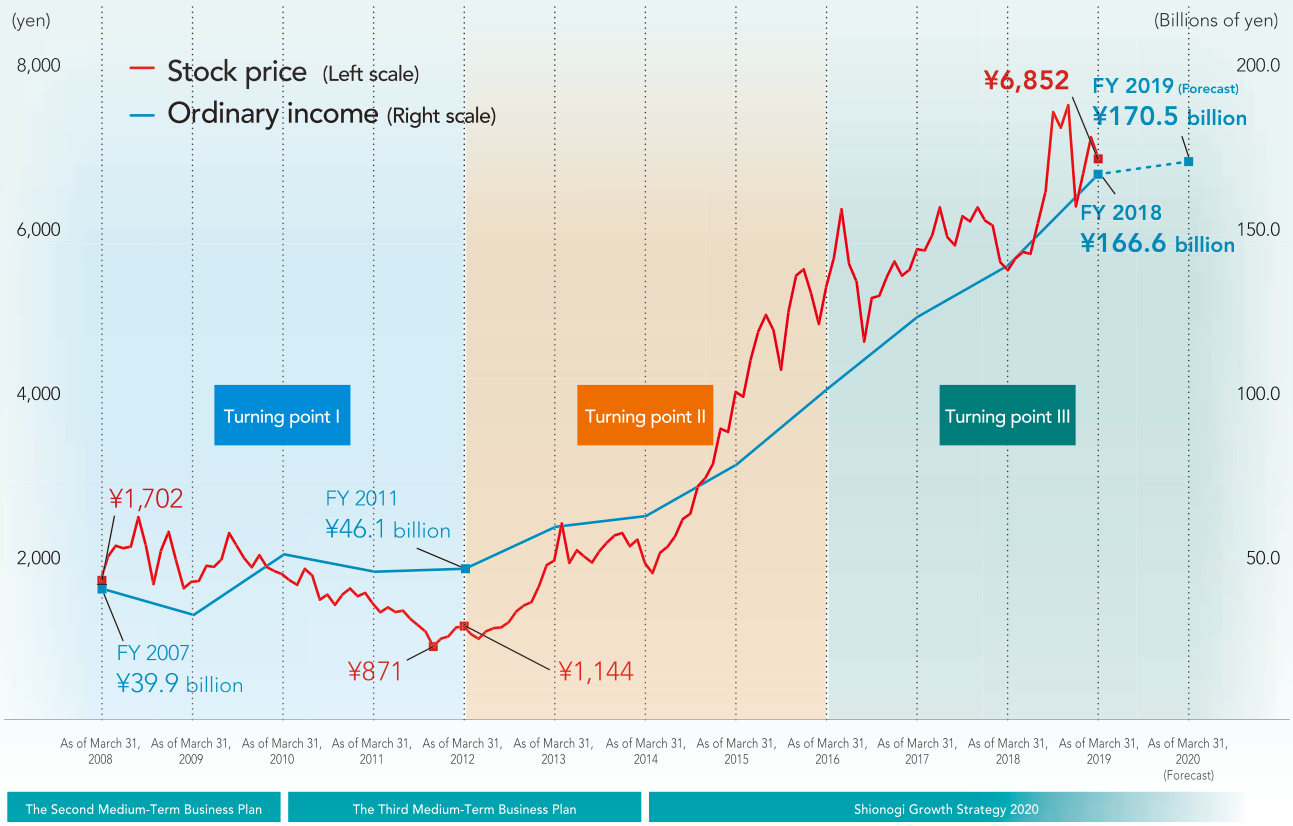
Shionogi's efforts to create sustainable corporate value

–Three key phases of business risk unique to the pharmaceutical sector (FY2008–)–

Shionogi was founded 141 years ago in 1878 as Shiono Gisaburo Shoten, a drug wholesaler in Doshomachi, Osaka. Since then, Shionogi has grown into a major pharmaceutical manufacturer on the back of key accomplishments along the way – the proprietary development of *Shinomin*, a sulfonamide drug; the in-house discovery and launch of *Shiomarin*, the world's first oxacephem antibiotic; and the success of blockbuster drug *Crestor*, a hyperlipidemia treatment. Growth has been driven by the Japanese market, but more recently, Shionogi has made a full-scale push into the US market, starting with the acquisition of US-based drug company Sciele Pharma, Inc. However, business performance deteriorated rapidly not long after the acquisition due to the global financial crisis triggered by the collapse of Lehman Brothers and a series of failures in drug development, ending the prospects of several promising new drugs. *Crestor*, which had been driving earnings, also faced its patent expiry – one of the inevitable challenges of operating in the pharmaceutical sector. Shionogi then had to develop strategies to overcome the so-called "*Crestor* Cliff" to ensure the Group's sustained and steady growth.



Turning point I : Learning — Fiscal 2008-2011

Sciele Pharma acquisition and disruption in US business

On September 1, 2008, Shionogi acquired US-based drug company Sciele Pharma, Inc. for roughly ¥150 billion to support a full-scale push into the US market. However, barely two weeks after signing the deal, the collapse of Lehman Brothers triggered the global financial crisis. Business conditions deteriorated rapidly and Shionogi's share price slumped. In addition, two new drugs that were to be sold via Sciele Pharma dropped out in the final stages of development. All the time and cost expended on the drugs disappeared in an instant, leaving a gap of at least two years in the pipeline before the next drug candidate would be ready for approval. Meanwhile, some drugs sold by Sciele Pharma were approaching patent expiry and the company faced a string of operational issues related to product quality and supply, shaking the confidence of the company's employees.

