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Table of Contents and Frequently Asked Questions

INTRO: WHAT IS BIOGENERATOR FUNDAMENTALS? .............................................................................................................. 6
WELCOME TO THE LIFE-SCIENCE ENTREPRENEUR’S ROADMAP

Sue’s Story: I have an idea, how do I get started? .......................................................... 7
Sue’s Story: With whom can I talk safely about my idea? How can I learn from others without jeopardizing my ideas? .......................................................... 8
Sue’s Story: How can I find mentors and advisors to help? ........................................... 9

MARKET RESEARCH

What is a Market Analysis? ............................................................................................... 10
1. What is Market Research? ........................................................................................... 10
2. What is Customer Research? ...................................................................................... 11
3. What is Competitor Research? .................................................................................... 11
4. What are Barriers to Entry? ....................................................................................... 11
What are the basic questions of Market Analysis? .......................................................... 12
Sue’s Story: What does it mean to be “focused”? ......................................................... 12
How do I better understand my potential customers? ................................................... 13
What is Primary Market Research? .............................................................................. 13
What is Secondary Market Research? .......................................................................... 13
Sue’s Story: What can I learn from market research? .................................................. 13
How do I evaluate competitors? ..................................................................................... 14
Sue’s Story: How do I target a market, and what is a SWOT analysis? ...................... 15
Market Analysis Section Summary .............................................................................. 16
What are some useful resources related to market research? ....................................... 16

REGULATORY CONSIDERATIONS

How are drugs, biologics, and/or vaccine regulation by the FDA? .............................. 17
How are generic drugs regulated? .................................................................................. 18
What are Bio-Similars? .................................................................................................. 18
How does the FDA regulate medical devices and diagnostics? ..................................... 18
How are medical devices classified by the FDA? What are the differences between Class 1, 2, and 3 devices? ......................................................................................... 18
What are the primary review mechanisms for Class II and III devices and diagnostics? What is a PMA, 510(k), or IDE? ................................................................. 18
What is CLIA? What is a lab-developed test? ............................................................... 19
How does the FDA regulate dietary supplements? ....................................................... 19
What are the regulatory pathways for animal therapeutics? ......................................... 19
How are animal devices and diagnostics regulated? .................................................... 20
What are the regulatory mechanisms for animal feed additives? ............................... 20
Food additive petition through the FDA: ...................................................................... 20
Feed listing petition through AAFCO: .......................................................................... 21
How are animal vaccines regulated? ............................................................................ 21
How are GMO crops regulated? .................................................................................... 21
How does the FDA review new GMO crops? ............................................................... 22
How does the EPA regulate GMO crops? .................................................................... 22
What are some useful resources related to regulatory pathways? .............................. 22

BUSINESS FORMATION

Should I choose an LLC or corporation as the entity type for my startup? ............... 23
Corporations (also referred to as standard corporations): .......................................... 23
<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intellectual Property</td>
<td>27</td>
</tr>
<tr>
<td>What is Intellectual Property?</td>
<td>28</td>
</tr>
<tr>
<td>Why should I be concerned about Intellectual Property?</td>
<td>29</td>
</tr>
<tr>
<td>What is a Patent?</td>
<td>29</td>
</tr>
<tr>
<td>What are the parts of a Patent?</td>
<td>29</td>
</tr>
<tr>
<td>What are the Requirements for Patentability?</td>
<td>30</td>
</tr>
<tr>
<td>What are examples of patentable subject matter?</td>
<td>31</td>
</tr>
<tr>
<td>What are examples of non-patent eligible subject matter?</td>
<td>31</td>
</tr>
<tr>
<td>How does one determine if an invention would have value as a Patent?</td>
<td>32</td>
</tr>
<tr>
<td>How do I complete a preliminary Patentability and FTO Search?</td>
<td>33</td>
</tr>
<tr>
<td>How much does a Professional Patentability or FTO Search cost?</td>
<td>33</td>
</tr>
<tr>
<td>What are the steps to filing a patent?</td>
<td>33</td>
</tr>
<tr>
<td>What is a PCT Application?</td>
<td>34</td>
</tr>
<tr>
<td>How much does a patent cost?</td>
<td>34</td>
</tr>
<tr>
<td>How do universities handle their IP? How does a startup work with a university to commercialize their IP?</td>
<td>35</td>
</tr>
<tr>
<td>Why are Universities involved in IP?</td>
<td>35</td>
</tr>
<tr>
<td>What is the process for working with the university TMO for me as an inventor?</td>
<td>36</td>
</tr>
<tr>
<td>What is the process for doing Business with the TMO as a company founder?</td>
<td>37</td>
</tr>
<tr>
<td>What is an Option Agreement?</td>
<td>37</td>
</tr>
<tr>
<td>What is a Technology License?</td>
<td>38</td>
</tr>
<tr>
<td>What are the typical terms in a Technology License?</td>
<td>38</td>
</tr>
<tr>
<td>What are some examples of licensing terms and policies from local Universities?</td>
<td>40</td>
</tr>
<tr>
<td>Trademarks</td>
<td>42</td>
</tr>
<tr>
<td>How do I acquire rights to my Trademark?</td>
<td>42</td>
</tr>
<tr>
<td>Copyright</td>
<td>43</td>
</tr>
<tr>
<td>Trade Secret</td>
<td>43</td>
</tr>
<tr>
<td>What can I do before I talk to an attorney about IP?</td>
<td>43</td>
</tr>
<tr>
<td>Sue’s Story-Is my idea patentable? How do I gain access to university IP?</td>
<td>44</td>
</tr>
<tr>
<td>What are some additional resources covering intellectual property?</td>
<td>45</td>
</tr>
<tr>
<td>Team Building</td>
<td>46</td>
</tr>
<tr>
<td>What are the special challenges for building start-up teams?</td>
<td>46</td>
</tr>
<tr>
<td>How can I overcome the team building challenges posed by Start-ups?</td>
<td>46</td>
</tr>
<tr>
<td>How do I get started building my team?</td>
<td>47</td>
</tr>
<tr>
<td>What roles will my early team members play?</td>
<td>47</td>
</tr>
<tr>
<td>Why and how should start-ups use equity as compensation?</td>
<td>48</td>
</tr>
<tr>
<td>• What is Founder Stock?</td>
<td>48</td>
</tr>
<tr>
<td>• What is a stock grant/buyback program?</td>
<td>49</td>
</tr>
<tr>
<td>• What are qualified/non-qualified stock option programs?</td>
<td>49</td>
</tr>
</tbody>
</table>
WHAT ARE SOME ADDITIONAL RESOURCES RELATED TO FINANCING A VENTURE?
**Intro: What is BioGenerator Fundamentals?**

BioGenerator Fundamentals is a business-coaching program designed to support early, would-be entrepreneurs in the Life Sciences in St. Louis. Fundamentals offers two program tracks: Coaching and Resources (“C&R”), which offers training and resources to help for first-time biotech founders understand business principles, and Grants to Business (“G2B”), which helps life-science startups develop competitive applications for business grants with a particular focus on SBIR/STTR and other non-dilutive funding.

This roadmap is an important early step in our C&R program. In addition to offering this “Life Science Entrepreneur’s Roadmap”, the program provides a “one-on-one”, customized business learning experience (to build upon the classroom-style learning offered by several other local programs) for each participant. This “Roadmap” is an important tool referenced frequently by the BioGenerator C&R program for specific assignments to program participants.

**Focus on Founders** – The program and this roadmap are designed to train and support Founders of businesses. They do not provide the level of training necessary for an operational role in a start-up (such training is already provided by several other programs in St. Louis). This is because operational training can be too detailed and time-consuming for many company founders – such as busy academicians; PhD students and post docs – who frequently have innovative technology ideas but whose current career and/or lack of relevant business experience precludes taking on operational roles at this career stage.

Instead, the Program and Roadmap seek to convey a broad conceptual understanding of most operational business topics and then focus deeply on teaching certain skills and providing certain resources especially needed by company Founders. These include:

- Effective company incorporation and registration at low cost.
- How to create a viable business model using the Business Model Canvas.
- Market, Customer and Competitor research studies.
- Technical and business development consulting projects.
- Small business development and proof of concept grants.
- Access to a state-of-the-art biology and chemistry lab facility.
- Training and support for federal grant applications through our G2B program.

**Learning is Earning** – Program participants earn access to the program resources by achieving specific training and business development milestones to the satisfaction of the Program Director. This “meritocratic” approach allows the program to allocate these precious resources to those most likely to be successful.

**Broadly covers bio and life sciences** – The Program is targeted to founders starting a company in the bio and life science “space”, including: human and animal therapeutic products; diagnostic products; medical devices; animal and crop agriculture products; research tools, reagent and service companies, and Healthcare IT.

For more information, [click here](#) or contact:

Harry Arader – Program Director
312-933-5250; harader@biogenerator.org
Welcome to The Life-Science Entrepreneur’s Roadmap

Believe it or not, by seeking support from BioGenerator Fundamentals you have already demonstrated key aspects of a successful life-sciences company founder: You are passionate about your idea and you are ready to invest ‘sweat equity’ (your own personal efforts) into it. Congratulations, you are already on your way!

The Life Science Entrepreneur’s Roadmap for Company Founders – developed in cooperation with The BALSA Foundation – aims to serve as a guide to help you understand the basic concepts that entrepreneurs tackle in order to realize their business ambitions. It was designed to be used as part of the BioGenerator Fundamentals program but can be used by anyone interested in creating a start-up company in the life sciences. With the Roadmap as your reference, you will be able to initiate and begin building a successful business. We hope the Roadmap will help you confirm a need for your idea, establish your business as a legal entity, develop intellectual property, learn how to champion your idea to any audience, and pursue independent financing.

Although we aim to provide information that you can apply to your business idea, the Roadmap is by no means comprehensive. It covers the basic concepts at a level appropriate for a company founder. At appropriate junctures, it provides links to other sites where more detailed information can be found. Yet even these are no substitute for experience. The Roadmap should serve as a starting point for further independent reading. It is, in essence, an overview designed to help you understand the business concepts that will mainly be implemented by the operational team you eventually recruit to launch your business.

Throughout the Roadmap, we have provided a story about Sue, a university-based scientist who is – like you – founding a company. Sue’s story – which appears in italicized print at the end of each chapter – provides a fictionalized example of the kinds of issues frequently confronted by company founders.

Otherwise, the Roadmap is structured to be used in two ways:

- It can be read in sequence with each chapter building upon the previous ones
- It is also organized into “Frequently Asked Questions” (FAQ) format. You can use the Table of Contents to navigate to those sections you feel are relevant to your immediate needs – just click on the question that seems closest to the issue you are trying to address.

It is important to note that the Roadmap should not be regarded as advertising, solicitation, or legal advice of any kind. You should not act or refrain from acting on the basis of any Roadmap content without seeking appropriate legal or professional advice. Also, at several points in the document we provide links to other sources for business know-how and document templates. These are provided as instructional resources only. You should not execute (that is, sign) or ask others to execute documents relating to your business without the advice of an experienced attorney. Your lawyer is an important part of your start-up team. Make efforts to find one you can trust as soon as you can afford it. Let’s get started!

Sue’s Story: I have an idea, how do I get started?
Sue is a Post-Doc at Washington University. She has been working on a previously un-elucidated cellular export mechanism. Recent research has implicated a particular gene and gene variants in a number of disease states: One gene variant causes an inability to properly utilize ATP. Another variant shows promise as a marker for a particular type of tumor. Yet
another gene variant is associated with the inability to produce insulin in an animal model she developed.

Sue has been hearing a lot about entrepreneurship lately around campus. She wonders if her work – which is nearing publication – could be the means for creating an entrepreneurial future for herself. This idea seems particularly attractive in light of the scarcity of tenure track faculty positions in her field.

**Sue’s Story: With whom can I talk safely about my idea? How can I learn from others without jeopardizing my ideas?**

Sue's academic training did not prepare her for entrepreneurial pursuits and she is eager to talk to business experts – getting advice from knowledgeable people is very important in science after all. Why not in business? However, she has the impression that business people can be pretty competitive – maybe even more so than academics – and that even in academia it pays to be prudent when sharing ideas. The director at the Skandalaris Center explains that the question of what to disclose to whom is a very delicate trade-off. Being able to describe her idea to people who are trying to help is obviously crucial, but how can she avoid giving away her ideas and possibly hurting her ability to get her patent or, even worse, providing crucial insights to someone else who might “scoop” her idea and leave her in the dark? She learns that there are three principles she can use to guide her activities in this regard:

**Principle 1 – Honor the “need to know”.** This means only providing people with the minimum information they need to know in order to do their job. For example, she learns that those business experts she is seeking strategic advice from really do need to know all the nuances of how her invention works, while the person who is doing the bookkeeping needs no real depth knowledge to do the job. Other functions, Marketing consultants for instance, or Manufacturing vendors only need limited information. It is important to reveal only as much as a person needs to know in order to help.

**Principle 2 – Be clear about the difference between public disclosure and confidential disclosure.** It is very important to understand the difference between a “confidential disclosure” and a “public disclosure”. A disclosure is “confidential” only when covered by a written and enforceable Confidential Disclosure Agreement (CDA) – also called a “Non-Disclosure Agreement” (NDA). All other kinds of disclosures – regardless to whom they are made and verbal promises notwithstanding – should be considered public disclosures.

**Principle 3 – Assume the technology works.** One good way to avoid potential damaging disclosures is to develop the habit of describing what the technology does, without going into how it does it. The core inventions behind a business idea must not be discussed in public disclosures at least until the perfected “non-provisional” patent has been filed. However, many important people will not sign CDAs or NDAs. This includes many “pro-bono” advisors – people who “just want to help” for free may want to avoid taking on any kind of risk and are frequently shy about signing CDAs. Also, most investors will not sign CDAs until they have decided to seriously evaluate an investment and are ready to perform diligence on the opportunity – usually many months into a relationship. Therefore, Sue realizes it is crucially important to be able to tell a compelling story about her business idea (including what the technology does) without giving away key inventions (that is, how the technology does what it does) until she has perfected patent filings – and even then, only, very carefully. Fortunately, she learns, most interested people – including potential investors – do not need to hear the nitty-gritty about how the technology works until it is time to perform technical diligence, which typically is done under CDA.
Sue also learns there are two kinds of CDAs – “one-way” and “two-way”. In a one-way disclosure, Sue uses a form that protects disclosures she makes to the other party but does not cover disclosures back to her from the other party. This form of agreement is highly useful for most kinds of relationships – relationships where the information Sue wishes to learn is non-proprietary to the other party. General business advice, networking conversations, discussions of market conditions and trends are all good examples. In other circumstances however, Sue will be getting the kind of technical help that could bear on the novelty, obviousness or utility of her invention or help to refine the invention. The nature of the information Sue wants to receive should be the key determination – if the other party reasonably expects to provide confidential information back to Sue – and Sue is willing to be “contaminated” by such disclosures – then a two-way CDA is appropriate. Sue also learns that some people insist on two-way CDAs regardless of their having confidential information or not. Sue figures in that case she will just have to figure out if the relationship is worth the risk of learning something contaminating.

Sue learns that she must get comfortable with the notion that most people are not willing to be bound indefinitely by CDAs, and that most of the time such agreements expire within 2 – 5 years. This seems reasonable since any truly proprietary information that is truly valuable can become the subject of a patent filing if warranted during this time.

*Click here for a source where sample CDAs/NDAs can be found.*

**Sue’s Story: How can I find mentors and advisors to help?**
Sue has embraced the notion that the best way to explore how to start-up a business around her ideas is to share them with – and get the reactions from – knowledgeable people. She has learned to have such conversations under the protection of the “need to know” principle and to obtain really deep – and especially technical – advice under benefit of CDA. So, the question becomes, where can she find knowledgeable people:

a) **Business support entities in St. Louis:**
   (1) Skandalaris Center
   (2) Fundamentals
   (3) BioGenerator
   (4) Square 1
   (5) BALSA Group
   (6) BALSA Foundation
   (7) UMSL outreach
   (8) MedLaunch
   (9) SlingHealth
   (10) iTEN
   (11) Gateway VMS

b) **Personal networking**
   (1) Fellow inventors
   (2) Academic Advisors for intros to industry
   (3) Venture Café
   (4) LinkedIn
   (5) StartLouis
Market Research

“If you build it, they will come.” Unfortunately, the business world does not work this way; seemingly good business ideas often fail because the entrepreneur did not take the customer into consideration. One thinking about pursuing a business idea must begin with the question, “if I build it, will they come?” This question can be answered through a market analysis, which aims to determine whether potential customers are willing to pay for your product or service and whether the market of people (or other businesses that are the customers for many start-ups) who are likely to pay is big enough to support your business. Different types of businesses and business at various stages require different approaches and depth in market analysis depending on the specific product or service that an entrepreneur aims to provide. Here, we outline some basic components of a market analysis that are applicable to most businesses and use illustrative examples to explain the core concepts.

What is a Market Analysis?

Broadly speaking, a “market analysis” refers to any initiative taken to evaluate a product’s or service’s potential for success and includes an understanding of the following areas:

1. What is Market Research? At its simplest level, the Market Size is the total number of “units” and “dollars” paid for a particular good or service over a specific unit of time (usually a year). Stated as a formula, the Market Size = nU/t X pU (where nU/t = the number of “Units” of a good or service purchased per convenient unit of time – usually per year and pU = the “Price” per unit of an average order). For many markets, this information is available for free from a variety of sources available over the Internet. To cite an example most people are familiar with, let’s look at car sales in the US:

   For July 2015, 670,000 new cars were bought by customers in the US. The average price paid was around $31,000. Therefore, the Market Size for new cars in the US in July was just over $2 billion. Annually, that would be just over 8 million cars (units) per year and 20 billion in dollar sales.

   However, for most start-up companies, this simplest “Market Size” calculation is not all that useful – “Cars” are not all alike – an economy sedan does not “compete” directly for the same customers as a luxury SUV – and most people – especially investors – are interested in understanding the size of the narrowest market segment in which your product or service will directly compete. Cars vary by many criteria that could define a market: by format (sedan VS wagon VS convertible etc.) size (measured by weight, number of occupants), engine capacity (in cubic centimeters or cubic inches), fuel efficiency (EPA rating) and the availability of features (standard VS automatic transmission, trim levels seats etc.) The point is that different car models are “competitive” only within specific, comparatively narrow vehicle classes.

   A start-up company is unlikely to be successful trying to develop and market a whole line of cars. Instead they are much more likely to succeed with one or a few very special cars – think of Tesla Motors for example which only sells very expensive electric-powered cars. Tesla Motors is only interested in that small segment of the market that is highly motivated to buy cars similar to the ones made by Tesla Motors – for example, customers who are very interested in high tech/high prestige cars with extremely low environmental impact. Moreover, because most people expect to buy a new car only

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1 When the target customer is individual people, they are frequently called “consumers” and the start-up is said to be pursuing a “B2C” (Business to Consumer) business model. When the target customer is another business the start-up is said to be pursuing a “B2B” (Business to Business) business model.
once every several years, only some fraction of those who might be interested in such a car are actually potential buyers at a single point in time. For the purposes of its business then, the relevant Market for Tesla is not the overall US Car market but rather the customers who are actually in the market for a high-end, high performance, environmentally “green” car right now or in the next few months. This number is likely to be only in the low thousands of individuals as opposed to the 670,000 buyers for all cars in the month of July 2015 as cited above.

From this simple example, we hope we have made the point that investors and others who need to know about your business are interested only in the “relevant, accessible” market for your product or service. Understanding how many potential customers there are in the relevant accessible market at a particular point in time and place is the purpose and challenge of Market Research.

2. What is Customer Research? Once a business has determined the “relevant accessible market” for its product or service, it is essential to understand who the customer will be, what the customer needs are, and how the product or service you have in mind can potentially meet the needs of the customers. Understanding the size of the relevant accessible market (i.e. Market Research) is only part of the problem. It is also vital to learn what motivates customers in the relevant accessible market to buy. This includes such questions as how do such potential customers hear about new product offerings? which performance features they need to have? And which would they like to have? what motivates them to buy now vs. continue to evaluate? what they are willing to pay? etc. How these customer preferences in aggregate change over time (market trends) will also help you decide whether or not to pursue your business idea. These questions that inform a business on the features and benefits of its product or service and how to communicate these benefits are the discipline of Customer Research.

3. What is Competitor Research? If you have a business idea, you will want to know whether other businesses already provide customers with a similar product or service and what makes each competing product or service different from your idea including the advantages and disadvantage of each. By understanding the products or services currently available, and those products or services that will become available before or shortly after yours becomes available, you can play to your strengths (competitive advantage) and shape your product or service in a way that is unique and stands out. By way of contrast, if you find there are many competitors, you may decide not to pursue your business idea. This is the focus and challenge of Competitor Research.

