

## Stock options and beyond

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Throwing some light on the Byzantine rules surrounding stock options and other equity associated with startups.

If you decide to found a company, you need to understand how your investment in time, vision, savings, and blood, sweat and tears is likely to be compensated via equity-based remuneration, particularly stock options. You also need to appreciate how to attract, retain and motivate your employees through appropriately designed equity incentives. Similarly, if you are a researcher leaving academia to work in a startup or even an established biotech company, it would behoove you to familiarize yourself with the stock options or other equity awards that you may be offered as part of your compensation package and the reasons why you and your employer may have different preferences regarding the selection of the form of equity award.

In this article, we summarize the advantages and disadvantages of stock options, the important accounting, US tax and other regulatory constraints that you need to appreciate, and possible modifications or alternatives to stock option programs that may be available to you. (Also provided, in **Table 1**, is a list of some of the not entirely familiar compensation terminology with which you may have to acquaint yourself when you leave academia for a startup.)

### The basics

Over the past quarter century—at least until fairly recently—stock options have been the equity award of choice for US companies, particularly in the biotech space. Stock options provide employees the ability to participate in equity appreciation without an up-front investment of money and with control over the timing of recognition of taxable income. As a founder or other employee of a biotech startup, you may correctly consider these features attractive. That being said, it is important that you understand

that your ability to ‘cash out’ of these options is dependent on whether your company can find a suitable exit through the sale of the company or an initial public offering (IPO) of its securities—events sadly not as common as they once were.

Even if your company does manage to complete an IPO, you may not be able to divest all your holdings or otherwise monetize your options. Moreover, there is no guarantee that all—or even any—of your options will be ‘in the money’ (that is, with an exercise price below the price of the underlying stock) at the time of an IPO or will remain in the money after the IPO. This is perhaps the greatest shortcoming of stock options in an industry where equity values can be so volatile and unpredictable.

If you are a founder, and wearing your employer hat, you also need to recognize that the tax and accounting treatment of stock options is more complex and less favorable than it once was. In short, stock options may not be the perfect incentive device that they often have been touted as representing.

### Differences between stock options

Stock options may be either non-qualified or tax qualified, with the latter being governed by Section 422 of the Internal Revenue Code and labeled ‘incentive stock options’ (ISOs). Whether one is considering non-qualified or tax-qualified options—and despite changes in accounting rules, described below, that have removed certain extra incentives for the use of options—the ability of an option holder to delay income recognition (and the related need for liquidity to pay associated taxes) until exer-



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For any member of a startup, understanding the accounting, US tax and other regulatory constraints associated with stock option programs and their alternatives is paramount to maximize the financial reward.

cise or later continues to make these financial instruments very attractive to founders and other employees of nascent biotech companies.

A non-qualified stock option that is not subject to Section 409A of the US tax code (see below) generally is *not* taxable upon grant or vesting; instead, ordinary income tax is due upon exercise of the option based on the positive difference between the exercise price and the fair market value of the stock underlying the exercised option.

In contrast, provided that various conditions—most notably, an exercise price no lower than fair market value as of the date of grant (higher for certain substantial shareholder employees) and holding period requirements—are satisfied, ISOs are not taxable upon grant, vesting or exercise. Instead, the first related taxable event occurs upon the sale of the shares received upon exercise, with any appreciation above the exercise price paid being taxed as a capital gain. These potential benefits are what give ISOs their cachet, and are why you may have heard industry peers talk about them at social events.

However, in reality, typically very few ISOs qualify for this favorable tax treatment because employees rarely satisfy the requirement to hold the shares for at least one year from exercise and

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**Table 1 Common terms relating to stock options and equity**