However, Shionogi's president was unwavering in his belief that overseas markets offered the best business opportunities for the Group. The Company had taken a long time to build up its overseas sales network and there was no desire to step back now. When Shionogi launched proprietary drug *Crestor*, there was no option but to out-license it to UK-based AstraZeneca PLC due to a lack of overseas sales channels, so overseas revenue from *Crestor* was limited to royalty income. In an effort to change that situation, Shionogi decided to acquire Sciele Pharma, but the large acquisition completely changed Shionogi's financial position after being almost debt-free. Between around 2008 and 2011, Shionogi faced sustained challenges at the operational level in the wake of the Sciele Pharma acquisition, but the Company also learned a great deal during that period as it worked to put the US business on an even footing. The US business had operated at a loss until recently and is steadily moving in the right direction.

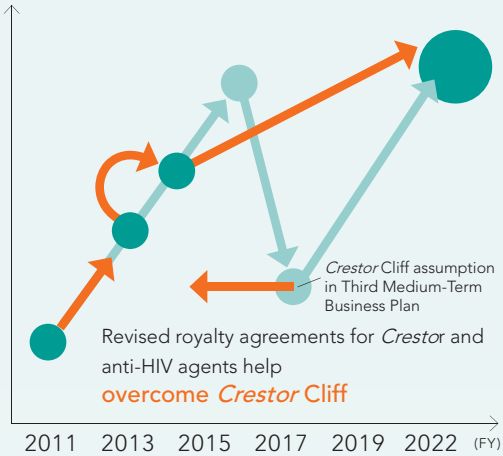
Turning point II : Confidence and Pride — Fiscal 2012-2015

Handling the *Crestor* patent expiry

Crestor became a blockbuster drug in Japan and overseas. In fiscal 2013, its peak year, *Crestor* generated royalty income of ¥65.7 billion on the back of strong sales overseas, driving Shionogi's earnings. However, patent expiry was fast-approaching. Drug developers face the so-called "patent cliff," when the end of patent protection for individual products can lead to a precipitous drop in profits. Products that generate royalty income face an even steeper patent cliff because out-licensed drugs are usually more profitable due to lower costs. Facing the loss of more than ¥60 billion in operating income in just a couple of years, Shionogi needed to do something to take the situation into its own hands, rather than awaiting a fate tied to conditions at another drug company.

In 2013, just three years before the *Crestor* patent expiry, Shionogi and UK partner AstraZeneca PLC agreed to modify the terms of the *Crestor* royalty agreement, lowering the effective royalty rate in return for extending the period of royalty payments until 2023 at the latest. While the new agreement brought forward the *Crestor* Cliff – the biggest issue for management at the time – it ensured Shionogi would continue to receive royalty income from the drug even after the patent expired, providing a source of income to support growth over the medium and long term.

Generating stable profits to support medium- and long-term growth



Anti-HIV agent *Tivicay* – a new growth driver

While efforts were being made to modify the royalty agreement for *Crestor*, Shionogi was also making steady progress with the development of a next-generation of strategic products.

One of those drugs was anti-HIV agent *Tivicay* (dolutegravir), developed in-house and out-licensed to UK-based ViiV Healthcare Ltd. *Tivicay* and combination drug *Triumeq* became blockbuster drugs, together generating global sales of £1.3 billion in 2015, the third year since launch. Despite the phased but large reduction in royalty income from *Crestor*, Shionogi's total royalty income grew to ¥114.9 billion in fiscal 2016. The revenue sharing agreement for *Tivicay* was initially based on the joint development of the drug by Shionogi and ViiV Healthcare, but the agreement was modified in 2012. Shionogi agreed to transfer the commercial rights for *Tivicay* and related products to ViiV Healthcare in exchange for a 10% stake in ViiV Healthcare. As a result, Shionogi started receiving dividend payments as a shareholder in the company, as well as royalty income for *Tivicay*. Dividends increased as ViiV Healthcare's earnings grew, with dividends received by Shionogi exceeding ¥10 billion in fiscal 2015. The changes to *Crestor* and *Tivicay* royalty agreements enabled Shionogi to comfortably overcome the *Crestor* Cliff.

Turning point III : From Complacency to Revival — Fiscal 2016-

Updates to SGS2020

The strong growth in earnings after the *Crestor* Cliff gave our employees' confidence, but there were also signs of a drop in intensity. The modified royalty agreements did not reinforce our underlying business; they had merely shifted the main source of royalty income from *Crestor* to the HIV franchise of dolutegravir-based drugs. Despite that, there was a growing sense of complacency within the Company that we had beaten the *Crestor* Cliff by increasing profits.

At the same time, changes in society and our business environment converged, prompting us to update the Medium-Term Business Plan (SGS2020) in October 2016 in order to sustain growth after 2020. Under the updated plan, we have channeled business resources into areas where Shionogi has a strong position, aiming to grow sustainably as a drug discovery-based pharmaceutical company contributing to a more vigorous society through improved healthcare and helping to solve social issues.

We are now in the final stages of the plan. Based on a shared sense of urgency, every employee is working together to achieve the plan's targets and laying the foundations for the next phase of growth from 2020, which will mean overcoming the "dolutegravir cliff" in about a decade.