4. What are Barriers to Entry? Depending on your business idea, you will be faced with barriers that make it difficult to sell your product or service for the first time (to enter the market). For example, government regulations may require you to prove your product is safe and effective (e.g. drug regulatory review and approval), you may need to have a large sales-force to compete effectively – even with a superior product, or potential customers may be very reluctant – or in fact, unable – to change from their current solution to buy yours. By identifying possible challenges your business will face, you will be able to build a strategy for overcoming them. This is crucially important because once you have overcome such Barriers to Entry, you may be able to rely on them as obstacles for those who might otherwise be motivated to compete with you. Therefore, barriers to entry are by no means solely a negative for a company – true, they may be difficult to overcome, but competitors entering the market after you will have to overcome these same – and ideally, additional – barriers.
What are the basic questions of Market Analysis? In your market analysis try to answer the following questions as best as you can:

- What product or service am I going to provide that meets a specific customer need? Why will customers buy my product or service?
- What is my target population of customers? Who am I going to target this product or service to? What do they need and/or want?
- How does this product or service meet the needs of my potential customers? What is the value that I am providing to my customers?
- What is the size of the market (How many customers are there in the entire market)? More importantly, what is the size of the relevant accessible market? How many customers in the relevant accessible market do I expect to have early on? What share will I take of the relevant accessible market in 3 years, 5 years etc.?
- Who else provides similar products or services? At what stage in development or commercialization are these products or services? How do their products or services compare to mine? How many customers do these competing businesses have?
- What barriers exist that may impede my product or service from entering the market? How does that affect my business? How do I overcome these barriers? How effective will these barriers be in keeping competitors out of the market once I have successfully entered?

A comprehensive market analysis should ideally reveal a large unmet need and help narrow down your target market and reshape your final product. It can also help you “fail fast,” and prevent unnecessary time and energy spent creating an offering that would have ultimately not be successful.

Sue’s Story: What does it mean to be “Focused”?

Sue wants to commercialize her postdoc research in cellular mechanisms that control cellular export. As previously discussed, her technology is broadly applicable – in fact after some thought she realizes she has 5 potential products (Cancer therapeutic, Diabetes therapeutic, Cancer diagnostic, Diabetes diagnostic, and novel animal model). Through the networks available to her in St. Louis (discussed during introduction) she has talked to about 20 business people about her discoveries and numerous business options. In these early meetings, she has consistently heard comments like: “You are trying to do a lot”; “Wow, you certainly have a lot of business ideas there”; and “your inventions go off in so many directions it’s hard to know where to start”. Sue is feeling frustrated because these first 20 interviews have all run out of time before she has been able to describe all her ideas – yet instead of being deeply impressed by all the “business potential” Sue believes might lie within her technology, the opposite seems to be happening – people are very kind and generally encouraging, but no-one really seems to be engaging with her. Finally, one of her contacts levels with her saying – “Sue, your technology is potentially broadly applicable but you aren’t going to get anywhere without Focus”. When she digs into this idea she is told – “you have loosely described about 5 different directions your technology could go – this is not a good thing! You have to figure out which one application shows the most promise and then focus mercilessly on this idea. The other ideas will have to wait until the most promising one is well underway.

**OK, the need to focus makes some sense – but how to go about doing so – surely it doesn’t make sense to write a separate business plan for each of her several ideas and see which one seems most appealing. Sue is fortunate at this point to learn about the “Business Model Canvas”. This is a business-planning tool that is deployed well before an attempt is made at writing a business plan. It is a “one page” approach to organizing her thinking about all the**
major aspects of her business ideas. She decides to do this “one page” exercise with the help of her most trusted business advisor for each of the 5 business ideas she has so far, specifically, Anti-Cancer Therapeutic; Diabetes control therapeutic; Cancer diagnostic; Diabetes “early warning diagnostic; Commercializing her “animal model”.

Here is a source where you can view a brief video about the Business Model Canvas.

Here is a source where you can create Business Model Canvas for your business.

After completing this exercise, she decides she needs to embark on some research to help her choose the ideal application of her discoveries. This leads her to perform a market analysis by going through the list of questions stated above. To start, she would like to validate the customers targeted by each of the potential products who would actually find it useful.

How do I better understand my potential Customers?
Customer Research, an important part of completing a market analysis, involves understanding your potential customers. There are two categorical approaches to collecting customer information: primary research and secondary research. Primary research means the information is collected first-hand through personal interviews, surveys, or questionnaires. Secondary research means the information is collected from a secondary source like published literature, white papers, press releases, market reports, and data vendors.

What is Primary Market Research? For primary market research, interviews and surveys are two common ways (there are others too esoteric to go into here) that you can gather information about end-users’ opinions. Generally, interviews collect data that generalizes market sentiments and helps you understand what aspects of a product or service might be important to the end-user/customer (e.g. price, convenience, accuracy, speed, value, etc.). Surveys, on the other hand, allow for the objective quantitation of various characteristics of the market.

What is Secondary Market Research? Secondary research is a quick and easy, though sometimes expensive, way of gathering helpful information already collected and published. Because anyone can search the Internet for these reports, that can be a great place to start. With secondary data, one can understand market size, market growth rates and market trends, identify competitors (see below), establish benchmarks and identify target segments. However, the information gathered using common Internet search engines is not always going to be specific, accurate, or up-to-date. To perform deeper searches, use local resources and talk to business insiders, like business journalists and writers.

Sue’s Story: What can I learn from market research?
After performing a combination of primary and secondary research (and thinking carefully about barriers to entry – which can be especially challenging for molecular diagnostics) it has become clear to Sue from some promising work in some animal models of cancer that the potential cancer therapeutic is her most promising application. It is here where both the need and opportunity are the greatest. Her target market will be physicians who might one day prescribe the therapeutic she plans to develop. In order to understand whether physicians would actually use her drug, she dives into a more detailed market analysis on this new target market. Among other things, she would like to determine the number of patients for whom there is currently no good therapeutic alternative and who might therefore actually benefit from the therapeutic she is proposing to develop.
Sue sends 100 emails to physicians, nurses, and hospital administration in oncology-related fields, 12 of these individuals agree to phone or in-person meetings. She finds out that a large proportion of her interviewees see triple-negative breast cancer (that is, negative for the genetic markers ER, PR, HER2) as an application in dire need of novel therapeutics. Of the 250,000 yearly breast cancer diagnoses in the US, 20% are classified as triple-negative. This suggests they will be extremely aggressive with higher rates of relapse and lower chances of in metastatic disease. There has been early data in her academic lab that her cellular export targets might be relevant in such cancers. This sounds like it might be a viable addressable market.

**How do I evaluate Competitors?**

Because of competition, and customer resistance to change, it is extremely rare for a product or service to achieve 100% market adoption. Every effective business plan contains a thorough evaluation of the competitive landscape highlighting the importance of knowing your competitors. A thorough analysis of the competition typically consists of: (1) a **competitive capabilities matrix** of the majority of current and impending companies with products that serve a similar market; (2) a detailed description of the most threatening competitors; and (3) a **Strength Weakness Opportunity Threat (SWOT)** analysis. A SWOT analysis describes the most important internal (strengths and weaknesses) and external (opportunities and threats) characteristics of the envisioned business in regards to the market and competitive landscape. In any business (but especially in life-sciences where the level of innovation is intense and product development time-lines are unusually long) it is crucially important to study not only the existing (already marketed) competition, but the competition in development as well. There are several secondary sources that provide “pipeline” data. Published papers are also an important source.

Sue decides to take a careful look at her potential competitors. She finds out that there are two large pharmaceutical companies with therapeutics in development targeting triple-negative breast cancers, and three startups touting great advancements but too early in their development process to have public data. After a careful competitor analysis, Sue tabulates her findings in the following table.

<table>
<thead>
<tr>
<th>Company</th>
<th>Molecular target</th>
<th>Stage of Development</th>
<th>Product Format</th>
<th>Clinical Advantage or Disadvantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Big Company P</td>
<td>Transcription Factor</td>
<td>Phase I</td>
<td>Injectable Biologic</td>
<td>Is rumored to have caused acute toxicity</td>
</tr>
<tr>
<td>Big Company M</td>
<td>Cellular Receptor</td>
<td>Phase I</td>
<td>Oral Small Molecule</td>
<td>Receptor is also expressed in Cardiac tissue, so cardiotoxicity is a risk.</td>
</tr>
<tr>
<td>3negCure</td>
<td>Lysosomal Storage</td>
<td>Pre-clinical</td>
<td>Injectable Biologic</td>
<td>Lysosomal storage is important in many tissues, therefore broad toxicity is a real risk.</td>
</tr>
<tr>
<td>Pharmasticy</td>
<td>WNT</td>
<td>Pre-clinical</td>
<td>Injectable Biologic</td>
<td>WNT pathways come in various forms and it has been difficult to find blockers uniquely active in WNT1 which is the pathway implicated in tumors.</td>
</tr>
<tr>
<td>Sue’s Company</td>
<td>Cellular Export Pathway</td>
<td>Discovery</td>
<td>Not yet determined</td>
<td>The Cellular Export pathway allows tumors to “defeat” cancer therapeutics. Therefore, a drug that blocks this pathway may leverage many other CA drugs as co-therapy.</td>
</tr>
</tbody>
</table>

**Table 1.** Competitive capabilities matrix for Sue’s cancer drug idea.
Understanding the competitive landscape will help form realistic expectation of the business and perhaps narrow down or re-focus the target market to a particular niche that presents an unmet need. This is because in every potential market, there is significant variability in a customer’s needs, tolerance of side effects, ability or willingness to pay for a product and many other factors. It is also very important to understand “who the customer is”. In the case of a cancer therapeutic, while the end user is the patient, this person is not really the key decision maker – the decision of which drug to prescribe is up to the patient’s physician, in this case the oncologist. Practicing oncologists frequently find it difficult to stay on top of new innovations – modern biology in Cancer has made huge strides since most oncologists left medical school. So, these oncologists must be educated about the latest trends in cancer research and rely heavily on “thought leading” oncologists who practice at one of several leading academic hospitals with strong reputations in oncology. The preferences and practices of these thought-leading physicians are crucially important. Another problem has to do with the high cost of cancer therapeutics. While the Oncologists care mainly about efficacy and safety, there is another “decision maker” who will be involved in the buying decision – “the payer”, either an insurance company or Medicaid for indigent patients. Because reimbursement for the prescription drug the oncologist recommends is crucial to the product’s success, the Payer is a key decision maker and must be considered “a customer” in the case of a therapeutic. By dividing the market into discrete segments and recognizing the differing motivations of the various decision makers involved you can identify a group of “customers: that must be motivated to adopt your product and can then develop targeted sales and marketing strategies to reach them.

Sue’s Story: How do I target a market, and what is a SWOT analysis?
Instead of trying to serve all members of the medical community treating breast cancer, Sue decides that it is better to target physicians who are more likely to treat patients with metastatic disease and have shown a willingness to try experimental treatments. By performing another round of interviews, she finds out that oncologists focused in large academic hospitals fit this description. She performs a SWOT analysis on this reformulated business idea targeting triple negative breast cancers that have metastasized and presents her analysis in the table below.

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of options on the market</td>
<td>Smaller market</td>
</tr>
<tr>
<td>Terminal patients tolerate higher side effects</td>
<td>More difficult application</td>
</tr>
<tr>
<td>Opportunities</td>
<td>Threats</td>
</tr>
<tr>
<td>Big pharma targeting application</td>
<td>several competitors exist</td>
</tr>
<tr>
<td>Expedited approval possible</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. SWOT Analysis

She also thinks about what payers will care about. She figures that the fact that her drug can make other cancer drugs more effective allows her to argue that her drug will cause fewer patients to relapse – or at least prolong the period of disease remission. By keeping patients healthier longer, her drug will then be instrumental in reducing overall healthcare costs and should therefore be cost effective compared to competing therapies.

Reaching the end of the list, Sue looks into barriers to market entry and they are primarily regulatory in nature. She begins to investigate these barriers, and that leads us to the next chapter of this roadmap…
Market Analysis Section Summary
A thorough market analysis is critical for the success of a business. It should be performed before starting a business, before making a business decision to launch a new project, or any time a business owner wants to re-evaluate if a product or service is still meeting the needs of the changing preferences of customers. Quantifying the addressable relevant market through Market Research, identifying target markets through primary and secondary Customer Research, performing Competitor Analysis, and considering Barriers to market Entry are the core components of a market analysis. Market analysis should be an ongoing process as it informs the revenue potential in the near-term and long-term.

What are some useful resources related to market research?
The Kauffman Foundation’s “Entrepreneurship.org” is a great resource for start-up companies and will be referred and linked to frequently in this Roadmap. Here is a useful discussion of market analysis that emphasizes the importance of customer interaction.

MO Source Link provides a list of questions that help assess the targeted market for a start-up business.
http://www.mosourcelink.com/startup/evaluate-your-idea
Regulatory Considerations

Because of the heavy involvement of regulatory authorities in approving and monitoring life science products, an important early step in developing a business model for a company is to consider what the regulatory path for a product will likely be. The regulatory path can greatly affect one’s path to market and even dictate a particular business model. In addition, regulatory concerns are seen as a main risk for investors in biotech companies given the significant time and money required and therefore an entrepreneur must be very clear about the relevant regulatory requirements when raising money.

In this section, we offer a table breaking down each type of regulatory body and clearances by product-type, and then follow with further details on the regulation required for each class of product.

<table>
<thead>
<tr>
<th>Product</th>
<th>Responsible Agency/Divisions</th>
<th>Regulation type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drugs</td>
<td>X</td>
<td>NDA, ANDA</td>
</tr>
<tr>
<td>Biologics and Vaccines</td>
<td>X</td>
<td>BLA</td>
</tr>
<tr>
<td>Medical Devices</td>
<td>X</td>
<td>510K, PMA</td>
</tr>
<tr>
<td>In-Vitro Diagnostics</td>
<td>X</td>
<td>510K, PMA, CLIA</td>
</tr>
<tr>
<td>Dietary supplements</td>
<td>X</td>
<td>DSHEA (none unless a “new ingredient”)</td>
</tr>
<tr>
<td>Animal Therapeutics</td>
<td>X</td>
<td>NADA; ANADA; CNADA</td>
</tr>
<tr>
<td>Animal Devices and Diagnostics</td>
<td>X</td>
<td>NONE</td>
</tr>
<tr>
<td>Animal Feed Additives</td>
<td>X</td>
<td>Feed additive Petition; AAFCO listing Petition</td>
</tr>
<tr>
<td>Animal Vaccines</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>GMO Crops</td>
<td>X</td>
<td>FIFRA</td>
</tr>
</tbody>
</table>

Table 3. Biotech applications and relevant agencies/regulations.

How are Drugs, Biologics, and/or vaccine regulation by the FDA?

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Clinical trials</td>
<td>In addition to preclinical testing, during this stage a company should first schedule a Pre-IND meeting with the FDA in which one’s regulatory pathway is discussed with FDA representatives. Then, when moving toward clinical trials, one applies for an IND certification (Investigational New Drug), to gain the right to conduct clinical trials and ship the drug across state lines</td>
</tr>
<tr>
<td>Phase 1</td>
<td>Testing in a small group of people for the first time. Evaluate safety, determine a safe dosage range, and identify side effects</td>
</tr>
<tr>
<td>Phase II</td>
<td>The drug or treatment is given to a larger group of people to see if it is effective and to further evaluate its safety.</td>
</tr>
<tr>
<td>Phase III</td>
<td>The drug or treatment is given to a group of patients large enough to determine efficacy at a pre-determined degree of statistical certainty and to collect information on adverse effects. Phase III Clinical Trials are usually the final step of clinical testing. Once the results are in, all the information from all the stages are collected into an application called the “New Drug Application” (NDA) for small molecule drugs or “Biologics License Application” (BLA) for biological therapeutics or vaccines. These extensive applications (NDA or BLA) include enormous amounts of information and take many months or years to approve.</td>
</tr>
<tr>
<td>Phase IV</td>
<td>In some cases, post marketing trials are required as a condition of approval. Such studies are done after the drug or treatment has been marketed to gather information on the drug’s effect in various populations and any side effects associated with long-term use.</td>
</tr>
</tbody>
</table>
How are generic drugs regulated?

ANDA – Abbreviated New Drug Application. This is the application process by which “generic” drugs are approved. In this case, once a patent on an innovator chemical entity has expired, the FDA will allow generic drug manufacturers to reference the pre-clinical efficacy and clinical studies that were submitted in the corresponding NDA that were the basis for approval of the innovator product. The generic manufacturer need only show that the generic product is substantially similar to the innovator product, and can successful complete the Chemistry, Manufacturing and Controls section for its product. The ANDA can be and usually is submitted to the FDA prior to the expiration of relevant patents and forms of regulatory exclusivity (such as “orphan drug” status). This greatly reduces the time and cost of bringing a generic drug to market once the innovator’s patent has expired.

Speedy mechanisms are available for expedited approval in case of drugs that are first-in-class or have significant advantage over existing treatments. Information about Priority Review/Breakthrough therapy/Fast Track/Accelerated approval can be found here.

What are Bio-Similars?

The FDA has been legislative mandate since 2010 to establish a system whereby “generic” biologic and vaccine products can be rapidly approved once the innovative biologic and vaccine product patents have expired. The difficult reality has been that exact “interchangeability” for biologically derived products has proved impossible to establish at the same level that is routinely achieved for small molecule drugs. The FDA has been managing a process to establish acceptable standards for such interchangeability but as of this writing are still working on such standards.

How does the FDA regulate Medical Devices and Diagnostics?

How are medical devices classified by the FDA? What are the differences between Class 1, 2, and 3 devices?

The FDA classifies medical devices and diagnostics into three categories. These categories largely determine the appropriate risk-dependent regulatory pathway.

Class I: Low-risk, ‘General Controls’, e.g., sunglasses, these are generally exempt from FDA regulation

Class II: Moderate-risk, ‘General and Special Controls’, e.g., blood glucose systems (Generally must go through pre-market review (510(k) or PMA))

Class III: High-risk, ‘General Controls and Premarket Approval’, e.g., heart valves (Always go through pre-market review)

What are the primary review mechanisms for Class II and III devices and diagnostics? What is a PMA, 510(k), or IDE?

PMA: Pre-Market Approval. Primarily for Class III Medical Devices. This is a more stringent
review process in which a new device or diagnostic needs to demonstrate it is both safe and effective.

510(k): Some class I, most class II, and (very rarely) class III devices and diagnostics may avoid the full PMA process and instead, at the FDA’s discretion, may be subject to a less stringent 510(k) clearance. A 510(k) is applicable if the new device or diagnostic is quite similar to an existing product (called a “predicate” product) that has already been approved for use. The company then needs to solely demonstrate substantial equivalency to the product already on the market.

Note, through a mechanism called “IDE” (Investigational Device Exemption) the FDA can grant the right to use a class II or class III product during clinical trials aimed at obtaining 510(k) clearance or PMA.

What is CLIA? What is a Lab-developed Test?

Diagnostic products may also reach the market through use as LDTs (Laboratory Developed Tests) in CLIA-certified laboratories. CLIA (Clinical Laboratory Improvement Amendments). Under CLIA, a clinical laboratory that obtains CLIA certification (a non-trivial process) has the ability to develop in-vitro diagnostic tests in their own laboratory that may then be used to diagnose disease in human biological samples (an LDT). A startup may utilize this mechanism by either building their own CLIA-certified laboratory or selling components to a CLIA lab that then develops a LDT in their laboratory with those components.

How does the FDA regulate dietary supplements?

The FDA regulates dietary supplements under a different set of regulations than those covering "conventional" foods and drug products. This set of regulations was promulgated in the DSHEA (Dietary Supplement Health and Education Act). Below are some general stipulations of this act:

1. Manufacturers and distributors of dietary supplements are prohibited from marketing products that are adulterated or misbranded. That means that these firms are responsible for evaluating the safety and labeling of their products before marketing to ensure that they meet all the requirements of DSHEA and FDA regulations. The FDA is responsible for taking action against any adulterated or misbranded dietary supplement product after it reaches the market.

2. In addition, supplements that contain “new ingredients” must register with the FDA. A "new dietary ingredient" is one that was not sold in the U.S. in a dietary supplement before October 15, 1994. The registration must demonstrate to the FDA why the ingredient is reasonably expected to be safe for use in a dietary supplement, unless it has been recognized as a food substance and is present in the food supply. Note: there is no authoritative list of dietary ingredients that were marketed before October 15, 1994. Therefore, companies are responsible for determining if a dietary ingredient was marketed before October 15, 1994 and providing documentation of this fact. Otherwise, it will be considered "new" and regulated accordingly.

What are the regulatory pathways for animal therapeutics?

There are three different types of new animal drug applications. Contact the FDA’s CVM (Center for Veterinary Medicine) Division for a consultation on which approach applies to your
NADA (New Animal Drug Application): This designation is used if the FDA determines that a substance for animal use will be regulated as a drug. Similar to human trials, the FDA’s Center for Veterinary Medicine (CVM) will, upon reviewing adequate pre-clinical information, grant an INAD (Investigational New Animal Drug) exemption so you may use the drug on animals during the trial process. The requirements for completing a NADA are very similar in structure and scope to the requirements for an NDA (discussed above).

