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Strategy

Japan's biggest biotech

By Karen Bernstein
Editor-in-Chief

Japanese pharmaceutical companies have historically been thought of as stodgy, insular and opaque, but that is changing fast. One year into the job, **Kyowa Hakko Kirin Co. Ltd.**'s CEO is building his company along lines that would sound familiar to any Western biopharma CEO: growing organically by combining the company's technology — much of which he helped discover — with targets out of academia.

Nobuo Hanai became president and CEO last March. To compete in today's environment, his senior management has concluded KHK must transform itself from a Japan-centric company into a global specialty pharmaceutical player.

To do so, the strategy has four basic components: creating new products based on KHK's core antibody-related technologies; strengthening its competitiveness in Japan in selected disease categories; expanding its business base in the U.S. and Europe; and building a biosimilars franchise.

KHK was created in 2008 through the merger of Kirin and Kyowa Hakko Kogyo Co. Ltd. The newco began its transformation in 2009 when it divested its food business under then-CEO Yuzuru Matsuda. In 2011, the company divested its chemicals business, leaving pharma and biochemicals.

> ***"The history of the company is the president is science-based. This affects the character of the company."***
>
> **Nobuo Hanai, Kyowa Hakko Kirin**

As a result of both moves, total net sales have declined by 28% since FY08, and the company's market cap has hovered around $6 billion for the last four years *(see "Kyowa's Sales by Segment").*

In the same period, however, pharmaceutical sales have grown by 19% to ¥249.7 billion ($3.1 billion).

The company made its first move outside Japan with the 2011 acquisition of ProStrakan Group plc for £292 million ($474 million). The U.K. company provided an EU and U.S. sales force, as well as U.S. and EU rights to pain drug Abstral fentanyl citrate, a sublingual mucoadhesive formulation of the mu opioid receptor agonist from **Orexo AB**, which reacquired the U.S. rights last year *(see BioCentury, Feb. 28, 2011).*

Also in 2012, KHK entered the biosimilars business by forming a joint venture with **Fujifilm Corp.** called **Fujifilm Kyowa Kirin Biologics Co. Ltd.**

KHK released a new medium-term business plan at the end of January. By the end of 2015, the company hopes to launch five new pharma products in Japan and to grow global pharma sales by ¥10.2 billion (4%) to ¥260 billion.

Overall global sales are expected to grow by ¥24.9 billion (7.5%) to ¥358 billion. That includes KHK's biochemical business, which includes amino acids and nucleic acids for use in pharmaceuticals and their intermediates, health foods, dietary supplements and cosmetics.

As the plan comes on line, the company projects only modest growth this year: it forecasts net sales of ¥338 billion ($4 billion), an increase of 1.5%, and operating income of ¥55 billion ($647.1 million), up 4%.

The payoff is slated to come later, after 2015, when KHK hopes to launch its first three home-grown products outside of Japan: Poteligeo mogamulizumab, an anti-CCR4 antibody; istradefylline (KW-6002), an adenosine A2A receptor (ADORA2A)

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agonist for Parkinson's disease (PD); and KRN23, a human antibody against fibroblast growth factor 23 (FGF23) for X-linked hypophosphatemic rickets/osteomalacia (XLH).

Thus, the next several years are all about execution — including testing Poteligeo in multiple cancer indications — after which the big drivers for sales will be Poteligeo and istradefylline.

Not your average CV

Hanai doesn't have the typical CV for a Japanese CEO.

He did a postdoc in biochemical oncology at the **Fred Hutchinson Cancer Research Center**.

He discovered the company's Potelligent technology, which enables commercial-scale production of antibodies free of fucose on their sugar chains. According to KHK, lower fucose content results in up to a hundredfold increase in antibody-dependent cell-mediated cytotoxicity (ADCC) in animal models compared to conventional mAbs.

Potelligent improves Fc receptor binding by increasing a mAb's affinity to Fc gamma receptor IIIa (CD16a; FCGR3A; FcgammaRIIIa), the major Fc receptor for ADCC in humans. The technology also allows lower dosing while decreasing the cost of goods.