Term	Description
Stock option	A contractual right granted to an employee entitling the recipient to buy shares of stock at a specified price (the 'exercise' or 'strike' price), typically subject to a vesting schedule whereby the option is not exercisable—and may be forfeited upon termination of employment—until it 'vests'. Once the option has vested, the holder typically may exercise the option (that is, buy the underlying stock by paying the exercise price) at any time within the remaining term of the option. Options customarily have a total maximum term of five to ten years, but usually remain exercisable for only a limited period of time following termination of employment. If, as of a given time after the grant of the option, the shares subject to the option have a value that is greater than the exercise price (such excess is known as the 'spread'), the options are referred to as being 'in the money'; if, on the other hand, the exercise price is greater than the value of the underlying stock, the options are described as 'out of the money' or 'underwater'.
Restricted stock	Shares of stock that are issued initially to an employee but remain subject to potential forfeiture upon termination of employment until they vest; in private companies such shares typically are also subject to transfer restrictions that extend beyond the vesting period and lapse upon a sale or IPO of the company. May also be subject to objective performance-based conditions to vesting: for example, successful clinical trials or the achievement of financial objectives (in which case it may be labeled 'performance stock' or a similar designation). Usually granted for no value other than services.
Restricted stock unit (RSU)	A contractual promise to deliver stock on a specified date in the future to an employee, subject to forfeiture upon termination of employment until they vest. RSUs may also be subject to the satisfaction of performance conditions (in which case they may be labeled 'performance units', 'performance share units' (PSUs) or a similar designation).
Stock appreciation right (SAR)	A contractual right granted to an employee entitling the recipient to receive (either in cash or stock) the positive difference (if any) between the value of stock at the time of grant and the value at the time of exercise, typically subject to a vesting schedule whereby the SAR is not exercisable—and may be forfeited upon termination of employment—until it vests. An SAR is effectively the economic equivalent of a stock option, but it does not require the payment of an exercise price; instead, the analog of the exercise price is simply deducted from the value of the shares at the time of exercise of the SAR to determine the amount payable.
Phantom share	A contractual promise to pay the cash value of a share of stock on a specified date in the future to an employee, subject to forfeiture upon termination of employment until they vest. In effect, a cash-settled RSU. Can be made subject to performance conditions as well.
Non-qualified deferred compensation	Various compensation arrangements in which payment is made in a taxable year later than the year in which the relevant services were performed by an employee. Frequently, non-qualified deferred compensation (NQDC) takes the form of supplemental executive pensions (SERPs) and deferred compensation plans pursuant to which employees may elect to receive part of their salaries or bonuses in future years rather than currently. These arrangements are labeled 'non-qualified' to distinguish them from 'qualified' plans, which include 401(k) plans and traditional pension plans. RSUs, SARs and phantom shares all are forms of non-qualified deferred compensation.

two years from grant of the ISO. Employees generally do not like to put up the cash to exercise options without almost simultaneously selling the shares received, or at least enough of them to cover the exercise price paid. For these reasons, as well as unattractive and often unanticipated Alternative Minimum Tax treatment of ISO exercises and the unavailability of corporate deductions for those ISOs that satisfy the conditions for favorable employee treatment, ISOs are rarely used by public biotech companies and probably are a questionable choice for private entities as well. In our experience, ISOs in effect make promises that they cannot keep.

### Tax considerations and Section 409A

Non-qualified deferred compensation arrangements have been commonplace in corporate America for many years, but the US Internal Revenue Service (IRS; Washington, DC) has long been concerned by what it perceived as frequent abuses and tax avoidance schemes hiding under the deferred compensation label. Scandals at companies like WorldCom (Clinton, MS) and Enron (Houston, TX), in which (among other things) executives accelerated the payment of deferred compensation to avoid their employer's default while rank-and-file employees had their savings stuck in 401(k) plans invested in soon-to-be-worthless company stock, spurred the US Congress to take action.

This action resulted in Section 409A of the US Internal Revenue Code and the complicated

and lengthy associated regulations subsequently adopted by the IRS. Section 409A governs all forms of non-qualified deferred compensation, which it defines broadly to include many arrangements—such as certain severance plans and agreements and equity-based incentive awards—not usually understood by researchers (or business people, for that matter!) to constitute deferred compensation.

In general, Section 409A imposes strict rules on the timing of deferral elections, permissible payment events and the ability to accelerate or further defer compensation once the original deferral terms have been set. The gist of these rules is to prevent the manipulation of the timing of income recognition. Although Section 409A does not prohibit the deferral of compensation, the statute greatly circumscribes the flexibility that previously applied. Failure to comply with Section 409A's rigid requirements has serious consequences for employees: accelerated income recognition and taxation; imposition of an additional 20% tax; and an interest charge.

Included within Section 409A's coverage are stock options with an exercise price per share below the fair market value of the underlying stock as of the grant date. If a typical US stock option were deemed to be non-qualified deferred compensation, it would violate Section 409A because of the absence of predetermined payment dates or events and consequently the holder would be taxed at ordinary income rates upon vesting of the options and

be subject to the 20% extra tax plus interest. Accordingly, you should make certain that any stock options granted to you are exempt from Section 409A.