ANADA (Abbreviated New Animal Drug Application): An ANADA is used to seek approval for a generic new animal drug. A generic new animal drug is a copy of an approved new animal drug for which patents or other periods of exclusivity are near expiration. Like ANDAs, ANADAs are generally approved rapidly upon expiration of the longest lasting patent or regulatory exclusivity.

CNADA (Conditional New Animal Drug Application) - Applications for conditional approval allow a drug sponsor to legally market a new animal drug intended for a minor use or for a minor species after proving it is safe, but before collecting all the necessary effectiveness data. The drug sponsor can keep the product on the market or up to five years, while collecting effectiveness data if FDA approves the sponsor’s annual renewal requests.

How are animal devices and diagnostics regulated?

Device manufacturers who exclusively manufacture or distribute veterinary devices are not required to register their establishments or list veterinary devices. The FDA though does have regulatory oversight over veterinary devices and can take appropriate regulatory action if a veterinary device is misbranded or adulterated. It is the responsibility of the manufacturer and/or distributor of these articles to assure that these animal devices are safe, effective, and properly labeled. The FDA recommends that manufacturers and/or distributors of veterinary medical devices request a review of their product labeling and promotional literature to ensure that it complies with the Act. This includes devices marketed in another country and offered for importation into the U.S.

What are the regulatory mechanisms for animal feed additives?

Food Additive Petition through the FDA: A manufacturer or other sponsor may petition the FDA for approval of a new animal food additive or they may petition for a new use of an already approved animal food additive. To demonstrate that the additive is safe for the proposed use in an animal food, the sponsor submits a food additive petition (FAP). The FAP must include sufficient information to establish that the food additive is safe and accomplishes its intended use, under the conditions of use specified in the petition; and once this has been demonstrated, FDA can issue a regulation addressing the food additive and its use. The regulation may specify the types of animal food that may contain the additive, the amount of the additive that may be used in an animal food, and/or the requirements for labeling the additive or for labeling the animal food containing the additive. Once approved, an animal food additive must be used within the constraints of its established regulation. Below is a list of the general information that should be included in a FAP.

1. Identity and composition of the additive including manufacturing methods and controls;
2. Intended use, use level, and labeling (cautions, warnings, shelf life, directions for use);
3. Data establishing the intended effect (physical, nutritional, or other technical effect);
4. Analytical methods (for the additive and for animal foods containing the additive);
5. Safety evaluation (target animal and human food)
6. Proposed tolerances for the food additive;
7. Proposed regulation; and
8. Environmental assessment

It should be noted that the FAP process is not required for feed-additives that are on the Federal “Generally Regarded As Safe” (GRAS) list. Under current law, manufactures can “Self Affirm” that the ingredients of their product are GRAS listed. Under this approach the manufacturer sends a notification affirming to the FDA that the ingredients are GRAS along with necessary supporting documentation. The FDA then has a limited time period during which it can object to the Self-Affirmation of GRAS status, thus requiring the manufacturer to go through the FAP process. If the FDA does not object within the time frame, it will send a letter of “non-objection”, and the manufacturer can then move forward to market the product.

Feed listing petition through AAFCO:
Once a product has been approved through the FAP process, or when a manufacturer has received its letter of “non-objection” for a GRAS product, the next step is to list the product with the Association of Animal Feed Control Officials (AFFCO). The AFFCO will then list the product in its annual publication. Pet Food makers and Animal meat production companies will not generally use a feed or feed additive until it is listed in the “AAFCO Official Publication”. Since the Official Publication is only published once per year, it is necessary for manufacturers to plan to submit its application for such a listing well in advance of the annual deadline in order to insure inclusion. Otherwise, the product will not be marketable as a practical matter.

How are animal vaccines regulated?

To manufacture and sell veterinary biologics, animal health companies must have both an establishment license and a product license, both of which are granted by the USDA. These licenses are given to manufacturers that have appropriate, inspected facilities, as well as qualified persons to run them. Before a product license is approved, the Center for Veterinary Biologics (CVB) requires all products to undergo an approval process to ensure compliance with the four characteristics outlined below:

1. **Efficacy** means that the product has the ability to produce the desired effect. In this case, efficacy means that the biologic has to be effective in preventing, treating or diagnosing a disease in animals.

2. **Safety** means that the biologic needs to relatively mild or infrequent side effects. Even after approval, firms maintain post-marketing surveillance for any side effects that were not discovered before release. These side effects usually have a very low occurrence in the population or are caused when the product interacts with other drugs or vaccines.

3. **Potency** means that the biologic needs to work before it expires. Because some veterinary biologics can degrade over time, regulations require each dose of the product to contain enough of the active ingredient to work properly – even on the day it expires.

4. **Purity** means the assurance that the product does not contain anything that might adversely affect potency, safety for the animal, efficacy and safety of the resulting human food products (for example, meat products). Veterinary biologics are tested for purity at each step of the manufacturing process and are then tested again before release.

How are GMO Crops regulated?
How does the FDA review new GMO crops?
The FDA review process for GMO crops is a process that includes several steps. Generally, the developer identifies the distinguishing attributes of new genetic traits and assesses whether any new material that a person consumed in food made from the genetically engineered plants could be toxic or allergenic. The developer also compares the levels of nutrients in the new genetically engineered plant to traditionally bred plants. This typically includes such nutrients as fiber, protein, fat, vitamins, and minerals. The developer includes this information in a Safety Assessment, which FDA’s Biotechnology Evaluation Team then evaluates for safety and compliance with the law. The FDA considers an evaluation to be complete only when its team of scientists are satisfied with the developer’s Safety Assessment and have no further questions regarding safety or regulatory issues.

How does the EPA regulate GMO crops?
The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) established procedures and labeling provisions for registering pesticides. The act provided the EPA with the authority to oversee the sale and use of pesticides. However, because FIFRA does not fully preempt state/tribal or local law, each state/tribe and local government may also regulate pesticide use. With regard to biotechnology, EPA’s jurisdiction under FIFRA covers regulation of the new substance and DNA in the plant when it is pesticidal in nature. For example, the substance produced by a plant that has been genetically modified to resist disease comes under FIFRA authority, whereas the substance produced by a plant that has been modified to resist drought does not.

Before the EPA can register a pesticide that is used on raw agricultural products, it must grant a tolerance or exemption. A tolerance is the maximum amount of a pesticide that can be on a raw product when it is used and still be considered safe. Under the Food, Drug, and Cosmetic Act (FDCA), a raw agricultural product is deemed unsafe if it contains a pesticide residue, unless the residue is within the limits of a tolerance established by EPA or is exempt from the requirement. The FDCA requires EPA to establish these residue tolerances.

What are some useful resources related to regulatory pathways?
2. On Biological License Applications: https://www.troutman.com/files/FileControl/c38042c0-a860-4179-8a50-12c1170d84fd/7483b893-e478-44a4-8fed-f49aa917d8cf/Presentation/File/Biologic%20License%20Application%20Checklist.pdf
3. On In Vitro Diagnostics; Laboratory Developed Tests and Genetic tests: https://fas.org/sgp/crs/misc/R43438.pdf
7. Find EPA Regulations at - http://www2.epa.gov/laws-regulations/regulations#find
Business Formation

Forming a company in the eyes of the State and the Federal IRS is the first step to becoming a real legal entity. The company serves as an external entity to the founders and thus protects the founders’ (and eventually, other shareholders’) personal financial assets from liabilities (most importantly debts that can’t be repaid and lawsuits) that might arise from business dealings. Entity creation is done at the state level. In this Roadmap, the entity options are a LLC and a Corporation – not a C-Corp per se, because it is not an entity rather a tax election. By default, a corporation is taxed as a C-corporation, but can elect to be taxed as an S-corporation.

The LLC has many tax elections available. A single member LLC is considered a disregarded entity, therefore, it is completely ignored by the IRS for tax purposes, unless it elects corporate income tax treatment, and may choose either C-corp or S-corp status. An LLC with more than 1 member by default is taxed as a partnership. Nonetheless, the multi-member LLC can elect to be taxed as a corporation and choose either C-corp or S-corp taxation status. Generally, entities (LLCs or Corporations) taxed as a C-corporation are subject to double taxation.

In this section, we provide an introduction to the two primary for-profit business types pursued by biotechnology firms (LLC and C-Corp) and then briefly discuss the advantages and disadvantages of each. The section ends with some details on how to register your entity through LegalZoom (use advised with a competent attorney) or utilizing the UMSL SBTDC.

Should I choose an LLC or Corporation as the entity type for my startup?
There is some debate in the biotech startup world as to whether new companies should incorporate as LLCs or Corporations. Corporation status is usually required by professional investors (like Venture Capitalists) but LLCs may offer some potential tax benefits to young startups if they anticipate making profits before having to take on significant investment. In this section, we present the benefits of both entity types. Note that switching from an LLC to a corporation is not too arduous of a task (In an uncomplicated and undisputed business situation and if handled by a legal professional it costs $2k and takes 1 week). It is, of course, up to you to decide which is best for you and your business. When in doubt, you should consult a competent attorney.

Below is a brief intro to each entity type focused on the key differences; a more detailed table comparing and contrasting the two follows.

Corporations (Also referred to as standard corporations): A corporation is a legal entity owned by shareholders. Any individual or corporation can create a new corporation. As a primary benefit, it protects the owners from personal liability. Without such legal protection, your creditors could come after you if your business goes under owing money. Also, without such legal protection your personal assets could be at risk should there be a lawsuit. So, the major advantage is this “limitation of liability” which all forms of corporations offer their founders and owners.

Limited Liability Company (LLC): Limited liability companies can be formed by any business or individual. An LLC offers liability protection similar to that of a corporation but is able to “pass through” its income tax burden to its owners, avoiding corporate income tax. This makes LLCs popular for companies that will generate profits prior to needing major investment. Also, LLCs
can pass through losses for tax purposes which is attractive to some investors (most often Angel Investors).

**Tax Election:** Standard corporations and LLCs can elect to be treated under Section C of the Internal Revenue Code (“C-corporation” or “C-corp”) or under Section S (“S-corporation” or “S-corp”). C-corporations are subject to corporate taxes, which means profits are not “passed through” directly to the owners. This means profits will likely be subject “double-taxation,” meaning the corporation has to pay corporate income tax on the profits and then owners have to pay personal income tax when receiving profit distributions (called dividends) from the corporation.

S-corporations pass revenues through to the shareholders, so the profits are only taxed once. LLCs often elect to be taxed as an S-corp to benefit from tax passthrough. While having the S-corp election, the business can only issue one class of stock and can only have up to 200 shareholders. In certain circumstances, an S-corp may make sense for some companies. Read here.

However, for various reasons, C-corps are much more favorably viewed by professional investors. The major reason for this is as a taxable entity, all of the burden of tax form preparation and compliance falls on the C-corp and is not passed through to the investors. Another reason is that C-corporations are not limited to only one form (or class) of stock – they can create as many classes of shareholders as they want. This limitation makes the business unwieldy for investors, prompting them to elect C-corp taxation and permitting more classes of stock to be issued for investors.
Sue’s Story-Business Formation, what kind of entity should I choose?
Sue is wondering which kind of corporate entity she should use. The answer she learns is that “it depends”. Her advisors tell her that:

- If her business model suggests her company is highly likely to generate profits before she needs to take on substantial investment, then the LLC form will allow her to avoid the “double taxation” problem identified above.

Table 4. Comparison of LLC and C-Corporations

<table>
<thead>
<tr>
<th>Liability</th>
<th>LLC</th>
<th>C Corp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Owners protected from legal liability</td>
<td>Owners protected from legal liability</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ownership and Management</th>
<th>LLC</th>
<th>C Corp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Members are owners who have equity interest and right to vote on a limited set of actions. Managers run the business. Managers can be, and often are, members.</td>
<td>Shareholders are owners, Management comprises Officers and a board of directors.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Taxation</th>
<th>LLC</th>
<th>C Corp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single taxation – Normally profits or loss are passed directly to members and taxed only at that level. However, LLCs can elect to pay corporate income taxes if so desired.</td>
<td>Possibility of double taxation exists- Company income is taxed and then shareholders are subject to personal income tax on any profits/distributions taken out of company</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Registration protects company name</th>
<th>LLC</th>
<th>C Corp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Unlimited number of owners</th>
<th>LLC</th>
<th>C Corp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Business Duration</th>
<th>LLC</th>
<th>C Corp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indefinitely</td>
<td>Indefinitely</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Benefits</th>
<th>LLC</th>
<th>C Corp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pass-Through taxation (single taxation): Income/loss would be reported on the personal tax returns of the members according to how these profits and losses are distributed (the members can make distributions how they see fit and are not required to use ownership as the only basis for distributions).</td>
<td>Much more likely to be the required organizational form to receive money from professional investors.</td>
<td></td>
</tr>
<tr>
<td>Flexible management structure</td>
<td>Owners can hold different types of stock interests (Preferred vs. Common Stock).</td>
<td></td>
</tr>
<tr>
<td>Simplest structure to begin a company with little overhead administrative management needed.</td>
<td>C-Corps allows investors the prospect of receiving dividends. Dividends must be made on the basis of ownership.</td>
<td></td>
</tr>
</tbody>
</table>
• However, most life-science companies pursuing business models that involve extensive product development will require large infusions of capital (i.e. anything over $1,000,000 or so) will need to access professional investors and might as well use the C Corp since that will most likely be required by the investors.

Because it’s clear to Sue that her cancer therapeutic company will operate at a loss for many years while it develops its products, she knows she will need to bring in professional investors well before she has profits. So, she decides to incorporate her company as a C Corporation. Because creating a C Corporation is so simple, one of her business advisors suggests she can do this quickly and inexpensively using Legal Zoom or even do all the steps herself (see discussion below). However, her advisor tells her, this does NOT mean she doesn’t need a transactions attorney. The process and documents for most substantive transactions (like raising money, taking licenses or forming collaborations of various kinds and many others) are very complicated and so she is advised to develop a strong relationship with an experienced transactions attorney as soon as she can afford to. He provides her with several lawyers to consider who specialize in start-up businesses similar to hers.

If you are at all in doubt, you should discuss the question of which kind of legal entity to use with an experienced lawyer. Ideally, having read this discussion you can abbreviate this discussion and avoid substantial legal costs that might otherwise be incurred getting educated by the lawyer. If you are 100% confident about which form to use, it is now uncomplicated and inexpensive to form your company online. Since LegalZoom is quite popular in this on-line company creation market, we are providing a sense of what that service entails. (Please note, we are not recommending you use this service or any other service – such decisions can only be made by you, the entrepreneur).

Establishing a corporate entity through LegalZoom
A quick and simple way to establish either an LLC or C-Corp is through LegalZoom. If you determine to use LegalZoom, we recommend using an experienced corporate attorney to review the operating documents or the shareholder agreement terms.

Forming an LLC in LegalZoom:
The process of establishing an LLC on LegalZoom takes approximately 20 minutes of your time. With a variety of packages, LegalZoom provides the opportunity to have an almost fully functional company established in as soon as 7-10 business days. Depending on the scope of services from State filing fees, Web Domain Setup, Bank Account Setup, Legal Consulting, Payroll software, and Access to hundreds of legal forms; LegalZoom can cost between $199 and $700 to setup an LLC. The most minimal package will cost $149 and does not include the State filing fee ($50 in Missouri), and will take approximate 30 days complete the registration process. Note that most LLCs also construct an operating agreement, and C-Corps must have shareholder agreements/bylaws. According to a survey of attorneys in St. Louis, you should typically expect to pay around $3,000 for the lawyer’s drafting of an Operating Agreement. Legal fees for creating Bylaws for a C Corp. are much lower.

Summary:
• Total Time (not including operating agreement): 19 Minutes
• Time until business registration: 7-30 days
• Total Cost: $149 - $700
• Services offered (Operating Agreement not included):
Missouri State Filing Fee for Article of Incorporation $50.00
Federal Tax ID (EIN) Obtainment (The IRS issues every company a unique Employee Identification Number (EIN) for the purposes of administering taxes). $49.00
Registered Agent Fee (A registered agent is responsible for receiving all legal documents and state notices for your company). $159.00
Annual Compliance Calendar Subscription. Let LegalZoom help keep you on task. $69.00

Forming a C-corp in LegalZoom:
The process of establishing a new C-corp or converting an existing business or partnership follows the same path in Legal Zoom. The main difference between establishing a C-corp vs. an LLC on LegalZoom is the requirement that C-corps require one to include the volume and share price for each of the owners. Otherwise the process and questions follow the same process as the LLC path.

Summary:
- Total Time: 22 Minutes
- Time until business registration: 7-30 days
- Total Cost: $199 - $700
- Services offered:
  - Missouri State Filing Fee for Article of Incorporation $50.00
  - Federal Tax ID (EIN) Obtainment - The IRS issues every company a unique Employee Identification Number (EIN) for the purposes of administering taxes). $49.00
  - Registered Agent Fee. (A registered agent is responsible for receiving all legal documents and state notices for your company). $159.00
  - Annual Compliance Calendar Subscription Annual Compliance Calendar Subscription $69.00

Utilizing UMSL’s SBTDC to form your entity
Kevin Wilson from UMSL Extension’s SMALL BUSINESS AND TECHNOLOGY DEVELOPMENT CENTER can assist with Business Plan Presentations. If interested in utilizing his services, please contact him at wilsonkr@missouri.edu.

Sue’s Story-When is LLC the best entity type?
While Sue was completing her market analysis, she decides she really has two distinct businesses she wants to launch; one will sell her novel animal model while the other will develop a cancer therapeutic. As mentioned above, she decides on a C Corp structure for the cancer therapeutic company. Because creation of a C Corp is so simple, she decides she can handle this herself using Legal Zoom. For the animal model company, she decides an LLC is the most logical entity type, as she does not foresee needing significant investment, and imagines the company as small and run primarily by the managers. She also quickly realizes that the Operating Agreement for an LLC is so complicated that she might as well engage a lawyer for this purpose. She decides that the lawyer for the LLC can also serve as the lawyer for the C Corp once she needs transaction advice for that company.

Intellectual Property
As you develop your innovation and your company begins to take shape, your ideas and inspiration begin to accumulate value. As your idea, company brand, and company image increase in value, you want to be sure they are protected. In this section, we provide an introduction to the information needed to develop, and then implement, an intellectual property strategy that best protects your invention, product, or brand. We recommend in the strongest possible terms that you obtain legal advice on intellectual property. This advice should come from an experienced Patent Attorney/Agent with knowledge of the technical field in which you operate (NB this is NOT the same lawyer you need for the transactional side of your business!) Since a lawyer’s time is expensive however, we offer in this section a very general understanding of how to protect your ideas so that you can use your attorney more wisely and avoid some of the legal fees associated with elementary “learning curve”.

What is Intellectual Property?

The term “intellectual property” or “IP” generally refers to “creations of the mind,” which are considered property and are protected by the law. Given that IP is treated much like physical property, it can be owned, licensed, assigned, bought or sold, and generally refers to four distinct categories.

1) Patents: Protection of novel, new, non-obvious, useful inventions for a limited period of time. In the life-sciences product development costs are comparatively very high. Therefore, early patent coverage of key innovations is crucially important and is the asset base for the vast majority of successful companies.

2) Trademark and Service Mark: Designations used to indicate the source of a product or service, respectively. Will my business have a name (e.g., McDonald’s, Great Clips), slogan (e.g., “Just Do It”), and/or logo, which a consumer will closely associate with my product or service?

3) Copyright: Protects a variety of different original and creative works and is immediately created when the work is “fixed” in a “tangible medium.” Increasingly in the life sciences, innovative ideas can become “tangible” through the medium of a computer or via the Internet. In these cases, relevant computer code may be copyrighted and thus become an important asset.

4) Trade Secret: Commercially valuable information that is offered protection through confidentiality / non-disclosure agreements (e.g., Coca-Cola formula, KFC Fried Chicken Recipe) as opposed to being protected by patents. Although protected under the law, a trade secret is not protected if the information can be reverse-engineered by someone else. Did my company come up with a product or process that may not be eligible for patent protection, but is unlikely to be easily reverse-engineered by a competitor (e.g., Google search algorithms)? Because they are generally easy to reverse-engineer from the detailed information made available through the regulatory process, trade secrets are not common forms of IP in the life-science industries.

Take time to consider which one or more of these categories of intellectual property apply to your business.
Why should I be concerned about Intellectual Property?

Intellectual property can prevent others from hurting the reputation of a business, can prevent the sale of unlawful fakes or knockoffs, and can protect an invention from being copied by competitors.

A potential investor or acquirer will evaluate a company’s intellectual property to assess how well the business is protected. If a competitor could easily copy or duplicate an invention because the intellectual property is not protected, an investor will most likely not invest in the company. Even worse, if a competitor has a pending patent application or granted patent that covers a company’s invention, they can bring legal action against that company seeking monetary compensation for “damages” from possible patent infringement and can prevent them from making or using that invention. Under certain circumstances – such as “willfully infringing” a patent, this can result in triple (3X) actual damages!

