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 stocksettled stock appreciation rights (SARs), cashsettled 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/

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 neurode-

generative 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,

hi

SciCafé



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.