As you can imagine, the determination of the fair market value of a startup company can be a difficult and occasionally speculative undertaking. Under Section 409A, in the case of stock not "readily tradable on an established securities market," fair market value means "a value determined by the reasonable application of a reasonable valuation method." There is a presumption that an independent appraisal results in a reasonable valuation for a period of 12 months. This presumption may be rebutted by the IRS upon a showing that the valuation method or application of the method was grossly unreasonable. This may occur, for example, if a board of directors relies on a valuation even though the board has good reason to believe there have been fundamental changes to the business since the date of the valuation.

Given the substantial adverse tax consequences under Section 409A of an option being deemed in the money on the date of grant, great care must be taken by startups to establish strong support for the valuation used to set the exercise price of options.

### Other considerations

Although this is perhaps of minor interest to a non-management employee, if you end up founding a company or otherwise being part

of a biotech company's management team, you should familiarize yourself with some of the other technical considerations that can affect the choice of whether to use options or other forms of equity awards, particularly if you hang around with the company long enough that it ends up floating on the public markets to raise finance. These considerations include the deductibility of incentive compensation under Section 162(m) of the Internal Revenue Code, and the accounting treatment of stock options and other equity awards, which can have a profound impact on your company's earnings or profits reflected in its financial statements provided to investors.

Following a post-IPO transition period, a newly public biotech company will become subject to Section 162(m) of the Internal Revenue Code, which limits the deductibility of annual compensation in excess of \$1 million paid to the company's CEO and three (or two, in the case of "Emerging Growth Companies": newly listed companies with annual total gross revenues of less than \$1 billion) most highly compensated executive officers—other than the CFO—listed in the summary compensation table contained in the compa-

ny's proxy statement (the disclosure document distributed to public company shareholders in connection with the company's annual meeting and the matters, including the election of directors, to be voted on). The most substantial relief from this deduction limitation is the exception for "qualified performance-based compensation," and the easiest way for a company to deliver incentive compensation to executive officers in compliance with this exception is by granting at-the-market stock options. Unlike other forms of exempt performance-based compensation, stock options need not be subject to pre-established, shareholder-approved performance conditions—the mere fact that they have no realizable value unless the company's stock price increases is enough for the Section 162(m) deduction limitation not to apply. This fact, together with the favorable accounting treatment accorded options until the adoption of new accounting standards described below, is the principal reason for the explosion in the use of stock options in the US in the 1990s through the mid-2000s.

### Box 1 Possible fixes for underwater options

Underwater options are less of a headache for those working for a startup than for those at a publicly held company. Private companies may re-price underwater options relatively easily, although, as with public companies, incremental accounting expense will be recognized in an amount equal to the excess, if any, of the fair value of the option as modified over the fair value immediately before modification. The most direct approach is simply to lower the price of the existing options. For purposes of Section 409A, such a modification would result in a deemed new grant but, so long as the new exercise price is not lower than the fair market value of the underlying stock as of the date of the modification, no violation of Section 409A will result.

In contrast, public companies face substantial practical constraints in dealing with underwater stock options. Among other things, the stock exchanges require shareholder approval of 'repricings' (which is very broadly defined to include not only direct reductions in exercise price but also various transactions by which underwater options are replaced by new awards with substantially identical accounting value) unless the relevant equity plan approved by shareholders expressly authorizes repricings. This, however, is highly unlikely to happen, as the two major proxy advisory firms, ISS (Rockville, MD) and Glass Lewis (San Francisco, CA), will recommend against shareholder approval of any equity plan that permits repricings. In addition, those firms and institutional shareholders will not abide simple exercise price reductions because of both the incremental accounting expense and ever-increasing governance concerns.

As a practical matter, then, any public company that wants to implement a repricing will need to obtain specific shareholder approval of an exchange of the underwater options for new awards of equal value. Often, this involves the issuance of a number of at-the-market options lower than the number of underwater options being replaced or of even fewer restricted shares or restricted stock units. Furthermore, unless the relevant plan would permit unilateral action by the company to replace the outstanding awards (which is improbable), a typical value-for-value exchange is likely to require participant elections through a registered exchange offer filed with and cleared by the US Securities Exchange Commission (SEC), a not-so-simple undertaking. This is because the new awards have a different economic profile than the underwater options that they would replace, so that the employees' election involves an investment decision between different securities, thereby triggering an SEC filing.