Similar protection is needed for company trademarks or service marks. As a company product and/or service becomes recognized, value is added to the company’s brand, which can be realized as the company logo, name, or slogan. A trademark, or a service mark in the case of companies that provide a service, protects a company’s brand and ensures no other companies can use any aspect of the brand. Generally, the value of “Brands” increases with marketing investment and resulting exposure. Thus, it is only rarely a major concern for early stage companies. Still, you have to start a brand somewhere somewhere!

What is a patent?

A patent is a right given by law to inventors to preclude others from using or otherwise exploiting, their inventions for a limited period of time (20 years from filing is the global standard and is now adhered to by the US as well). By granting the inventor a temporary monopoly in exchange for a full description of how to perform the invention, patents play a key role in developing industry around the world. US law confers "the right to exclude others from making, using, offering for sale or selling the invention throughout the United States or importing the invention into the United States." A patent, however, does not grant an individual the right to make, use, offer for sale, sell, or import the invention if doing so would violate any law (e.g., a new drug may be patentable, but it will be illegal to make, sell, possess, or use the drug until it has received regulatory approval). Keep in mind that patents are business property and should fit into the overall strategy. Improperly or cheaply filed patents can result in poor coverage or expensive fixes in later prosecution.

What are the parts of a patent?

Cover Page: The cover page presents information that is primarily bibliographic in nature. None of this information, including the abstract, has any legal import for interpreting the patent. The data provides notice of historical facts and identifying elements, such as the application filing date and the serial number.

Specification: The specification (also called the disclosure) is the most important part of a patent application. It describes the invention and its uses. It must do so in sufficient detail to allow a person trained in the field of the invention to practice the technology. The Claims of the patent (see below) must be directly supported in the specification. The specification must support the novelty of the invention by differentiating it from all the similar “Prior Art”. It must show that the invention is “practicable” (can be reduced to practice). It must be clear about the "inventive step" and should show why the invention would not be considered obvious to someone practiced in the "prior art”. The specification should include the following information:
(a) Title of the invention;
(b) Cross-references to related applications;
(c) Statement regarding federally sponsored research, if applicable;
(d) Background of the invention;
(e) Summary of the invention;
(f) Description of any drawings;
(g) Detailed description of the invention;
(h) Claims;
(i) Abstract.

The **Claims** are a very important part of an approved patent application as they define the invention and the scope of protection. The claims should contain:

- A preamble that explains the class of the invention, and optionally its primary properties, purpose, or field. For example, "An apparatus...;" "A therapeutic method for treating cancer...;" "A composition having an affinity for protein X...." This preamble may also reference another claim.

- A "transitional" phrase that characterizes the elements that follow. The phrases "comprising," "containing," and "including" are most often used and often preferable, as it means "having at least the following elements" and are therefore open (inclusive) and do not exclude additional limitations. The phrases "consisting of" and "consisting essentially of" are more limiting, as they mean "having all and only" or "virtually only" and are therefore closed (exclusive). Any good lawyer will apply more inclusive language than exclusive language in the patent claims. It will be the aim of the patent examiner (who works for the relevant patent office) to narrow the claims. This is the major thrust of negotiation with a patent office once there is agreement that novel IP exists.

- A set of "limitations" that together describe the invention: "an X, a Y, and a Z connected to the X and the Y." The elements should be described as though they interact or cooperate to achieve the desired result. Fewer limitations, on thus shorter claims, are broader in scope and coverage.

**What are the Requirements for Patentability?**

Besides being a process, machine, manufacture, or composition of matter, an idea or invention also must be 1.) **New,** 2.) **Novel,** 3.) **Non-obvious,** and 4.) **Demonstrate utility,** i.e. be useful in some context.

1) **New:** Is required for Patent eligibility as described below (Patentable Subject Matter).

2) **Novelty:** In the U.S. prior to March 2013, ownership of an idea or invention was awarded to the person that could prove she or he was the first to invent the idea. This legal principle was referred to as "First-to-Invent". After March 2013, U.S. patent law changed such that ownership of an idea or invention was awarded to the person that first filed the patent, also known as "First-Inventor-to-File". One must be still an inventor, not just the first one to file. Often, attorneys will ask whether any “prior art” exists concerning your idea or invention. Prior art refers to any public disclosure (e.g., a printed publication, presentation) made before the effective date of filing the patent application.

3) **Non-Obviousness:** If the creation of an invention requires very little creative effort and, therefore, is obvious to a “Person Having Ordinary Skill In The Art,” a patent will not be granted. In other words, if someone who is familiar with the relevant art, with average intellect and average creativity walked into a room with all of the most relevant prior art and necessary materials available, would she or he be able to come up with the
invention? If so, then the invention is said to be obvious. If the invention is non-obvious, the patent must be written in a way that enables a similarly skilled individual to practice the invention as claimed without undue experimentation.

4) **Utility**: In order to be patentable, an invention must be useful. Generally, to assess an invention’s usefulness one asks, “Does the invention do anything?” or “Does/will the invention work?” The requirement of an idea to be useful also implies that the invention can perform the intended purpose it was designed to do. This is rarely a problem in the life sciences domain.

**What are examples of patentable subject matter?**

1) **Process**: "mode of treatment of certain materials to produce a given result; an act, or a series of acts, performed upon the subject matter to be transformed and reduced to a different state or thing."
   a. **Ex.** A new set of steps involved in an organic chemistry reaction to create a commonly used chemical, resulting in a manufacturing “process” that is cheaper and faster than traditional methods.

2) **Machine**: “instrument that consists of parts or elements that are organized to cooperate, when set in motion, to produce a definite, predetermined result (apparatus, mechanism, device, engine).”
   a. **Ex.** A novel and more efficient flow cytometer.

3) **Manufacture**: “the production of articles for use from raw or prepared materials giving those materials new forms, qualities, properties or combinations, whether by hand labor or machinery; also, anything made for use from raw or prepared materials."
   a. **Ex.** The synthetic route for a small-molecule drug.

4) **Composition of Matter**: "all compositions of one or more substances and all composite articles, whether they be the results of chemical union or of mechanical mixture, or whether they be gases, fluids, powders, or solids."
   a. **Ex.** A newly synthesized chemical that does not occur naturally, has never been produced before, and which has utility, for example as a drug; or, the formulation of a previously known compound as a therapeutic.

**What are examples of non-patent eligible subject matter?**
Some ideas are not eligible for patent protection because they are already in the public domain as “Prior Art” (i.e. published by someone else). It’s important to stress that prior art need not be patented in order to be relevant – it only needs to have been published. The standards for what constitutes “Published” are very low – a poster presented at an academic conference would definitely be considered prior art and would preclude the possibility of filing a patent on the relevant idea once the poster is presented (except for the inventor, who can file during a period of up to one year from first public disclosure).

**Non-patent eligible** subject matter includes:

1) **Laws of Nature**: Laws concerning thermodynamics and conservation of energy, level of a biomarker unless it is non-obvious. (Case law is evolving on this point. Talk to your lawyer.)

2) **Abstract Ideas/Mental Processes**: A mathematical method for converting binary coded decimals into binary numerals
3) Naturally Occurring Items: A newly discovered plant in the rainforest, a newly discovered genetic mutation.

How does one determine if an invention would have value as a patent?

There are two evaluations performed to help answer this question. First, a Patentability Search must be completed to evaluate whether there exists prior art relevant to your technology that would prevent any claims you file from issuing. Obviously, a patent must ultimately issue in order to have value. In order for your innovation to meet the standards of “Patentability” you must be able to establish “novelty” and “non-obviousness” of your innovation over all existing art in the public domain. A Patentability Search consists of evaluating the scientific literature and any public information as well as patents (published applications, and issued patents, expired or unexpired) for features, concepts, or principles that are similar to your technology.

Ideally, in order to have value, a patent will stand on its own and not be “dominated” by other patents. However, it is frequently the case that an issued patent falls under the dominance of an earlier patent. In this case the value of the new patent may still potentially be considerable but it will be constrained by the earlier one. To address this reality, a Freedom To Operate (FTO) Search (also known as infringement or clearance search) should be completed to ensure your technology and commercial product will not infringe on existing patents. A FTO Search examines the claims portion of all relevant unexpired patents.

The ideal situation of course is that both the “Patentability” and “FTO” searches come back clean – showing no potential for infringement. This is pretty rare however – usually there is lots of potentially relevant art. All this art should be referenced and – in fact – should drive the drafting of the specification and claims sections of the new patent filing – care should be taken to differentiate the new invention from all existing art. If the new idea cannot be differentiated from all published art then it’s likely not to be patentable. In this sense, a patentability search that turns up directly relevant art that cannot be differentiated is likely to be fatal – that is a patent is unlikely to issue and therefore the cost of prosecuting the patent cannot be justified.

Freedom-to-operate searches are less likely to be “fatal” in this sense. Note that a new innovation can in fact be new, novel, non-obvious, useful and, therefore, patentable, but still partly infringe on an existing patent. Here is an example: A pharmaceutical company has an issued patent for a drug with “Composition of Matter” claims relating to the actual chemical structure of the drug and some “Methods of Use” claims relating to its formulation and indications. A new inventor later discovers a use for the same drug that was not mentioned in the specification or claims of the original patent. In this case, the new inventor can get a patent on the previously unanticipated use of the drug assuming it’s not obvious. In this case, the new inventor cannot use the drug without violating the first patent, but – once it issues – the original inventor cannot use the drug for the newly patented use without violating the second patent. This situation – called a “cross block” in business development jargon – is usually not fatal and is in fact frequently resolved with a license – for example the original and new inventors can execute an agreement allowing the new inventor to market the drug for the new use in return for a royalty stream paid to the original inventor.

Although a professional patent agent or attorney is recommended for more definitive Patentability and FTO assessments, such searches can be very expensive (thousands of dollars). Today, several excellent searchable databases are available free of charge and any inventor or entrepreneur can and should conduct initial searches of the patent space to gain initial, and free, perspectives on patentability and FTO. As mentioned above, these searches
are in fact integral to the drafting process itself as it is very important to draft new patent applications with a very clear impression of existing art in mind.

Finally, the question of “how valuable is a patent?” can only be answered in a commercial context. There are thousands of patents issued every year and, while all of them meet the test of “utility” relatively few of them are extremely valuable. The only way to ultimately derive value from a patent is to figure out how to use it as the core of a business model that enables a product or service to be sold uniquely by the patent holder (and/or licensees) in large quantities and at an attractively high price.

**How do I complete a preliminary Patentability and FTO Search?**
For a Patentability or FTO Search, any public description of a similar technology can be used to describe prior art. Basic searches on the Internet are a good place to start, including searching Google Scholar. Several free online resources are available specifically for researching previous patents that allow you to search for keywords in patents directly. These sources include Google Patents, the US Patent and Trademark Office, and FreePatentsOnline. Google Patents provides a useful navigation and querying interface, but note they do not have a 100% complete database.

**How much does a professional Patentability or FTO Search cost?**
As an individual inventor, the basic patentability search is more relevant and costs roughly $1,000. FTO Searches are some of the more expensive searches - they typically start around $5,000 but can get much more expensive with corporate firms paying $50k+ for such work. Written legal opinions interpreting these results are an additional cost.

**What are the steps to filing a patent?**
The steps that lead up to and include filing a patent with the United States Patent and Trademark Office (USPTO) can be complicated and confusing (see Timeline below). Fortunately, your patent attorney should have a good understanding of the entire process. You, however, should be aware of two application steps: 1.) filing a provisional patent and 2.) filing a non-provisional patent. Once the patent has been drafted, it can be filed as a provisional application. The provisional patent is not examined by the Patent Office and serves as a placeholder or stamp that declares that you have filed a patent. The day you filed the provisional patent is the “Priority date” for the purpose of who filed first (see “First-Inventor-to-File” above). You will have one year from the date of filing to convert (or “perfect”) the provisional patent into a non-provisional patent, which will be examined by the USPTO, or a PCT application (described in more detail below). Preparation of a provisional patent can cost much less than a non-provisional patent. The one-year time period for “perfection” gives you time to decide whether to invest in the full non-provisional patent application or not. A non-provisional application will only be prosecuted by the relevant patent office of the country in which it is filed (in the United States Patent Office for example), thus the granted claims will only be enforceable in the relevant country (the United States in this example). Alternatively, the Patent Cooperation Treaty (PCT) application discussed below gives you the opportunity to pursue foreign patent rights simultaneously with a single application.
Figure 1. Patent Preparation, Prosecution, and Post-grant maintenance Fee Timeline.

What is a PCT Application?

Here we present a brief introduction to PCT applications, as a full primer on The PCT is outside the scope of this roadmap. We recommend researching through the links at the end of this paragraph as well as consulting a patent attorney on the topic. The Patent Cooperation Treaty (PCT) system simplifies the process of filing international patent applications by consolidating the early process to one general entity as opposed to hundreds of foreign country patent offices. Submitting a PCT application delays the expenses associated with applying for patent protection in numerous countries and allows the inventor more time to assess the commercial viability of her or his invention. Under the PCT, an inventor files a single international patent application in one language with one patent office. One can choose to have that PCT office give an opinion on the patent, or just wait a defined time-period to “nationalize” and file your patent application to be prosecuted to the up to 148 countries accessible through The PCT.


How much does a patent cost?

The cost of researching existing patents to determine infringement, drafting the patent, filing the provisional and non-provisional patent, and other tasks vary depending on the time needed and the type of invention. Below are ranges of fees and attorney costs associated with filing patents to protect the invention.

Patentability and Freedom-to-operate search: $2,500-$15,000

Provisional patent application preparation: $2,500-3,000 for bare bones applications (e.g., starting with a manuscript or other disclosure, adding some model claims and a page or two of additional description to clearly support model claims).

Filing fee of provisional to the USPTO: $130
Preparing the non-provisional application: $2,500-$5,000 (can be more if it's a complicated or very broad patent with many claims or, less if the provisional patent was more complete).

Filing fee to the USPTO for non-provisional patent application = $435-$1,740 (depending on number of claims)

Patent Prosecution: $10k to $20k+. These are the costs you might expect from your legal team responding to correspondence with the patent office and adjusting the claims in a patent accordingly until it is ultimately accepted.

Foreign filing fees: If one submits a PCT instead of a US non-provisional, these are the fees associated with then preparing the submitting the PCT as full patent application to each country in which you desire coverage. Least expensive would Canada @ about $2500-3000. More expensive would include Australia, Europe, Japan, Korea at about $4-5k (not including substantial translation costs for Japan and Korea which can range up to $2,000).

Foreign attorney fees: Estimate around double to quadruple initial foreign filing costs.

Annuity fees: Also referred to as Maintenance or Renewal fees, these can introduce significant cost burden in case of foreign filings.

How do universities handle their IP? How does a startup work with a university to commercialize their IP?

Why are Universities involved in IP?
Universities are involved in IP because they are the major source of technological innovation with a long history of creating value for society in the US and Globally by supporting intellectuals, many of whom come up with novel, useful ideas. Over the last many decades, universities have evolved towards being more sophisticated in their understanding of innovation and commercialization. So much so that in the US in the late 1970s, it became increasingly obvious that a new approach to managing innovative technologies invented in universities was needed.

Prior to 1980, inventions developed under federal funding were owned by the US Government. This was an inefficient system – at the time only 5% of federally funded inventions were commercialized through non-exclusive licenses. Since most new technologies were either not patented at all, or when patented, were available to all comers through non-exclusive licenses, it was difficult for industry to commercialize university IP. To help solve this issue legislation was passed in 1980 requiring research universities to retain ownership and all licensing revenue from inventions developed during federally funded research. Called the Bayh-Dole Act, this legislation holds the university to a few important obligations related to patents of work funded by federal funding:

- The University must take reasonable steps to protect and commercialize innovations created with federal support. As a practical matter, this means they must have some kind of administrative arm that deals with patents and licenses (usually called an Office of Technology Management (OTM) or Technology Management Office (TMO)) and then follow reasonable peer practices.
• The government retains for its own use a non-exclusive license to the patent. (In theory, this license will only be exercised when there is a compelling Federal interest involved. In practice, this license is almost never exercised).
• The licensee is encouraged to manufacture in the US.
• Universities are encouraged to license to small businesses capable of developing and manufacturing the invention.
• A portion of the revenue from licensing a patent must be shared with the individual inventor(s).
• Any remaining revenue must go to support the licensing function, scientific research and/or education at the university.

The enactment of this legislation in essence mandated the modern Technology Management Office (TMO), the entity within a university that manages all the university’s IP (variously called the Tech Transfer Office or Office of Technology Management) and Foundations such as WARF (Wisconsin Alumni Research Foundation). If your startup is currently, or might in the future, utilize IP created at a university you will become quite familiar with a TMO. Following are some key processes that occur at TMOs related to IP, and then a summary of the terms used in most university licenses.

What is the process for working with the university TMO for me as an inventor?

The Invention Disclosure: Upon creating what an academic inventor feels is unique intellectual property, before making any kind of public disclosure (such as a publication or poster presentation at an academic meeting) they alert their technology management office to the potential IP through an invention disclosure. At most universities, this is a standard form where they encourage the inventor to provide information related to the invention and other work (prior art) in the field. Most university TMOs enable inventors to file disclosures online. The technology management office then utilizes the invention disclosure, often in conjunction with outside legal counsel, to decide whether the IP is new, novel, non-obvious, practical AND has substantial potential commercial value. If the answer is yes to all these questions, they may then fill a US provisional patent application and/or PCT application.

The Patent go/no go decision: The provisional period then gives the university time to decide whether to spend the money required to turn the provisional into a full patent, or if a PCT file internationally. This might involve seeing how far the inventor has furthered the research, if the inventor wishes to commercialize the IP, seeing if there is any interest in the IP from the business community (larger companies or startups), or conducting patentability, FTO, or market validity assessments. Ultimately the university technology management office must decide if there is a probability of return on the money they spend turning the provisional into issued claims.

Rights assignment: If the TMO decides not to patent, (or later decides to abandon prosecution of a patent), it will usually be willing to “assign” its rights in the invention to the inventors at no cost. In the instance of a rights assignment, the inventors then must then take on the task of managing the patent and the costs of prosecution.

University patent prosecution: In cases where the TMO decides to patent (and therefore to not assign rights back to the inventor), it will undertake the management task and costs of prosecution itself (at least for a time). Typically, a member of the TMO staff is given the management task. A law firm that advises the TMO staff member and inventor, works with the
inventor to draft the patent filings and otherwise “prosecutes” (i.e. handles the actual implementation) of the patent.²

**What is the process for doing Business with the TMO as a company founder?**

So far in our discussion of working with the TMO we have described how the university-based inventor interacts with the TMO as a university employee-inventor. For many academics, this is as far as it goes – they do not get actively involved in commercialization beyond their role in prosecuting the patent. However, in the last several decades and for a host of reasons it has become increasingly accepted – and indeed encouraged – that university personnel take a more active role in commercialization if they so desire. The remainder of this discussion addresses how to do business with the TMO assuming the inventor wants to take on the role of company founder.

Typically, most research universities cannot afford to take all their patent prosecutions all the way through patent issuance. For this reason, TMOs are under tremendous pressure to find “licensees” (further explained below) who will convincingly undertake such tasks and costs. Start-up companies have advantages and disadvantages here: on the one hand, TMOs like to work with start-ups because they frequently involve important faculty members who have a strong interest in commercialization and serving the faculty is an important part of the TMO’s mission. It's also true that – other things being equal – start-up companies have a better record of ultimately commercializing technology than do large companies (large companies frequently “sit on” technologies – i.e. don’t really develop them – either through corporate bureaucracy or for strategic reasons). However, large companies are much better able to take over the majority of prosecution costs much sooner than are start-ups. Managing these trade-offs is a constant headache for TMOs. In order to effectively qualify for a license, start-ups must be far enough along to be credible licensees. In order to insure it does not lose the opportunity to license, and yet still have the opportunity to make sufficient progress towards being a credible licensee, start-up companies frequently negotiate and sign a special kind of agreement – an Option Agreement – which holds the licensing opportunity open for a time, allowing the start-up to make necessary progress.

**What is an Option Agreement?**

An option agreement is a written agreement between the TMO and a potential licensee that states the university will – in return for a nominal fee – hold open an option to consummate an exclusive license to a technology for a pre-determined time-period (usually 6 months). During this “option period” the TMO will not grant a license of any kind with anyone other than the option holder. Option agreements are useful because, even though a startup may see value in a piece of IP, as a practical matter, it may be too young yet to meet convincing criteria for obtaining a full license. Or, the potential licensee may choose to delay taking a full license to a piece of IP for any number of reasons. Putting an exclusive option agreement in place creates the time for the start-up to get its commercial plan together, find early financing, perform diligence, test the technology in its own facilities etc. The university is frequently willing to do

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² The word prosecution can be confusing in this context. In patent law, prosecution does not mean to go to court. Instead, “prosecution” in patent law means the process of drafting the patent filings, negotiating the processes put in place by the national and international patent offices and negotiating with the patent examiners in those offices, ultimately resulting in an “issued patent”. At any point in the process and especially after issuance, patents may and often do end up being taken to court for resolution of patent disputes. This process of adjudicating patent disputes is called patent “litigation”.
such an option (or right of refusal) for several months in the hope that this will make the start-up more credible with potential investors, collaborators advisors etc. and thus lead to a stronger commercialization prospect which benefits both parties.