In 2003, Hanai started and ran KHK's BioWa Inc. subsidiary in Princeton, which was created to form partnerships in the U.S. with antibody developers interested in Potelligent.

Hanai also led the team that created the second KHK technology that BioWa licenses, called Complegent. It is designed to enhance complement-dependent cytotoxicity of antibodies via isotype chimerism, in which portions of IgG3 are introduced into corresponding regions of IgG1.

Hanai and his research team at KHK also discovered Poteligeo, KW-2871 and benralizumab (KHK4563), a humanized antibody against IL-5 receptor alpha (IL5RA; CD125).

Poteligeo, the first marketed drug that uses Potelligent, was approved in Japan in March 2012 for adult T cell leukemia-lymphoma. A companion diagnostic was approved at almost the same time.

Under a 2008 deal, **Amgen Inc.** has exclusive rights to mogamulizumab for all non-cancer indications outside of Japan, Korea, China and Taiwan.

KW-2871 is a chimeric mAb that binds to GD3 ganglioside, a cell surface antigen expressed on 90% of melanoma cells. KHK licensed it to **Life Science Pharmaceuticals Inc.** in 2007. It is in Phase II trials in malignant melanoma.

Under a 2007 deal, benralizumab is being developed as MEDI-563 outside of Japan and other Asian countries by the **MedImmune LLC** unit of **AstraZeneca plc**.

Benralizumab is in Phase II trials in Japan and Korea to treat asthma. MedImmune has it in Phase IIb trials in severe refractory eosinophilic asthma and in Phase IIa studies for eosinophilic chronic obstructive pulmonary disease (COPD).

Hanai noted KHK's last two presidents also were scientists. "The history of the company is the president is science-based," he told BioCentury. "This affects the character of the company. I'm not a marketing guy, so I have an eye to see the long-term future, not the short-term future."

Indeed, Hanai is focusing the company's strategy on organic growth based on KHK's three technology platforms for the discovery of therapeutic antibodies.

In addition to Potelligent and Complegent, the third platform is the KM mouse, which combines what was Kirin Pharma's technology for producing human artificial chromosomes (HACs) by transferring a fragment of a human chromosome into a mouse with Medarex Inc.'s technology for producing human antibodies. Medarex is owned by **Bristol-Myers Squibb Co.**

"Technology is the key to success," Hanai said. "Kyowa Hakko Kirin is not a global big pharma. It's not a small biotech company. But as long as we have strong technology, we will have good relationships with academics in Japan and the U.S. The basic model is getting targets out of academia and applying our technology."

KHK typically looks for novel targets at academic institutions and then applies its technologies to develop molecules against those targets.

Hanai cited Poteligeo as an example.

"I approached a **University of Tokyo** scientist, Dr. Koji Matsushima, and said we have Potelligent, you have chemokine technology, let's work together. That became the molecule that was just approved," he said. Matsushima is a professor in the department of molecular preventive medicine.

Benralizumab's target also came out of Japanese academia, and KHK made a humanized mAb using Potelligent.

Although KHK hasn't disclosed its collaborator, University of Tokyo professor Kiyoshi Takatsu published multiple papers in the early 1990s describing the cloning and characterization of IL5RA. Takatsu filed patents covering the discoveries and subsequently was named on patents filed by KHK covering the development of antibodies against the receptor.

The cloning and characterization of the receptor at roughly the same time also was reported in a series of separate publications by a team of **Roche** scientists.

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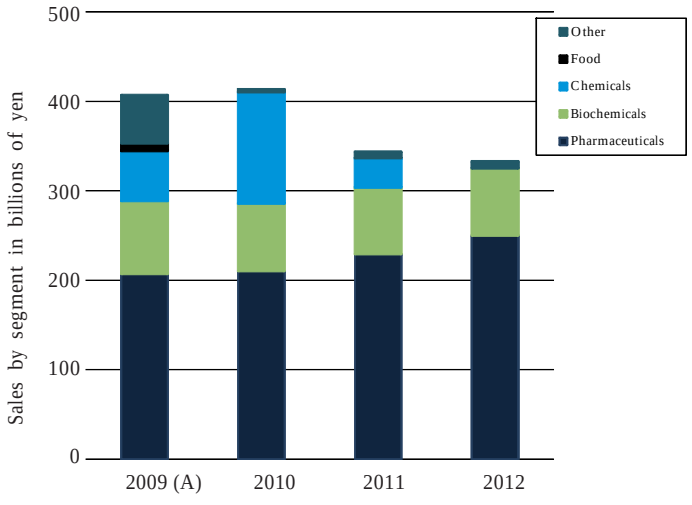
Kyowa's sales by segment