### Accounting implications

The Financial Accounting Standards Board (Stamford, CT; a not-for-profit self-regulatory organization of the US accounting profession, known as FASB), with the blessing of the US Securities and Exchange Commission (SEC; Washington, DC), establishes the accounting standards (US GAAP) applicable to audited financial statements in the United States, including those contained in securities filings by listed companies. As a consequence, earnings and other financial measures of company performance must be determined in accordance with US GAAP, and in turn earnings can be materially affected by how compensation expense is measured. Until late 2004, the then applicable US GAAP rule (APB 25) provided that an option with a strike price set at or above the fair market value of the underlying stock at grant would generate no compensation expense to the issuing company. In other words, the issuance of options would not reduce the earnings of the issuing company released to the public. This was because under APB 25's 'intrinsic value' accounting, the only expense generated by a typical stock-based award was the 'spread' at grant. For a restricted share or restricted stock unit granted for services rather than cash, the application of this methodology generally meant that the expense would be the stock price at grant; for standard options, the expense would be zero. For many companies, particularly startups, stock options seemed like 'funny money'—a form of compensation that was perceived by employees as highly valuable but that required no outlay of cash by employers and no accounting charges which would reduce company earnings.

Although the accounting profession recognized for many years that APB 25's treatment of options did not reflect economic reality, the move by FASB to fair value accounting (which attributes to the option itself, for purposes of calculating compensation expense, a 'fair value' based on Black-Scholes or other option pricing models developed by academic economists) was delayed for many years by intense lobbying efforts from the private sector (particularly the technology industry) and members of the US Congress representing districts with large concentrations of tech startups. The opponents of fair value accounting argued, among other things, that the favorable accounting treatment of options under APB 25 was a key driver of the success of the US technology industry and prophesied disastrous consequences if it were to be abandoned. These prophesies have not come true, but the accounting change did affect the prevalence of options.

Once the US GAAP rule (FAS123(R), subsequently redesignated as ASC 718) came into



effect in December 2004, many companies (and almost all public issuers) moved away from an exclusive reliance on stock options. Today most use a mix of options and other forms of equity awards, predominantly restricted stock or restricted stock units (which, if also made subject to performance-based conditions, are often referred to as 'performance shares' or 'performance share units'). Although this can in part be attributed to the change in accounting rules, it also reflects the impact of the options backdating scandals (in which some companies were found to have retroactively set grant dates to take advantage of lower stock—and hence option exercise—prices), corporate malfeasance and meltdowns at WorldCom and Enron (arguably contributed to by executives who tried to artificially prop up stock prices) and, more recently, the financial crisis.

### Pitfalls of stock options

When you are offered or elect to take stock options in a biotech company, you need to keep in mind some key issues. The foremost of these relate to company liquidity and the underperformance of company stock.

**Private company liquidity issues.** As noted above, the ability to defer taxation until the exercise of stock options (and potentially later in the case of ISOs) is one advantage of stock options as a means of compensation. However, the deferral potential of a stock option is not unlimited, as most options have a maximum term of between five and ten years. Moreover, to the extent that they are not forfeited upon termination of employment, options typically are (and to qualify for ISO treatment must be) exercisable for only a limited time following termination. This means that a stock option holder may be required to put up cash to exercise options before having the ability to sell the shares to recoup the cost. (Shares in a private company typically are subject to transfer restrictions preventing shareholders from selling their shares until an IPO or sale of the company.) Private equity, venture capital and other financial investors in biotech startups are unlikely to be willing for the startup to extend loans to fund employees' exercises of stock options, and in any event such loans would run afoul of Section 402 of the Sarbanes-Oxley legislation if the company were to go public. (Section 402 prohibits employer loans or other extensions of credit to officers arranged by US public companies.) As a result, risk-averse employees may leave options unexercised, particularly where, as is often the case with biotech companies, the prospect of a corporate liquidity event (that is, an IPO or sale of the company) may seem too distant.

Founders and their management teams that

seek to extend the term of stock options to mitigate liquidity problems need to consider the consequences under Section 409A of the Internal Revenue Code. Although the amendment of a non-qualified option's terms to extend post-termination exercisability (but not beyond the ultimate, maximum term of the option or ten years from grant, if earlier) will not endanger the exception from Section 409A, an extension of the maximum (typically five- to ten-year) term of an in-the-money non-qualified stock option will result in the option being deemed subject to, and in violation of, Section 409A from the date of grant.