**What is a Technology License?**
A license is an agreement between an owner of IP (the licensor) that allows another party (the licensee) to use, modify, and/or resell the IP in exchange for some sort of compensation. The compensation can be an upfront payment; royalties based on future revenue or company liquidation events. For this section, we are going to focus on licensing agreements between startups and academic universities. However, most if not all the aspects of a technology license described here would apply to technology licenses more generally (between two companies for instance). In the text, we will specifically refer to “universities” when the point is peculiar to them, and “licensors” when the point is generalizable.

(Please see the attachment at the end of this section for discussions from the Wash U and UMSL OTMs summarizing their technology transfer process as discussed above.)

**What are the typical terms in a Technology License?**

*Exclusive vs. semi-exclusive vs. non-exclusive:* An exclusive license means that only the licensee has rights to commercialize under the patent and the licensor cannot issue any additional licenses. A non-exclusive license means the licensee has rights to the IP but the licensor can issue additional non-exclusive licenses to other entities that would also then have rights to practice the invention. A semi-exclusive license can exist when there is more than one licensee, but each licensee has an exclusive right within a limited geographical area or within a limited field of use.

*Field of Use definition:* A Field definition is an important part of any license. Often licenses may be granted for all fields of use. In such a case, the licensee has an obligation to make reasonable efforts to pursue commercialization in all fields. In other instances, it makes sense as a practical matter to limit the field of use. For example, a chemical that may be useful as a drug for human use is frequently useful in other mammalian species. Or the same chemical may have other non-medical uses altogether. In such cases one company may obtain the rights to human medical use, another the rights to non-human medical uses and still another may be granted a license to the chemical for use in non-medical applications. The definition of such rights occurs in the Field of Use definition.

*Geographies:* Most licenses specify the geographical areas where the right to commercialize the technology obtains. This may be as broad as “The World” or “In all localities covered by relevant patents”. In other instances, however, it may make sense to exclusively grant a licensee an exclusive license only in geographies where that licensee can make a convincing case of its ability to commercialize. For example, rights under life-science patents are frequently divided up into “North American Rights”; “European Rights”; “Japan”; “Rest of Asia”; “Rest of World.” or other similar geographical divisions. When start-up companies are involved, it is frequently the case that it cannot win the right to all geographies.

*Sublicense Rights:* It is advisable for start-up companies to obtain the right to “sub-license” the technology to other companies for commercialization in fields of use or geographies outside of the ones of core interest to the start-up. This way, the start-up maintains some control over the overall commercialization strategy, yet the licensor is assured that the start-up is not over-extending itself. Start-ups should be aware however, that when a sublicense right is granted, the university will likely insist on segregating the “sub-license revenues” from “product revenues”
so that they can charge a much higher royalty on the sub-license revenues (see Revenue Stream).

**Revenue stream**: Universities can create revenue streams numerous ways through licenses. Here are the most common such streams:

**Upfront payments**: Some licenses will require the licensee to pay an upfront payment at the time the license is signed and becomes effective.

**Patent cost reimbursements**: The university will require the licensee to reimburse all of the “out of pocket” patent costs the university incurs in filing and prosecuting the IP covered by the license. The only question is one of timing. Obviously, it is in the best interests of the Start-up to delay the requirements of reimbursement as long as possible. Ideally, the license agreement should postpone such patent cost reimbursement until the company attains substantial sustained revenue. Many university licenses insist upon reimbursement prior to revenues. As a practical matter, this would mean that the licensee’s investors would have to reimburse the university. Most investors will not agree to invest with this requirement hanging over the company and will insist on a renegotiation of the license prior to investment. This gives the start-up company a strong argument in favor of postponing reimbursement for patent costs until after sustained revenues.

**Milestone payments**: Milestone payments are payments to the licensor by the licensee triggered by reaching development and commercial benchmarks. They serve to compensate the licensor as the value of the licensed technology increases. Examples of the triggers for milestone payments for a human therapeutic product might be: first use in man, completion of clinical trial phases 1, 2 and 3, submission of NDA, approval of NDA, first revenues and attainment of pre-agreed revenue targets.

**Royalties**: Royalties are paid when products that use the IP are sold. Royalties are usually calculated based of a percentage of total sales or fee per unit basis.

**Equity**: Licensors sometimes take an equity stake in the licensee as part of the license agreement. This equity stake becomes a revenue stream when the company or product is acquired or if the company is successful in “going public” through an IPO allowing the University to sell its equity stake.

**Performance Milestones and “Claw-Back” rights**: Licenses usually require that milestones will be met and that the associated payments will be made in a timely fashion. The licensor’s recourse in situations where the milestones/payments are not met/made is to “Claw-Back” (that is, cancel) the licensed rights. Other Claw-Back rights can be triggered if the licensee does not pursue commercialization diligently in all Fields and Geographies, or if the licensee does not meet reporting requirement commits fraud or other illegal acts. In essence, the performance milestones assure the licensor that commercialization will proceed in a timely manner, and the “Claw-Back” right ensures the licensee will face consequences if it fails to commercialize.

**Minimum payments**: A license might have minimum payments to the licensor that must be reached by certain time intervals after the signing date of the license. If the licensee does not generate royalty payments or other returns at least at the minimum they may have to pay the cash outright to retain control of the license.

**Patent prosecution and defense**: Most licenses are pretty specific about “who will do what” as far as patent prosecution and defense are concerned. As stated above, the licensor cannot afford to prosecute patents indefinitely unless its costs are reimbursed or otherwise paid. Once
they can afford to do so, it is likely in the best interest of the licensee if it takes over not only the cost of prosecution but the patent management responsibility as well, by hiring a single outside party acceptable to both the university and the licensee. Do not neglect to discuss the "Right to change Council" at licensing. Otherwise, the licensee will pay twice for patent prosecution – once for the licensor’s counsel and then again for the licensee. (While this may seem reasonable, it is not by any means a “given” that all licensors will agree to it).

Even in the period during which the licensor retains both the management and costs of prosecution, it will want to make sure the licensee will cooperate on all matters relating to patents. Thus, both parties are highly motivated to make sure that the license is very clear about who has what responsibility under which circumstances.

At a minimum, the Licensor’s responsibilities typically include:
- The management of prosecution and the payment of all application and legal fees.
- Monitoring potential infringement and to litigate against infringers.

Under this scenario, The Licensee’s responsibilities typically include:
- Monitoring potential infringers.
- Notify the licensor of potential infringement.
- Cooperation in all litigation.
- The payment of all patent associated costs as required by the license in a timely manner.

What are some examples of licensing terms and policies from local Universities?

**Washington University in Saint Louis:** Wash U offers a “quick start” license to university inventors, it has fixed terms in an effort to simplify and accelerate the process of negotiating a license. Some of the key terms appear below, the full license can be seen at this link along with additional details about the Washington University OTM.

- An exclusive license with right to sublicense
- No payment for past patent costs – future patent costs to be paid by Licensee
- No upfront, annual or milestone fees
- Financial and diligence performance milestones based on a detailed business plan
- No equity for Washington University
- A fixed 2% patent royalty rate on sales of any product(s)
- No minimum annual royalty payments
- A sliding sublicense revenue starting at 15% that steps down to 5% over five years
- A 0.95% “success fee” at an exit event of the company

**Saint Louis University Office of Technology Management (OTM)**

**OTM Mission:**

- Enhance and support SLU’s economic, academic and social-based initiatives
- Create economic value from SLU’s intellectual property (IP)
- Stimulate and sustain innovation, creativity and economic growth in St. Louis and region

**OTM Goals:**

- Encourage new invention disclosures from SLU faculty and staff
- Secure patent protection for selected technologies
- Start technologies toward early commercialization with competitive grants and awards
- Commercialize SLU research through both global corporations and local startups
OTM Processes:
• Make valuable discoveries available to end users as new products and services
• Solicit new invention disclosures (IDs) from faculty
• Assess commercial potential and patentability
• File patent applications for selected IDs
• Commercialize through strategic and startup licensees

OTM Startup Support:
• Strongly encourages and supports formation of startups as licensees for SLU IP
• It informs, guides and facilitates faculty startups in all needed aspects including:
  • Conflict of interest management
  • Startup entity formation
  • Independent advisors
  • Company management
  • Equity and grant financing
  • Initial commercialization plans
  • Office and/or laboratory location

OTM Startup Options & Licenses:
• SLU OTM recognizes the risks inherent in startup businesses, especially when funding is limited, and encourages their use of straightforward low-cost option agreements
• Options provide startups with a low cost exclusive evaluation period, typically 6 months, and give potential investors and granting institutions confidence as to their rights in IP
• Options also provide an exclusive period for negotiation of a license
• Startup management may negotiate a license term sheet with the option or later
• In either case, the term sheet and license will include but not be limited to:
  • Patent rights, field of use and territory
  • License issue fee potentially in the form of equity
  • Royalties, sublicense rights and pass-through royalties
  • Milestones for diligence purposes and performance payments
  • Patent expenses including past, ongoing and future expense
  • Progress reports, insurance and indemnification terms
  • Initial development and commercialization plans
  • Success fee on agreed liquidation events
• SLU OTM is committed to completing licenses that will proactively assist and support startup financing and viability going forward.

SLU OTM Contacts:
For further details please contact Graeme Thomas or Malcolm Townes, as follows:
- D. Graeme Thomas, Director  
  Tel: 314-977-7721  
  Email: dthoma42@slu.edu
- Malcolm S. Townes, Business Development Manager  
  Tel: 314-236-9096  
  Email: malcolm.townes@slu.edu
Trademarks

A trademark can be a name, logo, slogan/tagline, character, symbol, color, sound, or even scent that is used by individuals, businesses, and organizations to identify and distinguish their product or service by indicating the source of their product or service.

Figure 2. Examples of famous trademarks.

Consumers use trademarks to identify and compare as well as distinguish products/services. A trademark may offer an assurance of the quality or consistency of a good or service. For example, if you buy an Apple computer, you can expect the computer to be the same standard of quality that Apple is known for. In many cases, a trademark can be the most valuable tangible asset of a business.

How do I acquire rights to my Trademark?

Common law trademark rights are acquired upon using the trademark in connection with a good or service. Therefore, if you put your company's unique logo on your website in connection with the products or services you are offering, you acquire common law trademark rights.

To strengthen your protection and increase the scope, you may register your trademark as “In-Use” or as “Intent-To-Use.” By registering, you obtain the exclusive rights to use the mark nationwide, prevent registration of confusingly similar trademarks, increase the chance of getting trademark protection in foreign countries, and gain the ability to use “®” to designate that your trademark is registered.

Instructions on how to electronically register your trademark with the USPTO can be found here: http://www.uspto.gov/trademarks/teas/

Types of trademarks, from weakest to strongest protection, are described below:

- **Generic** (e.g. E-MAIL, ASPIRIN, ZIPPER, CARS): Device that is or has become synonymous with a general class of the product or service. For example, you would be unable to achieve trademark protection if you started a car company called “Cars” because “Cars” refers generically to the product offered. A trademark can become generic when the mark loses its primary meaning, such as “ASPIRIN” and “ZIPPER” which were both originally trademarks designed to designate a specific “brand” but became terms used to describe the category of goods. (Trademarks must be used carefully to ensure that they don’t become generic. So, once you have established a mark and plan to use it extensively in a market campaign you should get legal advice on how to use it properly.)

- **Descriptive** (e.g. BANK OF AMERICA, SPORTS ILLUSTRATED): The trademark describes the good or service and must establish secondary meaning by becoming distinctive to function as a trademark. For example, consumers must see the Bank of America trademark and connect it with Bank of America banking services rather than an American bank before trademark protection is secured.

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• Suggestive (e.g. JAGUAR, MICROSOFT, COPPERTONE): Marks that suggest the quality or characteristics of the good or service. For example, MICROSOFT suggests software for microprocessors.
• Arbitrary (e.g. APPLE): Trademark has a common meaning and that meaning has no relation or inherent connection to the goods or services being sold.
• Fanciful (e.g. EXXON, BUICK, KODAK): Devices that have been invented for the sole purpose of acting as a trademark and has no other meaning aside from connecting a good or service to the trademark. Considered the strongest type of trademark protection.

Copyright
Copyright law protects original creative works by rewarding authors and artists with a set of exclusive rights. Federal copyright law grants authors and artists the exclusive right to make and sell copies of their works, the right to create derivative works, and the right to perform or display their works publicly. These exclusive rights are subject to a time limit and generally expire 70 years after the author’s death.

Copyrightable works include the following types: literary, musical, dramatic, pictorial/graphic/sculptural works; pantomimes or choreographs; audiovisual works, sound recordings, compilations, and architectural works.

If you create or hire someone to create an original logo or character for your company, copyright protection allows you to stop others from using that same logo or character in addition to any trademark protection that may be afforded.

More recently, copyright protection has been discussed in the context of computer code, exactly as written, as an alternative to patent protection. Presently, the consensus is that computer code, specifically as it is written, is afforded copyright protection as a literary work.

Trade Secret
In some limited cases, trade secret protection may be appropriate for some inventions or ideas. A trade secret can be a formula, practice, process, design, or instrument that is not generally known and not reasonably attainable and that gives a business a competitive advantage. Trade secret protection is indefinite (i.e. forever), but if another party reverse engineers the protected invention entirely on their own, the trade secret holder has no way of preventing the other party from using the invention. Generally speaking, trade secrets are not a viable technological basis for start-up life science companies.

An attorney should make the determination of whether trade secret protection is appropriate for your invention/idea. Often, a complex invention (e.g. Google’s search algorithms) or recipe (e.g. Coca-Cola, KFC Fried Chicken), which may not be patentable or easily reverse engineered, is appropriate for trade secret protection.

What can I do before I talk to an attorney about IP?
1) Educate yourself. Beyond this Roadmap, try to learn as much as possible about when IP is needed and when it is not. File for IP protection when you and your attorney decide the time is right. However, it is important to reiterate that any public disclosure prior to filing your provisional application for patent protection can count as prior art towards your invention. Thus, it is important to discuss with an attorney your invention prior to a public disclosure. A public disclosure can be a publication, a presentation, a conference
abstract, a grant application, or anything that provides enough information about your invention that allows others with ordinary skill in the art to make or use your invention. Even discussions of the invention with others can count as a public disclosure if a CDA is not in place. As you speak to others about your idea, avoid disclosing critical and unique aspects of your idea or invention except under a CDA and then only after careful consideration of the necessity/value of making such a disclosure.

2) Search for filed patents or trademarks and for similar products or ideas. For both patents and trademarks, be aware of products or businesses that may be similar to your idea or business. Collect any information you find on websites, blogs, patents, or any other public resource and present them to your attorney. The information can help your attorney decide how to write the claims of a patent or whether to file for a trademark. Providing your attorney with the most comprehensive view of the closest prior art will allow her or him to draft your application such that you will more likely be able to overcome the prior art during prosecution.

   a. Patents: A “patentability search”, also referred to as a “prior art search”, is a comprehensive search for anything in the public domain (i.e. publications, patent applications and awarded patents) that is similar or may have some overlap with your idea or invention. The best way to begin a patentability search is to query key words that describe the idea or invention using Google Patents4. Through your Competitive Analysis (see the “Market Analysis” section), you should have a good idea of competitors and potentially similar products or businesses.

   b. Trademarks: If your trademark is a word or phrase, search the Internet for the word or phrase and similar combinations. In addition, search the USPTO Trademark Electronic Search System (TESS)5 for any registrations of the mark or phrase.

3) Plan your strategy. Before you speak to an attorney, be able to clearly and succinctly describe in writing your IP, whether an idea, invention, logo, etc. A clear outline of your invention and its novelty and non-obviousness over the prior art will enable a more efficient conversation with your attorney thereby potentially reducing costs associated with drafting, and down the road, prosecution of your patent application. Importantly, if you are not the sole inventor, be sure you confirm with your co-inventors what exactly needs to be protected.

4) Identify inventors. If you feel anyone else has contributed to your idea or inventions be sure to communicate to them your intention of filing a patent or trademark. Before speaking to an attorney, be certain of the people that should be included on the patent.

Most firms that specialize in patent filing employ patent agents. Although not attorneys, these individuals have technical specializations, are licensed to practice patent law, and can help you perform prior art searches or draft a patent at a fraction of the cost of an attorney. When you do decide to reach out to an attorney, carefully evaluate several attorneys on their specialty, background, price, reputation, etc. You should consider your attorney as a business partner that you will turn to not only as you establish your business but also as you grow your business.

Sue’s Story-Is my idea patentable? How do I gain access to university IP?
Sue has heard that a patent is an important way to get started on creating a business and recollects hearing about the Office of Technology Management (OTM) during orientation when she began her Post Doc some time ago. So, she decides to get in touch with the office. With the approval of the PI with whom she works, she contacts the OTM Director. She learns a couple crucial things:

4 Patent Search: www.google.com/patents
5 Trademark Search: https://www.uspto.gov/trademarks-application-process/search-trademark-database
i.) That her technology ideas may very well be patentable

ii.) That the process for determining if the University’s OTM will invest in a patent starts with her filling out and submitting an “invention disclosure”.

iii.) That it is preferred that this invention disclosure be filed well before (at least a few months prior) any publications (From a strictly legal point of view, patents can be filed in the US up to a year after the inventor first publishes the idea, however this strategy is risky since publication may stimulate others to file variants or improvements on the idea. If they file first the original inventor’s ability to get a patent – even on the original idea, may be constrained. Ex-US this one-year “grace period” is not available). Sue mentions that the publication process is pretty slow and so doesn’t see any problem. She mentions that “No, we haven’t even submitted to a journal yet. We are only doing poster sessions at this stage”. Her OTM contact points out that poster sessions at an open scientific forum are in fact “publication” and may preclude or interfere with the possibility of obtaining a patent. Sue checks her schedule and discovers there are about 3 weeks remaining prior to the first poster session.

iv.) Notebooks should be updated timely and eye-witnessed by someone who is not an inventor

Working with her OTM contact, Sue and the University’s patent counsel prepare a provisional patent application based around the planned poster presentation and a draft manuscript that she and her fellow inventors have prepared. She learns that this takes some of the pressure off and that she can now publish her idea. However, she also learns that she has only one year to “perfect” the provisional filing with her “non-provisional” patent application.

After the provisional is filed, Sue is able to negotiate an option to the patents filed by the OTM covering her technology with only a small dip into her savings ($1k). This gives her one-year to build the company, raise money, and begin R&D, while still negotiating the full license. Meanwhile the time-period to perfecting her patent application is also one year.

What are some additional Resources covering intellectual property?
The SBTDC at Warrensburg offers assistance with patents and trademarks; for more information on their services call (660) 543-4402 or visit https://missouribusiness.net/sbtdc/

For more information on IP Protection, please visit Kauffman Founders School webpage - http://www.entrepreneurship.org/Founders-School/Intellectual-Property.aspx
Team Building

What are the special challenges for building start-up teams?

One of the most important contributions a company founder makes to a successful start-up is to identify, attract engage and motivate great people to do the work of the company. This is a lot more of a challenge than most people might realize – even (or maybe especially) if they have had significant experience hiring people in traditional academic or industrial environments.

There are several aspects of team building in a start-up that pose special challenges:

- Working for a start-up entails significant risk – much more so than in most other human endeavors. By “risk” in this case we mean that the start-up will almost certainly struggle and the likelihood of outright failure is high. As a practical matter, this means that compensation for team members – especially cash compensation – will not be anywhere near as reliable as in a more established company or institution. Many otherwise qualified people simply cannot take on such financial risk.

- Because start-ups are generally thinly funded there is constant pressure to find ways to economize on everything – people, equipment, rent, you name it. Every potential dollar of expense must be squeezed until it becomes a quarter – or better, a dime. This means getting advice and services for free, working with borrowed equipment, outsourcing much of what is not truly strategic, shopping around for the best price on everything, and not being afraid to ask for deep discounts even off an already low price. People who come from large companies especially will find this “cheap, cheaper, can I get it for free?” culture challenging at first and many will never adapt.

- Start-up companies generally must be very flexible and evolve their business models constantly in order to adjust to changing trends and perceptions of customer market needs and the vagaries of financial markets. As a practical matter, this means that projects can be altered or cancelled with very little notice, people can be reassigned to new projects frequently and everybody is probably going to be responsible for several projects that must be frequently re-prioritized. As priorities change even basic responsibilities may need to be re-assigned – and such decisions must be made very rapidly. Most people’s work styles developed in Academia or Industry are not well adapted to a start-up situation that likely will frequently appear chaotic.