Over the last four years, **Kyowa Hakko Kirin Co. Ltd.** (Tokyo:4151) has simplified its business to focus on two main revenue streams — pharmaceuticals and biochemicals. Since 2010, total sales have declined by 19% to ¥333.2 billion ($4.2 billion) in 2012, as KHK shed its food business in 2009 and its chemical business in 2011. Pharmaceutical sales, however, have risen 19% to ¥249.7 billion ($3.1 billion) in the same period. Figures represent sales to external customers and do not include sales within KHK. (A) Adjusted to reflect calendar year — KHK changed its fiscal year end from March 31, 2010, to Dec. 31, 2009; *Source: Kyowa Hakko Kirin*



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KHK's key academic relationship in the U.S. is with the **La Jolla Institute for Allergy & Immunology**. "We have had a good relationship with La Jolla for over 20 years," Hanai said. "Our research facility is in the same building so the scientists can communicate easily. Our technology and their science has become our pipeline."

As an example Hanai cited KHK's anti-LIGHT antibody. "The molecule was discovered by La Jolla scientists. We used our KM Mouse to produce the antibody. Then we invited **Sanofi** for development. This is our style."

In 2009, KHK granted Sanofi exclusive worldwide rights to the human mAb against tumor necrosis factor ligand superfamily member 14 (TNFSF14; LIGHT; CD258), except in Asia where the companies share co-development rights and KHK has marketing rights.

SAR252067 is in Phase I trials in Crohn's disease and ulcerative colitis (UC).

KHK's business development group also looks for very early technology as well as later-stage opportunities.

"I will fight for a late-stage or mid-stage compound, but I want to keep the research pipeline full. That's essential for Kyowa Hakko Kirin to survive for the future," said Tamao Watanabe, head of global licensing and business development. "We have a team dedicated to early stage. Usually Japanese companies focus on later stage. We want to do both. Business development and research are the two wheels to go forward."

At least 17 of the 25 compounds that KHK or its partners have in the clinic are against novel targets. The company's R&D is split about 50-50 between antibodies and small molecules *(see "Kyowa's Pipeline," online)*.

Indeed, to be successful, it is clear KHK will have to make good on first-in-class or best-in-class molecules. Its five biggest products today represent an aging portfolio of which three drugs come from the Amgen-Kirin side of the merger and two come from the Kyowa Hakko side. Together they accounted for ¥135.9 billion ($1.7 billion), or 54% of 2012 pharmaceutical sales *(see "Kyowa's Top 5 Drugs")*.

