

# perfumer & flavorist®

## Novel Compounds Point Toward the Future of Healthier, Better-tasting Flavors

Inside Redpoint Bio's discovery and development of bitter blockers and flavor enhancers

The sequencing of the human genome has elucidated, among countless other things, the taste signaling pathway in the tongue. Meanwhile, the desire for healthier food options among food and beverage companies and consumers—particularly the reduction of sodium and sugar—has increased exponentially. As a result, a number of biotech firms have emerged to tackle the manipulation of taste receptors and signals in the interest of modifying flavors.

Building on the core knowledge of founder Robert Margolskee (professor of neuroscience, structural and chemical biology, and pharmacology and systems therapeutics at Mount Sinai in New York), Redpoint Bio (Ewing, New Jersey) approaches the research and discovery of sweet and salt enhancers, bitter blockers, and spice modulators from a drug discovery background. CEO Ray Salemme explains that the company has applied that background to the science of flavors, originally focusing on bitter blockers for orally dissolving prescription drug and OTC tablets and films. Whether it's the delivery of acetaminophen, diphenhydramine hydrochloride or ranitidine, aversive taste is a primary roadblock for the feasibility of these orally applied drugs. The efficacy and toxicological advantages of such drug delivery created the company's first avenue of research, which quickly expanded to applications for foods and beverages as researchers discovered taste enhancers. Aside from expanding its expertise, the move into developing materials for flavors presents the added advantage of a relatively brief approval process. While clearing a material through the US Food and Drug Administration can sometimes take more than five years, approval of a flavor material via the Flavor and Extract Manufacturers Association's GRAS process costs significantly less and takes just 12–18 months.

### Sweet and Savory/Salt Enhancers

The guiding principle of Redpoint Bio's research is to improve the nutrition and taste of foods and beverages. As Scott Siegel, vice president of corporate development, notes, the ability to reduce sugar and sodium content in products has mutually beneficial health and fiscal ramifications so long as there is no attendant loss of flavor quality. Rather than focusing on cell surface receptors on the tongue, Redpoint Bio's

technology largely works downstream in the cellular pathway, targeting the transmission of receptor signals. The company's enhancers and blockers work, respectively, by holding the TRP5 taste channel open or closed, a phenomenon Siegel likens to "turning the volume up or down" on targeted taste sensations. (There is additional evidence, based on the work of Margolskee and others, that these taste signaling modulators could also be used to treat diabetes and obesity by manipulating the body's metabolic reaction to tastants sensed in the human gut. See: RF Margolskee, J Dyer, Z Kokrashvili, KSH Salmon, E Ilegems, K Daly, EL Maillet, Y Ninomiya, B Mosinger and SP Shirazi-Beechey, T1R3 and gustducin in gut sense

sugars to regulate expression of Na<sup>+</sup>-glucose cotransporter. *Proceedings of the National Academy of Sciences*, **104** (38), 15075–15080.)

In the development of these compounds, the company's research eschews trial and error by applying a pharmaceutical-based approach. Salemme explains: "Instead of having [panelists] taste things, we have a specific receptor that we know is responsible for a particular taste sensation. We can create high-throughput biological assay systems and test tens of thousands of compounds very rapidly and efficiently." Throughout this process, Redpoint Bio has been issued 11



Ray Salemme, CEO

US patents and 15 international patents. More than 70 patents are reportedly pending.

So far, the company's research has led to a partnership with Givaudan for sweet and savory applications. Redpoint's agreements mirror typical biotech industry agreements. The company is strictly focused on discovery, while its partners take on the marketing and commercialization, with milestones and/or royalties paid to Redpoint Bio upon development and commercialization.

### Health, Wellness and Flavor

As the cost of goods and public health consciousness ramp up, and as taste remains the key reason for product acceptance, the largest markets for taste enhancers center on the savory and beverage categories. According to Mariner Analytical data cited by Redpoint Bio, the total estimated global market targeted for taste enhancement exceeds \$1 trillion. On the sweet side, this includes soft drinks, milk products and confectionary, totaling ~\$455 billion. These numbers are particularly significant when considering that 24 million Americans suffered diabetes

in 2007, a figure that is only expected to rise in coming years. On the savory side, this includes soups, prepared foods and snack foods, totaling ~\$565.

Meanwhile, the potential for bitter blockers in liquid and oral-dissolve pharmaceutical formulations is vast. (These materials also have potential applications in foods containing processed soy and cocoa.) The current total market for this category, according to Valeo Partners data cited by Redpoint Bio, is more than \$2.7 billion. Improving the taste of these formulations is of great importance due to their use in pediatric and geriatric applications, in addition to their safety, convenience, and improved efficacy. To underscore the potential, Redpoint Bio points out that unpalatable antibiotic liquid formulations are a top factor for patient noncompliance. The company adds that its blockers can be added to formulations in minute amounts compared to the amount of present active pharmaceutical ingredient in a given dosage.

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