In short, it takes a very special person with a super strong work ethic, flexibility, good team skills and positive attitude to thrive in the start-up environment.

How can I overcome the team building challenges posed by Start-ups?

Every start-up business is different of course and the specific team-building approach will be dictated by many things – the nature of the technical challenge; the degree to which the work of the company can be “contracted out”; how much funding is available and other factors. So, the onus is ultimately on the founder to learn about and ultimately decide what is most important for the team being built. However, there are several general principles that apply and things you almost certainly will need to do.
How do I get started building my team?

Many of you reading this document will have lots of experience identifying, hiring and managing employees (including post-docs for you academics). However, finding the earliest team members for a start-up company is actually quite different from this experience in several important ways.

Most fundamentally, it is usually not wise to hire employees when first starting-up your company. Instead you want to identify, attract, engage and motivate highly experienced mentors, contractors and consultants as your early team members. This is mainly because the early challenges for a life-science company have a lot to do with setting technical goals that are responsive to clear business strategies and then putting together detailed technical plans to accomplish those goals. These tasks usually require seasoned people with lots of specifically relevant technical and high-level business skills. Generally extensive start-up experience (ideally both successes and failures!) is a must.

Such people are not easy to find, and generally don’t want to work as employees for a single company anyway – they may want to spread their expertise across many start-up companies. So, you must forget all about the standard ways to find “employees” and instead learn how to tap into the real expertise offered by relevant experts.

The only sure-fire ways to find such experts is to use your existing professional network AND to learn about and tap into the professional networks that exist (to a greater and lesser extent) in every entrepreneurial community. In St. Louis, we are fortunate to have access to many networking nodes for finding real start-up expertise. The BioGenerator Fundamentals program itself is such a node. You can find information about other nodes in the CET’s St. Louis Startup Ecosystem map, which is linked on page 60 (Getting Started of this guide).

As a founder of a start-up you need to be able to describe the basics of your business idea succinctly and clearly. (See page 8 for a tool called the Business Model Canvas to help you refine your idea. See page 56 for a brief discussion of “pitching” your idea, the link immediately above and pages 60 – 64 for lists of organization who can help you develop this crucial skill.)

Once you have your elevator and brief pitches down, you should first avail yourself of free advice from as many experienced people as will talk to you. With these people, it is very important to spend as little time as possible “telling” and as much time as possible listening. Use questions rather than statements whenever possible. Make it clear you are eager to listen and learn. As these highly experienced people develop confidence in you and your business idea they will usually be willing to introduce you to others who can help. This is the process of networking. You should make it a point to try to talk to 30 - 50 knowledgeable people about your idea – if you are talking to the right people this should allow you to start focusing in on people who can really help.

What roles will my early team members play?
The first people you should recruit through the networking process are called “Mentors”. These are people interested enough to be willing to devote considerable time to you and your idea for free. They should be generally knowledgeable about start-up businesses in your general area (therapeutics, diagnostics etc.) but by no means need to have deep technical knowledge. Mentors should be able to provide effective business advice and introductions to experts with deeper relevant sector expertise for you to tap.
The next category of people you will need to recruit to your effort is generally technical advisors. These should be technical experts in your field or a closely relevant field depending on where your business strategy needs to take you. These people will usually meet with you once or twice for free, but will eventually want to sell you their expertise (see discussion of equity immediately following this section). You should test the technical knowledge of these people carefully yourself first. Assuming you are initially satisfied, you should then carefully check their bona fides with your Mentors and with references. Don’t rely solely on references provided by the technical expert. You should ask for such references of course but the best kind of references are people you find yourself who are likely to know the person in question. When checking references be sure to check not only the candidate’s technical expertise, but also their experience and ability to work well in a start-up company. Once you have decided to move forward with a technical expert, try to agree on a limited project whereby you can check out their work without making a long-term commitment.

The last and most important recruit you should expect to make as a founder is your first “C” level team member. Most frequently, this is the Chief Executive Officer (CEO) or, in special circumstances, the Chief Operating Officer (COO). It is very important and wise to evaluate these people very carefully. In addition to taking all the steps above, it is important to check to make sure the CEO has extensive successful experience raising money. This person should also be able to specifically cite extensive experience building and leading an operational team. Don’t be shy about enlisting potential investors (along with Mentors and Technical Experts of course) in finding and evaluating this important recruitment candidate.

Once you have identified a CEO, see if you can arrange a trial assignment of some kind – a special consulting assignment that is crucial to the business but which can have specific deliverables and a near term endpoint is ideal. This way you can try out the CEO candidate prior to making this very important commitment. Once the CEO is on board, you should then expect to largely delegate further team building to this person but be sure they understand the extent to which you want to be kept in the loop as the team building progresses.

**Why and how should start-ups use equity as compensation?**

One fundamental principle of effective start-up team building is to use equity as compensation. This is crucial to the success of a start-up because cash is very difficult to come by and compensation with equity reduces the need to compensate with cash. Equity is also a good idea because it is a well-observed fact that people work harder, smarter, and more cooperatively when everybody has a significant stake in the outcome. Compensating team members with equity provides a powerful incentive to work hard and aligns the team towards shared goals.

There are three major forms of equity compensation in start-ups, each with its own advantages and disadvantages:

- **What is Founder Stock?** Common stock in the Corporation (or units in an LLC) are issued to the founders of the company based on an agreed ownership arrangement – usually best if the stock is distributed proportional to the value of the individual contributions prior to and up until the creation of the company. Frequently founder stock is also distributed in anticipation of future contributions from each individual founder (this can be problematic – see Disadvantages immediately below.)
  - Advantages: Conceptually simple, easy to document, creates a sense of shared purpose and fairness. Also, financial gain realized from the eventual sale of
common stock when the company is acquired or goes public are all treated at the “capital gains” tax rate which is generally lower than the tax rate on “individual income” – thus founders generally pay lower taxes on the value created by their company than they would on a corresponding amount of ordinary income.

- Disadvantages: Founder stock is difficult to “take back” (essentially impossible to take back without mutual consent). This can become a big problem if one of the founders is unwilling or unable to perform what was promised. (This problem can be overcome by putting a specific “vesting schedule” in place. This way the founders stock must be earned over time. If the majority of shareholders are dissatisfied with performance, they can alter or terminate the arrangement prior to the stock “vesting” (i.e. before it becomes the unencumbered property of the holder). This approach is strongly advised if founder stock is granted in anticipation of promised future performance.)

- Here is a link to a more detailed discussion of founder stock.

- **What is a stock grant/buyback program?** As discussed above, as a start-up gets underway it will be wise to work mainly with contractors, consultants and other team members who are not employees. Under the stock grant/buyback approach, shares of stock are granted for a very nominal fee to non-employee team members with the understanding and under a legal agreement that specifies the stock can be “bought back” at the same low price if there is lack of performance by a certain date (this buy back is also commonly called a “clawback” and is at the company’s discretion). The participants in a stock grant/buyback program can then file an “83(b)” election with the IRS, basically a letter that declares a low value for the stock thus granted. This very low value is treated as regular income but because the stock grant has low value it has low or no real tax impact.

- Advantages: Assuming the grantee does a good job and the stock is not bought back by the company, when the stock is ultimately sold, all the gains are taxed at the lower capital gains rate. In this case the grant/buyback program is a good way to avoid unattractive tax treatment for team members who are not company employees. In the case of poor or non-performance, it is simple for the company, at its sole discretion to “buy back” the shares at a nominal fee if the grantee doesn’t perform as promised. This protects the company from unnecessary financial dilution.

- Disadvantages: Can be difficult to explain.

- Here is a link to a more detailed discussion of 83(b) elections and stock grant/repurchase programs: stock grant/repurchase programs.

- **What are qualified/non-qualified stock option programs?** Once a company can afford employees, it is well advised to create a stock option program for employees. These are programs specifically created to incentivize employees. Qualified stock options (also called Incentive Stock Options or ISOs) are designed in such a way that they protect employees and the company from possible undesirable tax impacts and (usually) from potential disputes.

- Advantages: Incentivize and create goal alignment among employees. Additional option grants in a qualified option plan can easily be made to reward great performance and provide additional incentives without negative tax impact.

- Disadvantages: Complicated to initiate properly, must be carefully administered, difficult to explain to inexperienced employees.
Here is a link to a more detailed discussion of employee stock option plans, both qualified and non-qualified.

Compensation with equity is an essential part of most successful start-ups. However, it is a very complicated area, and it is very important to get it right because plans that are poorly conceived, managed and/or explained can quickly become demotivating, thus defeating their purpose. You are strongly advised to use your transactions attorney to put these kinds of agreements and plans in place.

**Accounting, financial documentation, and projections**

Through the course of your business life, your business will have many financial transactions. In fact, essentially every substantive action a company takes is recorded as a financial transaction in the accounting record. In this section, we will introduce the principles of accounting for some common activities including Financing, Investing, and Operating. We then illustrate how all these accounting activities are documented through Income Statements, Balance Sheets, and Cash Flow Statements. Finally, we work through an example of a financial statement for a company that is operational with step-by-step explanations.

**What accounting practices are relevant for financing activities?**

Having decided on a business idea, your top priority is to find money to create your business; this is also known as financing your business (also see “Financing” section below). Financing activities are transactions between business owners and investors (for example venture capitalists) and creditors (banks, equipment financing companies). Later in the life of a company, the company rewards its creditors by paying off loans with interest and its investors by paying a dividend to shareholders, or by arranging an “exit” (either an IPO or an acquisition) whereby the shareholders can sell their stock at a profit. Although you may be able to receive money through grants or gifts from family and friends, most business are started through debt or equity financing.

**Debt Financing - Liabilities**

Debt financing refers to cash (money) received from lenders in exchange for a commitment to repay principal at a specific future date, with a specific interest rate. A typical example of debt financing is receiving a loan from the bank. In accounting terminology, a loan is considered a “liability” because, like other forms of debt, must be paid back.

**Equity Financing - Owners’ Equity**

Equity financing refers to cash (money) received from an individual or from individuals in exchange for part or full ownership of the company. Individual(s) who own a portion of a company own “shares” of the company (or “units” in the case of an LLC). These shares entitle the owners to (but do not guarantee) potential payments (dividends – these are rare for start-up and early stage companies) and can increase in value as the company becomes more valuable ultimately creating an opportunity for shareholders to make a profit (by selling their shares at an increased price during an “exit” – this is by far the most common way for shareholders of early stage companies to benefit financially).

- **Contributed Capital** – The money contributions a business received from owner(s)/shareholders.
• **Common Stock** – is issued by the company to the Founders in return for their start-up efforts and for start-up cash. Common stock is also issued to Employees, Directors and Advisors in return for their efforts, either through a stock grant or, more commonly, through a stock option plan.

• **Preferred Stock** – is issued by the company to investors in return for their contributed capital. It is called “preferred stock” because it carries extra rewards and rights that are not offered to common shareholders.

**Convertible Note Financing**

• **Convertible Note** – debt that converts into equity. In this form of financing, an investor loans money to a company, and rather than get their money back plus interest, investors receive shares of preferred stock of the value of the loan, including accrued interest, at some future date.

**SAFE (Simple Agreement for Future Equity) Financing**

• An alternative to convertible notes, SAFE requires the negotiation of only one item “Valuation Cap” by both the company and the investors and allows money to be raised at very early stage. The investor and the company agree on the valuation cap, mutually date and sign a safe and the investor sends the company the investment amount. When the company decides to sell shares of preferred stock in a priced round, an outstanding safe will convert into shares of preferred stock. There is no threshold amount that the company must raise to trigger the conversion.

• Additional details on SAFE can be found here - https://www.ycombinator.com/documents/

**What accounting practices are relevant for investing activities?**

Once you have financed your business, your next priority is to invest the raised cash (money) in company assets. In accounting terminology, an asset is anything of value that can be converted into cash (i.e. sold). Examples of investing activities include the purchase (or sale) of:

• **Plant, Property and Equipment (PP&E)**, which are tangible assets with a useful life longer than one year, such as buildings, land, and machinery.

• **Intangible Assets**, which are not physical items but have monetary value (e.g. patents).

• **Marketable Securities**, which consist of financial assets, such as securities (e.g. shares) in another company.

**What accounting practices are relevant for operating activities?**

Once you have invested in the establishment of your business, you will need to manage the day-to-day operations: the **purchasing and selling of goods/services**. Consider a contract research company that purchases reagents and lab supplies and rents a laboratory for performing its research services:

**Purchasing Goods/Services**

The purchase of goods (e.g. reagents and lab supplies) or services (e.g. lab rental and utilities) takes place in one of three ways: cash, credit, or prepayment:

(1) A **cash purchase** is paid immediately at the time of purchase.

(2) A **credit purchase** is paid sometime after the purchase. Payments a business still owes to suppliers are called “Accounts Payable.”

(3) A **prepayment** to the supplier is paid before the purchase. Payments for which a business has not received the good/service yet, are called “Prepaid Expenses.”
Typically, if the contract research company is small and does not have a credit history, then it will have to pay immediately using cash or credit card to its reagent suppliers at the time of purchase (Type 1: cash purchase). For its utilities, the shoe making company will receive services one month and pay the following month (Type 2: credit purchase – also called “payment in arrears”), and for rent, the contract research company will prepay the landlord for using the laboratory for the coming month(s) (Type 3: prepayment).

Selling Goods/Services
Cash receipt from customers for the sale of goods (e.g. an assay kit) or services (e.g. a contracted experiment done by the company on behalf of a customer) also takes place in one of three ways: cash, credit or prepayment:

(1) A **cash sale** is payment received at the time of sale.
(2) A **credit sale** is payment received after the sale. Payments for a sold good or service that a business has not received from customers are “Accounts Receivable.”
(3) A **prepayment** from a customer is payment received before a good/service is provided. Payments for which a customer is still owed the good/service are “Advances from Customer.”

Small life-science business would prefer to operate by requiring a combination of prepayment and cash sales from its customers. (Note, credit card sales are considered to be cash sales since the business receives the cash immediately from the credit card company.) A typical pattern is some percentage (up to 50%) upon contract signing and the remainder(s) upon the completion of milestones and project completion. It is a fact of business life however that larger customers are slow payers (big pharmaceutical companies typically take 3 – 6 months to pay!) So, our Contract Research Company will likely have to make credit sales as a practical matter if it wants to have big, prestigious contracts from big companies.

**What financial statements will I need to understand and know how to prepare?**
All companies document the business activities listed above (and many other activities) using a combination of Financial Statements. These are the Balance Sheet, The Income Statement (also called the “Profit and Loss” statement or P&L), and The Cash Flow Statement (also called the “Statement of Changes in Financial Position”). These financial records are used by the company to assess its business activities and demonstrate the value and operation of their business to shareholders.

**How do I prepare a balance sheet?**
The Balance Sheet is a financial statement that summarizes a company’s assets, liabilities, and shareholder’s equity at a specific point in time. A company owns its assets and pays for them by borrowing money (liability) or selling ownership of the company (equity). This document is called a balance sheet because the assets must always balance out (equal) the liabilities and equity. These three balance sheet segments give investors an idea as to what the company owns and owes as well as the amount of money that has been invested into the company.
DEFINITIONS/EQUATIONS

Assets = Liabilities + Shareholders Equity

- Asset: an economic resource owned by a business expected to benefit future operations
  - Accounts receivable (A/R): money that is owed to a business but not yet received
  - PP&E: Property, plant, and equipment
  - Inventory: goods/materials a business holds for purpose of selling in the future

- Liability: payment promise to be fulfilled in future time periods: in service, products, or cash
  - Accounts payable (A/P): money that a business owes to someone that has not yet been paid

- Equity: owner’s claims to, or interest in, the business entity’s assets
  - Capital accounts: shareholders, members
  - Retained earnings: portion of a company’s net earnings that it doesn’t pay off to shareholders as dividends, but rather uses to reinvest in the business or pay off debts

How do I prepare an income statement?

Also known as a Profit and Loss (P&L) Statement, an Income Statement documents a company’s financial performance over a specific accounting period. The financial performance is assessed by summarizing a business’ revenues and expenses through operating, financing, and investing activities described above. The income statement shows the net profit or loss incurred over a specific period (e.g. fiscal year, quarter, month, etc.)
DEFINITIONS / EQUATIONS

Revenues – Operating expenses = Operating P/L

- Revenue: results from sale of products or services
- Expense: goods, materials, or services purchased & USED within the current period. Purchases not used in the period may be INVENTORIED or CAPITALIZED and are not included in the Income Statement.
- Variable Costs: are costs incurred when a unit of product or service is produced (e.g. labor or materials) and which increase in strict proportion with the number of units made. For example, if one hundred milliliters of reagent are needed for one assay kit product, the variable reagent cost is the cost of one hundred milliliters of reagent. The variable costs incurred by a company are reported in the P&L as either COGS: costs of goods sold or COSS: costs of services sold
- Fixed Costs: are costs that are not dependent on the number of products or services produced. For example, the monthly rent does not change whether a kit producer makes one assay kit or 100 assay kits.
- Other income/expenses not related to primary business operations: sales of assets, interest earned, interest paid, taxes, depreciation, and amortization.
- Gross Margin/Profit = Revenue – variable costs
- EBITDA: Earnings Before Interest, Tax, Depreciation, and Amortization

How do I prepare a cash flow statement?
A document showing aggregate data regarding all cash inflows a company receives from its ongoing operations and external investment sources, as well as all cash outflows that pay for business activities and investments during a given quarter. It is important to keep track of
operating cash at minimum on a monthly basis in order to see positive, break-even, and negative (underfunded) operating cash periods, and also not forgetting about accessible cash from your PP&E if you borrow against it. This allows you to see if you are able to accomplish goals requiring cash (i.e. pay bills or “make payroll”/pay employees)

\[
\text{Beginning Cash} + \text{Sales} - \text{Operating Expenses} = \text{Net Cash} -/+ \text{Capital Expenditures} = \text{Net Cash Balance}
\]

Sue’s Story: How should I handle accounting and financial projections?

For bookkeeping Sue has been using Quickbooks to track all expenses. The software, when kept up to-date, can produce any required financial report on demand. Sue has also enlisted an accountant from BDO to help her onboard Quickbooks and manage her taxes. With these steps, Sue feels confident about tracking current finances for her startup. But, she has learned she is expected to prepare projections of financial documentation before engaging in fundraising efforts. She decides to begin this fairly daunting task by working backwards, deciding the ideal exit point she sees for the company and her investors and then describing what needs to be done to get there.

After some online research on other how other cancer drug development startups where able to provide value to their investors and founders she has discovered that therapeutic products have to go through a very rigorous and expensive development path – dictated and closely monitored by the FDA – in order to get to market. She reads articles from the Pharmaceutical industry suggesting that the cost to get a product all the way to market can be over $1 billion!

To Sue, this number seems well out of the realm of possibility for her tiny company. In discussing it with her business mentors, she learns that indeed the cost to develop a product all the way through FDA approval is well beyond the fund-raising ability of a small company like hers. Fortunately, her advisors are able to explain that the vast majority of the costs to develop

<table>
<thead>
<tr>
<th>OPERATING ACTIVITIES</th>
<th>Year Ended December 31, 2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash from Customers</td>
<td>180</td>
<td>200</td>
<td>900</td>
</tr>
<tr>
<td>Cash to Suppliers</td>
<td>5</td>
<td>(65)</td>
<td>70</td>
</tr>
<tr>
<td>Cash to Employees</td>
<td>500</td>
<td>(500)</td>
<td>(500)</td>
</tr>
<tr>
<td>Cash paid in Interest</td>
<td>40</td>
<td>(40)</td>
<td>(45)</td>
</tr>
<tr>
<td><strong>Cash Flow from Operations</strong></td>
<td>725</td>
<td>(405)</td>
<td>425</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>INVESTING ACTIVITIES</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>PP&amp;E Purchases</td>
<td>0</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td><strong>Cash Flow for Investing</strong></td>
<td>0</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FINANCING ACTIVITIES</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equity Financing</td>
<td>5</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>Loan/Mortgage Financing</td>
<td>20</td>
<td>28</td>
<td>65</td>
</tr>
<tr>
<td>Paid Dividend</td>
<td>0</td>
<td>(6)</td>
<td>(12)</td>
</tr>
<tr>
<td><strong>Cash Flow from Financing</strong></td>
<td>25</td>
<td>30</td>
<td>68</td>
</tr>
</tbody>
</table>

| Net Cash Flow        | 750  | (325)| 593  |
| Beginning Balance of Cash | 0    | 750  | 425  |
| Ending Balance of Cash | 750  | 425  | 1018 |

Table 7: Company ABC’s Cash Flow Statement
a therapeutic product occur in late stage clinical trials designed to demonstrate efficacy and safety to a very high degree of statistical certainty – these very expensive trials are called “Phase III Clinical Trials”. In the vast majority of cases, start-up drug development companies need to take their product only into early stage human clinical trials – usually up to some point in “Phase II Clinical Trials” – greatly reducing the costs they have to cover, and then sell the product (or company itself in the case of a “one product” company) to a large pharmaceutical company who is willing to take over development from that point forward. She learns that large pharmaceutical companies now rely to a very large extent on small companies to do the early stage research, their product “pipelines” are worryingly thin in many cases, and are very willing to pay handsomely to acquire products (or companies with products) that successfully demonstrate early efficacy and safety in humans.

