling robot, it is easier to document your research because you can share the pipetting scripts and researchers can reproduce the data. Automation provides a very detailed explanation of what you can—and did—do.*

*Also:*

*When we developed our own platform, it was important to us that there was a high level of automation. In that sense, the OT-2 was a nice enhancement of one of our own key selling points.*

*Also:*

*We know our technology has the capability of providing very accurate data, but it is still biology where even small variation can affect the results. For the applications we work with—drug discovery, for example—we must make sure we're controlling as much of the experiment as possible. The ability to control the prep process makes for better results.*