**Underwater options.** The shortcoming of share ownership most commonly experienced by founders and employees of biotech startups is the phenomenon of out-of-the-money, or 'underwater', options. This especially plagues biotech firms, the financial results and stock valuation of which are highly volatile and subject to frequent and sometimes lengthy setbacks due to difficulties and delays in the regulatory or commercialization process. What companies can do, if anything, about underwater options is a more difficult, technical question.

Box 1 outlines some measures companies can take to fix them.

### Alternatives to stock options

Many biotech companies now supplement or even replace the use of options with so-called 'full value awards', equity awards that correspond to a share rather than an option or stock appreciation right, giving the holder a stake in downside as well as upside.

**Restricted stock.** The most traditional form of full value award is shares of restricted stock—actual shares granted or sold to employees subject to transfer and forfeiture restrictions and a vesting schedule. The vesting of restricted stock usually is time based, but performance conditions also can be applied. Restricted stock is subject to taxation under Section 83 of the Internal Revenue Code, which provides that restricted stock is taxed as ordinary income when it vests and ceases to be subject to a "substantial risk of forfeiture," although the recipient of restricted property can also accelerate taxation to the date of grant (thereby assuring that any subsequent appreciation will be taxed as capital gains at a lower rate than ordinary income) by making an election under Section 83(b) that is filed with the employer and the IRS within 30 days following the date of grant. Being subject to Section 83 means restricted stock is categorically excluded from coverage under Section 409A. Even during the heyday of stock options restricted stock was fairly frequently used at startups, particularly

for the senior-most executives and where initial valuation was low, making a Section 83(b) election attractive.

Note that time-based vesting restricted stock, unlike stock options and performance-based restricted stock, is subject to the deduction limitations of Section 162(m) of the Internal Revenue Code discussed above. This is because the performance-based exception to Section 162(m) can only be satisfied by either (a) awards the value of which is based solely on the appreciation of the stock from the date of grant (such as stock options and stock appreciation rights that are not in the money on the date of grant) or (b) awards the value and payment of which is based on the achievement of predetermined, objective performance goals. Unlike those two categories, non-performance vesting restricted stock has imbedded value and is not contingent on the satisfaction of performance goals, and therefore is not exempt from Section 162(m).

**Restricted stock units.** Restricted stock units (RSUs) are economically identical to restricted stock but subject to a different tax regime. Unlike restricted stock, they represent a contractual promise to deliver actual shares (or, less frequently, the cash value of shares) in the future rather than a current transfer of shares. As such, they are not subject to Section 83 and are taxable upon payment or settlement rather than upon vesting. That being said, RSUs issued by public companies often are settled upon vesting, thereby eliminating any real-life tax difference between RSUs and restricted stock.

Section 409A of the Internal Revenue Code will apply to any RSUs that are payable later than the March 15 of the year following vesting (the deadline for application of the so-called 'short-term deferral' exception to Section 409A). As noted in the discussion of Section 409A above, Section 409A imposes strict rules on the timing of deferral elections and the ability to accelerate or further defer compensation once the original deferral terms have been set. Furthermore, deferred compensation subject to Section 409A generally can only be paid on a specified date or dates or on certain permissible events, namely, separation from service, death, disability or a change in control (which does not include an initial public offering). Thus, if Section 409A applies to an award of RSUs, there will be very limited ability to accelerate or further defer the payment of RSUs after grant. Lastly, public company officers also may be subject to a mandatory six-month delay of payment upon separation from service. Despite these Section 409A-based limitations, many private companies avail themselves of the ability to defer settlement and taxation (and the related employee liquidity issues that they create) to Section 409A-compliant dates or

events likely to occur substantially in the future, when it is hoped that liquidity will be available.

RSUs often are subject to performance conditions, in which case they often are referred to as performance (stock) units (PSUs). Because time-based RSUs are subject to Section 162(m)'s deduction limitation, and institutional shareholders and shareholder advisory firms prefer performance-based awards, PSUs currently are the most frequently employed replacement or supplement to stock options at public biotech companies. The performance objectives usually are financial, but can also include product development milestones. Product-related performance goals can be particularly useful at biotech firms, where financial results may be less important in the short to medium term than making progress toward regulatory approval or commercialization.