Based on this input, Sue decides the most attractive exit strategy for her startup is to develop a few lead drug candidates against her target, perform some initial toxicity and animal efficacy trials, complete “Phase I” trials (these test the drug in healthy volunteers), move into “Phase II” trials (where the drug is tested in actual cancer patients) and then sell the drug and IP to a larger biopharma company that can complete the Phase II and Phase III trials and launch the product. In this way, she is able to cut down on the total amount of money she needs to raise and time it will take before she can provide a return to investors.

### How do I make expense projections?

So, to develop projections of what her financial documentation will look like in the future Sue decides she first must decide how much money will be required before she can reach her target exit. She notes that 3 cancer drug startups that exited at her target point of development (these are referred to as comparable exits) spent a total of $25-$50M on development prior to sale. With these numbers in mind she begins to think through how much money, and how many employees she will need to get the point of development she is targeting (Develop a screening assay, identify leads, optimize leads, initial tox screen, animal data, human trials). She comes up with the headcount projection below, and then combines these estimate with the $25M-$50M she knows others have spent to develop the expense projections that follow with the assumptions used in those projections.

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CEO</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>COO</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>1</td>
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</tr>
<tr>
<td>CFO</td>
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<td>-</td>
<td>-</td>
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<tr>
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<td>1</td>
</tr>
<tr>
<td>Scientific Operations</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lead Scientist (Mgr.)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Research Assoc.</td>
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<td>4</td>
<td>6</td>
<td>10</td>
<td>18</td>
<td>25</td>
</tr>
<tr>
<td>Biz Dev and Marketing</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biz Dev Manager</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Biz Dev Ascc</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>3</td>
<td>3</td>
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<tr>
<td>Financial</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Accountant</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<td>Administrative</td>
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<td></td>
</tr>
<tr>
<td>Human Resources Mgr.</td>
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<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Operations Mgr.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total Staff</td>
<td>3</td>
<td>8</td>
<td>11</td>
<td>21</td>
<td>31</td>
<td>38</td>
</tr>
</tbody>
</table>

Table 8. Headcount Projections
Equipment costs assume initial lab startup costs, a spike in 2018 when the group moves from an accelerator to their own lab space, and then estimates ongoing expenses.

Bulk Assay Components first two are based off of expected expenses, moving forward they are estimated at $300,000+ $50,000 per scientist.

Legal services through general counsel estimated at $20,000 for the year. IP costs are estimated at $75k per expected patent, plus an additional 10% per headcount.

Rent-expansion planned in 2018.

Insurance estimates are based upon a conversation with insurance agent at AHM Insurance.

Marketing/Fundraising expenses are website maintenance, marketing materials at conferences/etc., as well as costs related to fundraising opportunities (application/presentation fees, travel, etc.). I have estimated total of $15000 split over 12 months for the Seed B round, plus 4 people attending a conference at $12000 total.

Consultants will be FDA, grant writing, etc.

Personnel is based on headcount projection with an increasing average salary over time.

Sales/Admin is printing supplies, dues/subscriptions to online services, office supplies, etc. Estimates increase based on headcount.

Taxes are estimates from accountant.

Having completed the financial projections through Phase II, Sue is pleased to see that her detailed “bottom up” cost projections of just over $28 million have ended up being at the low end of the range of costs her literature searches and secondary research tell her they should be. So, this is going to be easy, she thinks – we just have to raise the money and do the research. She decides to raise $30M to fund her company. (Note, this line of thinking is continued as Sue refines her expense needs during the financing chapter of this roadmap.

How do I build a Revenue Model?

Sue learns from her advisors that she must create a “revenue model” for her company. This seems kind of silly to her – how can she be expected to project sales for a product that is at

Table 9. Expense Projections

<table>
<thead>
<tr>
<th># of Employees</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equipment</td>
<td>$250,000</td>
<td>$500,000</td>
<td>$750,000</td>
<td>$500,000</td>
<td>$500,000</td>
<td>$500,000</td>
</tr>
<tr>
<td>Bulk Assay Components</td>
<td>$150,000</td>
<td>$435,000</td>
<td>$990,000</td>
<td>$1,325,000</td>
<td>$3,350,000</td>
<td>$7,000,000</td>
</tr>
<tr>
<td>Legal/IP Services</td>
<td>$70,000</td>
<td>$126,000</td>
<td>$138,600</td>
<td>$152,460</td>
<td>$167,706</td>
<td>$184,477</td>
</tr>
<tr>
<td>Rent</td>
<td>$5,000</td>
<td>$5,000</td>
<td>$25,000</td>
<td>$25,000</td>
<td>$25,000</td>
<td>$25,000</td>
</tr>
<tr>
<td>Insurance</td>
<td>$5,000</td>
<td>$5,000</td>
<td>$15,000</td>
<td>$15,000</td>
<td>$15,000</td>
<td>$15,000</td>
</tr>
<tr>
<td>Marketing/Fundraising</td>
<td>$2,250</td>
<td>$2,250</td>
<td>$50,000</td>
<td>$60,000</td>
<td>$72,000</td>
<td>$86,400</td>
</tr>
<tr>
<td>Consulting</td>
<td>$5,000</td>
<td>$25,000</td>
<td>$37,000</td>
<td>$55,500</td>
<td>$83,250</td>
<td>$124,875</td>
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<tr>
<td>Personnel</td>
<td>$195,000</td>
<td>$520,000</td>
<td>$825,000</td>
<td>$1,575,000</td>
<td>$3,255,000</td>
<td>$3,990,000</td>
</tr>
<tr>
<td>Sales/Admin/BOD</td>
<td>$1,200</td>
<td>$10,368</td>
<td>$14,515</td>
<td>$20,321</td>
<td>$28,450</td>
<td>$39,830</td>
</tr>
<tr>
<td>Taxes/Accounting</td>
<td>$5,000</td>
<td>$5,000</td>
<td>$10,000</td>
<td>$10,000</td>
<td>$10,000</td>
<td>$10,000</td>
</tr>
<tr>
<td>Monthly Total Spend</td>
<td>$688,450</td>
<td>$1,633,618</td>
<td>$2,855,115</td>
<td>$3,738,281</td>
<td>$7,506,406</td>
<td>$11,975,581</td>
</tr>
</tbody>
</table>

Table 10. Revenue Projections
least 8 years from FDA approval and marketing and which will be ultimately developed (from Phase II on) and marketed by an acquirer? Having by now become an effective company founder, Sue makes some reasonable guesses about what the future revenue projections should look like. She starts with the total population of “triple negative” breast cancer patients she discovered from her market research. She then adjusts this amount by year to account for the projected growth of this patient population. She then makes some assumptions about her “Market Penetration” (what share of the market she expects her eventual acquirer will attain) estimates the “Price” of a course of therapy with the product, and then multiplies these variables to obtain a projection of “Total Revenue”. Knowing that the average “Cost of Goods” in the pharmaceutical industry is about 5% she can calculate “Cost of Goods” for her product and then subtracts this number from Total Revenue to obtain the “Gross Margin” for her product. She then makes some ballpark “Marketing and Sales Expenses” and finally arrives at the “Product Margin” (also called Product Contribution) which is the relevant number a big company acquirer might look at to evaluate her product as an acquisition target.

**How do I generate a Discounted Cash Flow?**

1. **What is a Discounted Cash Flow?**
A Discounted Cash Flow (DCF) is a valuation method used to estimate the intrinsic value of a company. Investors commonly use it estimate what a company may be worth today (present value) based on how much money it may make in the future (cash inflow) and how much money it will lose (cash outflow) before it becomes profitable.

For example, let’s say an inventor has a small molecule candidate that shows promise as a cancer therapeutic. The small molecule candidate works great in cell culture experiments. If it becomes a blockbuster cancer drug, then it could be worth billions of dollars. However, there are several **risks** to overcome before the small molecule candidate becomes a market-approved drug:

- Successfully complete animal studies,
- Successfully complete all three phases of FDA human clinical trials,
- Receive FDA approval,
- Achieve reimbursement from private and government insurance, and
- Successfully compete in the marketplace.

All of this is **highly risky and very expensive**. To determine today’s value of this potential billion-dollar drug, when it is still risky and unproven, investors frequently use a DCF model. It is necessary to not only project how much revenue the drug earns (cash inflows), but also the operating, development and commercialization expenses of the drug (cash outflows) over time. The investor nets these future cash inflows and outflows, and then “discounts” them back to a value today (present value), using a risk factor that accounts for the possibility of failure. They then typically use the DCF approach to sensitize several different scenarios to get a feel for the risks, vulnerabilities and revenue opportunities confronting a company in different hypothetical futures. The DCF model is a major tool used by investors to think systematically about their ultimate goal – a healthy “Return on Investment” (ROI).

2. **Why do we want you to make a DCF?**
Drafting a DCF is a great way to get a sense for whether your business is financially feasible. Plenty of brilliant scientific ideas don’t necessarily make great products – for example, sometimes the cost of bringing them to market is much higher than the revenues the product could ever generate. It’s also a useful tool to get a reality check on how long and how expensive it will be to bring your idea to market. Perhaps most importantly, when done right, it will force
you to think through your business idea at very granular levels – especially around those variables, inputs or assumptions that have a big impact on ROI.

3. How do you create a DCF?

1) **Develop a Corporate Timeline.** Firstly, develop a corporate timeline. Determine the key milestones of your business and how long it will take to achieve each of these milestones in order to launch your product.

2) **Create a Pro-Forma Income Statement.** Leverage the corporate timeline to forecast the operating revenue (cash inflows) and expenses (cash outflows) of your business on a yearly basis. The forecast period for this Income Statement (aka Profit & Loss statement or “P&L”) will likely extend for 10 years or more. You can learn more about income statements in this introductory tutorial about financial statements [here](#) (note: this tutorial also includes lessons on the other essential financial documents for business - cash flow statements and balance sheets. You don’t need to worry about them for this exercise). Because you are pre-revenue startup, your projections will be an estimate of what your revenue and expenses might be in the future. Some advice on financial projections can be found [here](#). A good rule of thumb is to project the Income Statement for three years beyond the point at which the product reaches peak revenue.

You will need to provide estimates for the following components of your income statement:

- **NET SALES (REVENUE)**
  - Determine your market size.
    - How many people could benefit from and would want to buy your product?
    - Estimate what fraction of that market you think you can capture each year.
      - Are there competitors or similar products on the market already?
      - What fraction of the market do they capture?
      - How much revenue do they generate per year?
  - Does a distribution partner take a percent of sales?

**NOTE:** It is normal to not generate revenue while you complete product validation studies, clinical trials, etc.

- **COST OF GOODS SOLD (COGS)**
  - What raw materials or reagents are needed for each unit of your product sold?
  - What labor costs are directly involved in making your product or administering the service you provide?
  - Will you need to contract with a manufacturer, and what will they charge?

Include all costs that are involved with directly creating the product or service that you sell.

- **SALES, GENERAL, AND ADMINISTRATIVE COSTS (SG&A)**
  - These will include the other costs involved in running your business. Include costs like:
    - Rent, support staff salaries, and executive salaries.
  - Importantly, think about how much market capture you’re projecting in your revenue line, and think about think about how your company will realistically generate that revenue (called the “Customer Acquisition Strategy.” Each of the following steps in
the Customer Acquisition Strategy comes with a cost (overall called the “Cost of Acquiring a Customer” or CAC)

- How will you make customers aware of your offering?
- At what point will you transition from Advertising and/or Digital Marketing to Personal Selling (i.e. with a sales representative)?
- How will you determine when they are interested enough to evaluate your offering?
- What tools will you give them to make this evaluation?
- Will you offer a sample or free trial in order for the customer to get comfortable with your offering?
- Who will keep the customer on task as they make the buying decision?
- Who will close the sale?
- Who will follow-up for repeat sales?

❖ **RESEARCH & DEVELOPMENT**

➢ How much R&D will you have to do?
➢ What will FDA trials cost?
➢ Are you relying on patent protection as a barrier to entry by competitors? If so, don’t forget to include patent costs or licensing fees/royalties.

❖ **EBITDA**

➢ To calculate EBITDA (Earnings before Interest, Taxes, Depreciation and Amortization), subtract COGS, SG&A and R&D from Revenue. Most start-up companies only need work through the details of the P&L down to the EBITDA, so for this exercise you can stop here.

3) **Calculate Net Present Value (NPV).** This can be a challenging concept to a first-time entrepreneur. If you would like to try this yourself, use the resources below to familiarize yourself with the concepts and calculate your NPV (Excel has a formula that can help you). Try changing some of your input parameters – what business decisions can increase your company’s value? If this is difficult, we can help you with this step once you’ve gotten your EBITDA projections finished.

- Investopedia: Present Value
- Investopedia: Net Present Value and the Internal Rate of Return


**What are some additional resources covering accounting and financial documentation?**


Financing your startup

What is a “Pitch”?
Now that your company is formed, your idea is validated, and your business idea is refined, it is time to raise money (“capital”) to support your operations. Before you begin meeting with potential sources of financing however, it is very important to develop a few context-sensitive “pitches” for your idea. In most cases you will be fine at explaining the details of your technology and business (otherwise you cannot succeed). **This is NOT what a pitch is for.** Explaining in detail comes much later in the process. The purpose of a pitch (regardless of length) to get someone intrigued enough with your business idea so that they agree to take the next step – first to get more information, eventually to invest. Suffice it to say that you will need an “elevator pitch” (less than 90 seconds) for networking events and chance encounters, an intro pitch (10 – 15 minutes pitch supported by a well-designed slide deck) for investor conferences and meetings and a detailed pitch (30-minute talk plus extensive prepared Q & A both supported by a well-designed slide deck) for invited investor meetings. Pitching your idea to investors (and to new team members for that matter) is a refined skill and cannot be effectively taught in a document like this. Fortunately, there are MANY organizations in St. Louis who can help with your pitches. It is a great idea to develop and practice your pitch with people who don’t know much of anything about your technology area. (Please see pages 58 – 62 for resources who can help with your pitches.)

What are the different ways of financing a new company?
New companies can be financed in different ways. Depending on your business goals and corporate structure (i.e. LLC, Corporation, Nonprofit, etc.), you may favor one funding source over another. In this section, we cover the different ways of financing a new company, the different groups of people or institutions that provide funding, and specific funding opportunities in St. Louis available to those completing the Roadmap with details aimed at helping you develop a strategy for raising your first funding round.

New and growing companies support their businesses through grants, debt, convertible notes, equity deals, crowdfunding, or “Impact” Investment.

**Grants** – An attractive way to finance your company is by federal, state, or private grants because, like the BALSA Foundation Entry Fund and the ARCH Grant program, grants are awarded without requiring any equity/ownership, in your company, or that the grantor is paid back over time. Most private and government grant funding sources award money with few strings attached other than requiring mandatory monthly, quarterly, or annual progress reports. Some grants are focused on certain industries, types of companies, or problems that need solving, while others are more general. Grants can take the form of a one-time award, milestone-based distributions, or as free professional services, also known as in-kind donations.

An important form of Grants for life science entrepreneurs is the Small Business Administration’s “SBIR” (Small Business Investigational Research) and “STTR” (Small business Technology Transfer Research) programs. These programs were created through a federal statute that requires all US government agencies that perform research to invest 3.5% of their research budgets with small companies (defined as < 500 people. In practice, very small companies with < 3 personnel can qualify). All the agencies thus affected solicit, evaluate, score and grant applications according to their own criteria and process. The agencies that are most important for the life sciences are:
The National Institutes of Health (omnibus and various agency solicitations)
The National Science Foundation
The Department of Defense (various branches have their own programs).

The SBA program grants are generally phased as follows:
- Phase I – up to roughly $225,000 (varies by agency)
- Phase II – up to roughly $1,500,000 (varies by agency)
- Fast Track – in order to streamline the application process, a fast-track application specifies
  the detailed research plan and specific success criteria for Phases 1 and 2. (The availability
  and specifics of this approach varies somewhat by agency).
- Phase IIb – $1 million per year for three years.

This source of non-dilutive funding is so important that the BioGenerator Fundamentals
program offers specialized training for these grants. The training covers the needs of all
relevant agencies) and – in select cases – one-on-one application coaching. Contact the
BioGenerator Fundamentals Program Director for details.

Debt – A loan, the primary means of acquiring debt, is a lump sum of money that must be
repaid with additional interest over a future period, or term. The interest rate charged is an
important feature of debt financing and usually reflects the level of risk the lender is willing to
take. Most lenders will require the following when assessing and giving a loan:
- Business Plan: Most lenders will utilize a business plan to assess the business
  opportunity. We have been advised a 3-5 pages document is sufficient, it must cover a
  description of the business, a marketing plan, financial projections, and funding
  requirements. Avoid “fluff,” technical jargon, and grammatical errors.
- Personal Financials: Most will require 3 years of personal tax returns and a personal
  financial statement
- Adequate Down Payment: 10-20% of loan for most lending institutions
- Collateral: If a business requesting a loan does not have collateral (e.g., land, buildings,
  equipment), the lender may ask for personal assets to be pledged as collateral.

Other debt opportunities do exist for those that can meet the above requirements from
traditional lending opportunities. For instance, “microloans,” are specifically focused on those
not able to qualify for traditional loans. Microloans are offered locally from groups such as
Justine Petersen. Given the risk profile of most life science innovations, traditional debt is
only available to start-up life-science companies under very unusual and rare circumstances.

Convertible Notes – One way of soliciting funds for your company is to accept money today
with the possibility of providing equity/ownership in your company at some future, mutually
agreed upon date. Through a convertible note, an investor can lend money to a company and
rather than getting their money back with interest as is the case with a traditional loan, the
investor has the option of receiving equity in the company. The company provides a ‘note’ in
exchange for the initial investment money, which a few years later, when the company
receives more significant funding, ‘converts’ into company ownership. Typically, in a
convertible note the investor is guaranteed a lower price per ownership unit because of her or
his willingness to invest in the early days of the company when the risk of failure is the
highest. The advantage to the company is that they do not have to put a value on the
company, determine how much ownership to give away per dollar invested, until a future time
point when calculating such a value should be less speculative. This streamlines what could
otherwise be a protracted and unnecessarily expensive transaction. This funding mechanism
is popular for pre-seed and seed stage investments because the extra time, expense and
potential for stalled negotiations to agree on a “valuation” for the company is considered a
waste of time until the company is sufficiently advanced to be comparable to a wide range of other deals in the relevant market. It is very rare for investments later than seed stage. In fact, most convertible debt is “converted” immediately after the seed stage, at the initiation of funding round “A”.

**Equity Investments** – A straight equity deal occurs when an investor exchanges money for an ownership interest in the company. The investor essentially purchases a portion of the company. The amount of equity the investor receives will depend upon the agreed upon monetary value of the company – this “valuation” is an important part of the negotiation for an equity investment. For example, let’s assume a start-up company wants to raise $500,000 to complete a proof of concept study and that they have an interested investor. In this case, the investor and the company have agreed that prior to the new investment the company is worth $1,000,000. In this scenario, the “Pre-money Valuation” of the company is said to be $1,000,000 and the Post Money Valuation would be $1,500,000.

**What are the different Classes of Stock?** – In the example immediately above, if the new investor is willing to take “common stock” (i.e. the same class of stock owned by the founders of the company) in return for the investment, then the ownership post money will be Founders 2/3s, new investors 1/3. In reality, however, most investors are not content with common stock and in fact require certain preferences in order to invest. In this much more usual case the investor receives “Preferred Stock” and the agreements that document the investment specify what these preferences are. The two monetary preferences most commonly seen in preferred stock deals are (but are no means limited to):

- **Liquidation Preference** - a liquidation preference requires that upon company liquidation (i.e. when the company is acquired) the preferred stock holders receive some multiple of their money back before the common stock holders receive any compensation. In the current funding environment, the multiple for a liquidation preference is typically 1X but it can be higher depending on the vagaries of supply and demand. So, to extend our example above, let’s assume the company is successful in accomplishing its Proof of Concept experiment and negotiates an acquisition for $3.5 million. In the case of a 1X liquidation preference, the preferred shareholders would collectively receive $1.5 million (a 1X liquidation = $500K plus 1/3 of the remaining proceeds = $1M) and the founders would receive $2 million (2/3 of the remaining proceeds after the liquidation preference is paid).