**Other incentive arrangements.** Other forms of long-term incentives include cash- or stock-settled stock appreciation rights (SARs), cash-settled RSUs and PSUs, and other long-term incentive plans paying bonuses based on the level of achievement of various financial, operational and product development metrics. Other than stock-settled SARs, which are accounted for in the same manner as stock options under

ASC 718, these other cash-settled forms of award are considered 'liability awards,' requiring so-called 'mark-to-market' expensing under US GAAP, whereby the accounting expense associated with an award, rather than being fixed at grant, is adjusted over time to reflect the award's changing value. For this reason, as well as the cash-poor nature of many private biotech companies and young public companies and the preference of institutional shareholders for the greater stockholder-management alignment of interests produced by equity-settled awards, these awards are used relatively infrequently.

### Conclusions

Although stock options continue to be a popular employee incentive device, in the past few years their advantages have been diminished through accounting and tax law changes, whereas their shortcomings have become more apparent in the biotech sector—in which a consistently growing stock price is far from assured, or even likely. As a consequence, biotech firms are moving away from an exclusive reliance on stock options and instead are using a mix of equity-based incentives, most commonly a combination of stock options and performance-based stock units.

From the perspective of a founder or other employee, the shift to a combination of stock options and some form of restricted stock or stock units should be welcome, making it less likely that the employee's awards will have no value at all. Unlike the corporate employer, an employee would prefer that restricted stock or stock units not be subject to performance conditions. As for a preference between restricted stock or restricted stock units, if the underlying value of the stock at grant is low enough that the employee could afford to make a Section 83(b) election (and thereby have future appreciation taxed entirely at capital gains rates), then restricted stock, rather than RSUs, is the way to go.

If you find the complexity of the rules described above daunting, seeking the advice of a financial advisor upon grant—and certainly before exercising or dealing—may be advisable. In some cases, the financial stakes involved could be sizeable. 

### COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

For more content on bioentrepreneurism, visit our Trade Secrets blog.

[http://blogs.nature.com/trade\\_secrets/](http://blogs.nature.com/trade_secrets/)

### Startups on the menu

In 2011, Steve Finkbeiner, of the University of California, San Francisco Gladstone Institutes and Taube-Koret Center, participated in the Bay Area SciCafé following publication of his paper describing small molecules that stimulate autophagy as possible treatments for neurodegenerative disease (*Nat. Med.* **16**, 1227, 2010). Key to this discovery was the invention of a patented high-throughput single-cell imaging platform that makes it possible to track the development of brain cells from patient-derived induced pluripotent stem cells.

### Nature Biotechnology: How have you built on the work described in the *Nature Medicine* paper?

**Steve Finkbeiner:** Initially, our efforts were directed at developing leads from our internal academic programs far enough that they warranted industry partnerships, using financial support from philanthropists or other non-dilutive funding sources. The goal was to catalyze the discovery of therapeutics by carrying out the early-stage discovery and development work necessary to de-risk the leads. However, as we developed innovative tools and deep biology expertise to do this work, industry sought access to our platform to advance their own programs.

### NBT: What types of challenges does commercialization of neuroscience research pose?

**SF:** Early-stage central nervous system drug discovery is viewed as risky,



so the extent to which discoveries must be de-risked is especially high. Collaboration and open innovation are ways to manage risk because it reduces the investment necessary to have an effective development infrastructure. Philanthropy is absolutely critical as well. It makes it possible to carry out the development of promising leads without adding encumbrances that would ultimately make those leads difficult to partner out. Industry partnerships are essential because they are uniquely resourced to afford and execute clinical trials. My impression is that philanthropy in this area is growing, and I hope that the message that philanthropists have the opportunity to make a major difference and can see the impact of their efforts entices even greater investment.

### NBT: What led you to pursue translational applications as well as fundamental research?

**SF:** Part of my work as an academic scientist led naturally to a focus on mechanisms of disease, which in turn led to the discovery of potential therapeutic targets. A few years ago, I was fortunate to be approached by philanthropists interested in one of the diseases we study, and with their help, created an infrastructure for developing discoveries with therapeutic potential from the academic research program. We raise about \$5 from other sources for every \$1 we receive in philanthropy. For example, the invention of a first-generation high-throughput stem cell platform was made possible with philanthropy. Our early successes using it attracted the resources to develop the technology further and attract pharma partnerships and sponsored research agreements.