- **Down Round Protection** – This preference provides some protection for the preferred stockholders from the financial impact of a negative impact on a company. Extending our previous example, let’s assume that an additional $100K turns out to be necessary in order for the Company to meet its Proof of Concept. For clarity let’s assume the new $100K is raised from a new investor but because management was unsuccessful in attaining its goal of completing the POC with the original investment, the new investor will only accept a (new) pre-money investment of $1.1 million (NB, a “down round” compared to the “post money valuation” of $1.5 million from the first investment. There are at least two kinds of down-round protection: Full Ratchet and Weighted Average. In Full Ratchet protection, all of the current preferred stock holders would get the value of their shares re-stated to the price per share enjoyed by the new investor. As a practical matter in full ratchet down-round protection, the full impact of the $400K “down round” would fall on the shoulders of the founders (i.e. the common stock holders), and the preferred stockholders would be getting the same economics as the new investor. In Weighted Average down round protection, the current preferred shareholders would be issued additional stock proportional to their contribution to the combined amount from both rounds, in this case 4/5s. As a practical matter, the current preferred shareholders share some fraction of the
impact from the down round (in this case, they would take an $80K “haircut” and the founders would take a $320K “haircut”.

- Non-monetary preferences – In addition to the monetary preferences exemplified above (there are several other forms of monetary preferences that may be encountered by the way), preferred stockholders typically obtain some control over the company through voting requirements and restrictive covenants. In the example cited in this section, the preferred shareholders only control 1/3 of the voting stock of the company and therefore do not technically have majority control (traditionally defined as 51% or more of the voting stock). However, the restrictive covenants traditionally required by preferred investors specify that all crucial decisions (hiring or firing of key personnel; changing strategy; spending large of sums of money over some maximum; partnering agreements; additional fund raises etc.) require a majority approval of the preferred shareholders. This effectively gives preferred investors control over most important decisions as a practical matter.

Crowdfunding – Raising money from the general public over the Internet is referred to as crowdfunding. Crowdfunding campaigns typically leverage the internet to access millions of people and can take four forms: 1. reward-based which offer tangible incentives for funding, typically a promise of receiving the product made by the company; 2. donation-based which ask individuals to part with their money for nothing in return; 3. lending-based which is paid back over time; and 4. equity-based which can offer equity for financing (the legal aspects of this last mechanism are not finalized, however).

**Which type/s of financing should I pursue for my startup?**

No matter whether a company (commercial, nonprofit, or hybrid) is developing a new medical device, providing beauty and hair services, or supporting efforts to combat domestic violence, all businesses go through rounds of fundraising. Depending on the business and how soon it can begin generating revenue, the company may only need to go through one round of fundraising. In the examples above, a medical device company will need to raise millions of dollars through many funding rounds to be able to pay for the research and development needed to create the device. A nonprofit with a mission to support reductions in domestic violence continuously finds funding to support its operations while a new salon may only need to go through one round of funding to raise enough money to purchase or lease building space and salon equipment.

Since grants are awarded without taking any portion of the company, every new business should consider soliciting grant funding from federal, state, or private institutions. Since some grant agencies have very specific requirements and only fund companies with specific characteristics, it can be challenging to find a grant source that matches a company’s mission, business model, or developmental stage.

Although there are no rules for fundraising, new companies typically fall into three categories depending on the business type (for-profit vs. non-profit) and business stage (time until first customer):

1. **Non-profits** – Organizations that have charitable or educational purposes are known as non-profits. Non-profits typically do not have owners and therefore cannot issue stock in exchange for an equity deal or convertible note. To finance the organization’s operations (e.g. office space, salaries, programming budgets), non-profits continuously raise money through donations from the public, through grants from private charitable organizations, and through grants from government agencies.
2. **Early Revenue Business** – Some newly founded business can quickly begin generating revenue from customers because they do not require significant resources to become
established. Businesses that provide a service (e.g. childcare, hairstyling, free-lance photography, legal advice) or that provide a readily available good (e.g. food trucks, restaurants, candy shop) generally under go one round of financing to purchase equipment, rent office space, and pay salaries before becoming revenue positive. These businesses should pursue grant and debt financing.

3. Late Revenue Business – Some businesses will need to raise money over the course of several years because they require significant funding and time to develop their product. Biotechnology companies, for example, may spend over 5 years researching and developing a biomedical device or drug and, therefore are years away from generating revenue or returns. These types of companies typically pursue all the funding types above but debt financing.

**Model Legal Docs for VC backed funding:**
The National Venture Capital Association (NVCA) provides model legal documents that can be used as a starting point in venture capital financings. Their aim is to reflect “best practices” and avoid hidden legal traps. This, in turn, reduces the time and effort for investors, management teams, and attorneys. Additional details can be found here. The original docs saw some changes in March 2018 which can be accessed here (Registration required).

**Who types of organizations provide financial support for startups?**
The following funding types could provide you with your first round of financing, typically anywhere from $10,000 to upwards of $500,000 depending on the source. Although more funding sources exist for more established companies (e.g., Venture Capital) and various organizations provide various types of financing, we focus on the people and organizations you should target first, specifically, government agencies, non-profit organizations, business competitions, friends and family, and angel investors. Examples, specifications, and instructions for applying to these funding sources are found in the following section.

**Government Agencies** (Grants, Debt) – State and federal governments have various funding programs that aim to spur economic growth by encouraging entrepreneurship. Some government entities serve as microlenders and offer small loans. Many, if not most, require attendance at regular meetings and mandatory business education programs before applying for loans. Perhaps most significant for Life-Science companies are the Small Business Innovation Research (SBIR) and Small Business Technology Transfer Research (STTR) programs.

**Non-profit Organizations** (Grant, Debt) – Many non-profit organizations provide grants or loans to individuals wanting to start a business or to individuals who have already started a business. Some non-profit, however, have specific requirements to the types of businesses or people that are eligible.

**Banks** (Debt) – Small business loans are a great mechanism for businesses that expect to generate revenue quickly to get off the ground. Banks, however, will often require a down-payment and individuals to provide collateral in return for a loan in case the individual defaults. An individual’s personal assets (e.g., home, car, property) are typically used as collateral.

**Business Competitions** (Grants, Convertible Notes, Equity Deals) – Business plan competitions provide financial support to early-stage companies that they believe will be successful. Most competitions request a fairly detailed business plan describing the company
and product as well as other details demonstrating a potential for business success. Competitions can be focused on a specific industry or industries and almost always have specific eligibility requirements. For example, a competition may require applicants to be affiliated, be at a certain developmental stage, or limit how funds can be used. Competitions typically award grants, either as a sum of money or in-kind services, and/or convertible notes.

**Friends/Family** (Debt, Convertible Notes, Equity Deals) – Friends and family who believe in an entrepreneur’s idea and potential success could provide initial funding. Friends and family could provide a loan to be repaid at a future date, issue convertible notes, or request equity in exchange.

**Angel Investors** (Convertible Notes, Equity Deals) – Angel investors are high net worth individuals wanting to invest in companies at their earliest stage with the hopes of receiving returns in the future. Generally, angels need to be accredited investors, meaning they have a net worth of at least $1 million and an annual income of $200,000 individually or $300,000 jointly with a spouse. Angel investors normally work in groups, or syndicates, in which they pay a membership fee to have the opportunity to invest. Generally, individual angels invest $25,000 and up into each company through convertible notes or equity deals. Although angels typically invest in any industry, individuals can have preferences for a specific industry, typically one they know well.

**What funding organizations are there in Missouri and St. Louis?**

**Getting Started** – The Center for Emerging Technologies (CET) has created an overview of the St. Louis startup ecosystem with information about mentoring, workspace, and funding resources in the St. Louis area. [Click here for their ecosystem slides](#); a map of the ecosystem can be found on slide 10.

**Government Agencies** – Each federal, state, or city funding program have their own applications process. They can be grants, debt (loans), or a mix of various types.

St. Louis County Economic Council Loan Programs – A number of loan opportunities are available from St. Louis county, for example: The Metropolitan St. Louis Loan Program, Minority/ Disadvantaged Contractor Loan Guarantee, Recycling Market Development Loan Program, SBA 504 Loan Program and Minority & Women’s Pre-Qualified Loan Program

**Eligibility:** For each of these programs, the individual must live and conduct business in St. Louis. Each has additional requirements that can be found in the link below.

**Funding:** Varies, but general range is $5k-$150k

**Timeline:** Rolling application

**Application and Details:** Details [here](#) for each of these programs

Missouri State Loan Programs – There are two main loan programs offered through Missouri state, The MO linked deposit for small businesses, and The Missouri export finance program working capital loan guarantees.

**Eligibility:** Both require residents in Missouri and are restricted to for-profit businesses.

**Funding:** Up to $1M

**Timeline:** Rolling application

**Application and Details:** Details on the linked deposit program can be found [here](#), and the Export Finance Program [https://exportmissouri.mo.gov/exports/financing](https://exportmissouri.mo.gov/exports/financing)
Small Business Innovation Research; Small Business Technology Transfer (SBIR/STTR) – Federal government grant agency for R&D aimed to bring a technology to market.  
*Eligibility:* US for-profit company with at least one full-time employee. Over 100 solicitations available at any time focused on specific or general goals.  
*Funding:* up to $4.7 million! ($225k – Phase I; $1.5 million – Phase II; $3 million – Phase III)  
*Timeline:* Application deadlines occur 3X a year for NIH, 2X a year for NSF & DOD.  
*Application:* Multi-page government grant proposal.

**MTC Tech Launch** – Grant matching program offered through the State of Missouri.  
*Eligibility:* Missouri science and technology companies who are going to raise at least $100,000 in equity elsewhere and have not raised more than $250,000 to date.  
*Funding:* You can request up to $100,000, if awarded, and you can raise $100,000 in equity elsewhere; they will match up to $100,000 through a convertible note.  
*Timeline:* Bi-annual applications  
*Applications:* [here](#)

**Non-profit Organizations**

**BioGenerator** – BioGenerator has two funding mechanisms for early-stage biotech ideas. You can read more about their resources [here](#).

- **Concept Grants:** up to $50k nondilutive funding for proof-of-concept experiments, market research, preliminary IP research, etc. Can include access to office and lab space within the BioGenerator facilities at Cortex.
- **Seed Funding:** dilutive equity funding in seed-stage companies  
  
  *Eligibility:* Early-stage bio-science company in Saint Louis 
  *Funding:* Ranges from low $1000s up to $50k nondilutive for concept grants, to $100k+ dilutive for seed funding investments.  
  *Timeline:* Apply any time of the year  
  *Application:* Fill out application form, which can be found [here](#) at any time of year

**Business Plan Competitions** – St. Louis business plan competition provide grants, convertible notes, and/or equity deals.  

**Arch Grants** – A non-profit organization that offers startups funding in the form of grants and in-kind services for startups as they become established or transition to the City of St. Louis.  
*Eligibility:* For-profit businesses in all industries. Startup companies must be located in or be willing to relocate its headquarters to St. Louis.  
*Funding:* $50,000 grant; pro-bono accounting, legal, marketing, HR, financial consulting, banking, and mentoring services.  
*Timeline:* Application opens in spring.  
*Application:* Competition occurs in three rounds, ending with a business plan and presentation.

**The BALSA Foundation** – A non-profit organization that offers first time entrepreneurs from all background and industries funding, resources, and networking connections.  
*Eligibility:* Any first-time entrepreneur at the earliest stages of business formation  
*Funding:* Up to $5k in grants  
*Timeline:* Application opens twice yearly  
*Application:* A one-page summary of a business idea and use of funds.

**Global Impact Award:** Washington University in St. Louis funding source aiming to fund start-ups that will have a global impact.
Eligibility: WUSTL-affiliated companies that have raised less than $1M at date of application.
Funding: Up to $50,000 grant.
Timeline: Once a-year business plan competition which begins in the Spring

Accelerate St. Louis Challenge – Business plan competition organized by Edward Jones and St. Louis Economic Development Partnership aimed at promoting entrepreneurship in St. Louis.
Eligibility: All industries. Businesses may be new or early-stage companies with no more than $100,000 in annual revenue. Applicant entities must be located in the St. Louis region. See website for additional rules and requirements.
Funding: 1) Top three winners will be awarded with a total of $100,000 cash, office space within STL VentureWorks incubator network, enrollment in Center for Business Growth mentoring program, as well as accounting, legal and marketing services. 2) Bright Future Entrepreneurial Inclusion Awards ($5,000) for minority, women, immigrant, and veteran entrepreneurs in the St. Louis region.
Timeline: Beginning of fall, online applications.
Application: Competition consists of several steps over six months, including initial application, business analysis, video pitch, presentation, and interview with the judging pane.

Helix Fund
Eligibility: The Helix Fund co-invests with specific partners to promote the growth of bioscience and related technology businesses in St. Louis County. Eligible companies must be referred to the Helix Fund for investment consideration by one of our partners. An eligible company that already has the support of one of our partners may also request funding directly, but only after the partner has committed funding to the specific opportunity.
Funding: $50,000
Timeline: Anytime
Application: Contact Christine Karslake, VP of Innovation and Entrepreneurship at the STL Partnership, CKarslake@stlpartnership.com

Capital Innovators – provides tech startups with $50k in equity financing, an incubator program, and connections for their business development.
Eligibility: Tech-related businesses or ideas, typically web-based, mobile, or other software-as-a-service (SaaS) startups. Tech companies at all stages during the life cycle of a startup, pre- or post-revenue, are eligible to apply. Companies with a functioning prototype of their product are preferred.
Funding and Accelerator details: $50,000 in seed funding in exchange for equity to five companies per class. Project-based mentorship from a seasoned pool of knowledgeable experts, networking, and follow-on funding opportunities over the course of 12 weeks.
Timeline: Capital Innovators run a Fall and Spring 12-week Accelerator Programs each year.
Application: Online business analysis, details here

Skandalaris Cup – Commercial business plan competition sponsored by Washington University in St. Louis’ Skandalaris Center for Interdisciplinary Innovation and Entrepreneurship.
Eligibility: Businesses in all industries. Applicant teams must include at least one WUSTL student or recent alum.
Funding: The winning team receives a $5,000 cash prize with the opportunity for further investment.
Brazen (earlier Prosper Startup Accelerator)

**Eligibility:** Brazen supports women-led startups with a focus on technology, health care, and consumer products. They define a women-led business as a company with at least one woman in a position of leadership and significant and meaningful equity.

**Funding:** $50k, and extensive training process

**Timeline:** Spring and Fall application deadlines

Angel Investors-

The process of soliciting angel funding is unique to each group and can take various forms. Angel groups normally require an online application which is pre-screened by the organization. Selected companies pitch to the entire angel group. If a few angels are interested in the company, the angel group then leads a due diligence process to further vet the team and business, which can take several months. If angels want to proceed with the investment, the angel and company negotiate terms of agreement.

**Billiken Angels Network** — Angel group associated with Saint Louis University.

**Eligibility:** Full business plan required, along with presentation. Only invest in St. Louis companies or companies associated or affiliated with SLU.

**Funding:** Typically, $250k-$1M in convertible notes

**Timeline:** Anytime

**Application:** Complete business plan online application through [gust](#).

**Saint Louis Arch Angels** — Angel group

**Eligibility:** Full business plan required, they invest in first-of-a-kind new ideas, rather than incremental enhancements to common products and services.

**Funding:** $250-$750k investments.

**Timeline:** Anytime, after submitting application they will hold a screening session to judge your pitch before deciding if it is ready for the full group.

**Application:** Complete business plan online application through [gust](#).

Crowdsourcing sites

**Kickstarter** — The most heavily trafficked crowdfunding site. An entrepreneur launches a project to try and raise funding for their finite work with a clear goal that they’d like to bring to life. The funding goal is the amount of money that a creator needs to complete their project. Funding on Kickstarter is all-or-nothing. No one will be charged for a pledge towards a project unless it reaches its funding goal. This way, creators always have the budget they scoped out before moving forward. A creator is the person or team behind the project idea; working to bring it to life. Backers are folks who pledge money to join creators in bringing projects to life. Rewards are a creator’s chance to share a piece of their project with their backer community. Typically, these are one-of-a-kind experiences, limited editions, copies of the creative work being produced, other tangible incentives, or simply a “thank you” and a promise to use the funding towards a creative and original project.

**Eligibility:** No restrictions other than a campaign cannot be used to fund charities or offer financial incentives. Creators must be US residents, over 18, and have driver’s license, bank account, and/or credit card.

**Funding:** All but 5% of the funds raised, which Kickstarter retains.

**Timeline:** A campaign can be started at any time.
Sue’s Story—How should I finance my venture?

Sue has previously determined she needs to raise $28M to fund her venture. When discussing this with her advisors she learns that the highly experienced and sophisticated investors who actually make investments of this magnitude will not be willing to advance her this money in one lump sum—in fact, they will only invest in smaller increments called “tranches”—much smaller investments meant to fund the company only through each of the several goals of development. Moreover, she learns, this is actually to the advantage of Sue and the team she wants to build—for if the company was to raise $30 million in a single round at her current level of progress she and her team will likely be massively “diluted” out of their ownership positions in the company as shown in the following table.

With the help of her advisors she then figures out what the major milestones for her product development campaign will be, and then works up cost estimates of what it should cost to get these goals accomplished. She then re-organizes her cost projections so they are presented by goal or “milestone” as shown in the table:

<table>
<thead>
<tr>
<th>Year</th>
<th>Milestone</th>
<th>Milestone spend</th>
<th>An Spend</th>
<th>Cum. Spend</th>
<th>Amounts Raised</th>
<th>Pre money</th>
<th>Post money</th>
<th>Common %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Assay done/Leads ided</td>
<td>$600</td>
<td>$90</td>
<td>$690</td>
<td>$500</td>
<td>$500</td>
<td>$750</td>
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<tr>
<td>1</td>
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<td>$2,290</td>
<td>$1,600</td>
<td>$2,500</td>
<td>$4,100</td>
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<tr>
<td>2</td>
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<td>$800</td>
<td>$800</td>
<td>$800</td>
<td>$800</td>
<td>$800</td>
<td>$800</td>
</tr>
<tr>
<td>3</td>
<td>Animal Efficacy</td>
<td>$800</td>
<td>$2,900</td>
<td>$5,190</td>
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<td>$5,500</td>
<td>$8,400</td>
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</tr>
<tr>
<td>4</td>
<td>Regulatorry</td>
<td>$2,500</td>
<td>$3,800</td>
<td>$8,990</td>
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<td>$10,000</td>
<td>$13,800</td>
<td>$13,800</td>
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<tr>
<td>5 &amp; 6</td>
<td>Phase I clinical</td>
<td>$15,000</td>
<td>$19,500</td>
<td>$28,490</td>
<td>$19,500</td>
<td>$25,000</td>
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<td>$28,490</td>
<td>$28,300</td>
<td>$28,300</td>
<td>$28,300</td>
<td>$28,300</td>
<td>$28,300</td>
</tr>
</tbody>
</table>

Table 11. Milestone-based financial projections

This Table is quite different from her first attempt at projections (see Accounting section) and—although it was a lot of work—Sue can see how this will be a much more useful approach with several advantages over the first approach:

- Because the model allocates money by project, it leaves open the question of whether or not the project will be done by employees of the company or by contract researchers. One of Sue’s advisors point out that while it may sound like a good idea to hire lots of employees, in reality, having a pay-roll to meet every month is a huge headache for an entrepreneur. And many tasks can in fact be accomplished much more efficiently (and professionally) by experts working under a contract as opposed to employees who—even if they have the necessary experience—must develop the systems to make the company run smoothly. Plus, Sue realizes, she will have to pay her employees regardless of whether they perform the assigned tasks properly or not. With contractors, she can always withhold payment if the contractor does not perform as promised.

- Because the projections are organized by project milestone, potential investors can easily see what goal she is proposing to invest their money against. This is much more useful (and even intriguing) for a potential investor.
• Because costs are organized by major milestone, the company is proposing to potential investors how the money should be “Tranched” (or broken down in to practical raises).

• In fact, using this method, Sue proves to herself that raising the money in digestible chunks is actually much better for her (and her team) financially. She compares the % of the company she and her Team (the Common Shareholders) end up owning under the “Tranched” approach as opposed to raising the money “all at once”, and finds to her amazement that she will end up to 3 or 4 times more equity at the end with the Tranched approach.

To see how this works, Sue starts in both the “Tranched” and “all at once” scenarios with a “Pre-money valuation” of $750,000 (she has been told that this number is not uncommon for an early stage valuation of a company like hers). In the “all at once” case, she would raise $28.3M on a pre-money valuation of $750,000 – that’s $750,000/29,100,000 = 3% meaning that the “common shareholders” (that is, Sue and all the employees of the company who are compensated by equity) will share 3% of the proceeds of the company (NB this is the BEST CASE scenario not counting liquidation preferences and other financial incentives the financial investors will get). In the “Tranched” case, each time Sue and her company raise a small chunk of money, if they achieve their objective they will be rewarded with an “up valuation” or “share appreciation” (meaning that the “Pre-money valuation” of each succeeding investment Tranche is somewhat higher than the “Post-money valuation” of the previous Tranche. This consistent record of performance yields a better return for the common shareholders who end up with 8% of the company by the end of the phase II trials (as opposed to 3% under the “all at once” scenario.)

What are some additional resources related to financing a venture?
For further insight as to determining if VC is right for your organization & how to find and approach VC negotiating, click here.