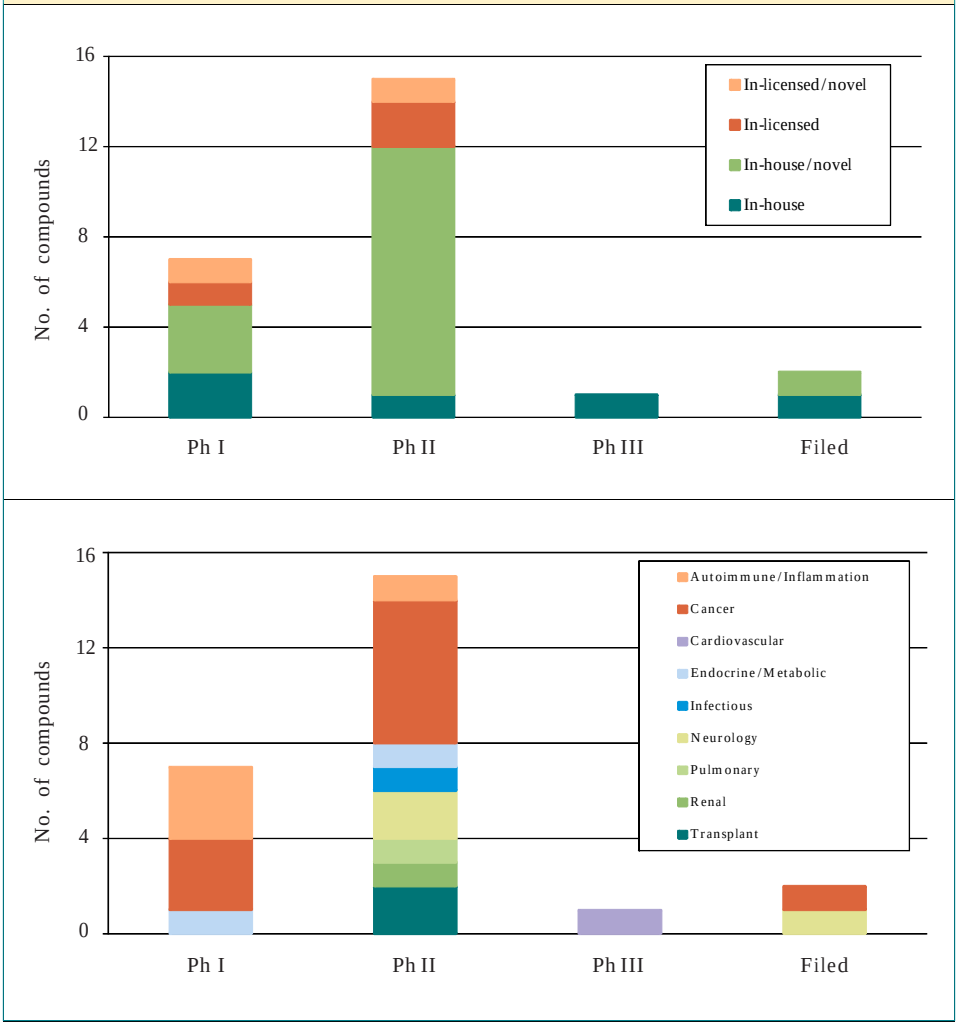
That success also requires turning ProStraken from a loss-making entity into a profitable one. The unit had 2012 sales of £129 million ($204.8 million) — mainly from Abstral for pain, Sancuso granisetron for chemotherapy induced nausea and vomiting (CIMV) and Rectogesic nitroglycerin ointment for pain associated with anal fissures — but an operating loss of £19 million ($30.2 million).

For 2013, KHK projects ProStraken sales of £154 million ($254 million) and an operating loss of £4 million ($6.6 million). By 2015, the company expects net sales above ¥20 billion ($235 million) and operating income above ¥2.5 billion ($29.4 million).

Kyowa's pipeline

Kyowa Hakko Kirin Co. Ltd. (Tokyo:4151) and its partners have at least 25 compounds in clinical development, excluding line extensions and drugs already marketed by the Japanese pharma in various territories. Twenty of the compounds were generated internally, while five were in-licensed. At least 17 of these are against a novel target — one to which no marketed drug binds. The majority — 10 — are in development for cancer. *Source: Kyowa Hakko Kirin*

Click here to view the Kyowa pipeline



Looking early

The company also is looking at new therapeutic modalities. "It's important for pharma companies to think of using new therapeutic technology like iPS and siRNA," said Hanai.

KHK has two RNAi deals: a 2008 product deal with **Alnylam Pharmaceuticals Inc.** and a 2010 technology deal with **Dicerna Pharmaceuticals Inc.**

The Alnylam deal gives KHK rights in Asia to ALN-RSV01, a respiratory syncytial virus-specific short interfering RNA (siRNA) that has completed Phase IIb testing to treat RSV. Alnylam CEO John Maraganore said the company plans to seek a partner before moving into Phase III testing; KHK is considering clinical trials in Japan, according to spokesperson Kazuhide Hasegawa.

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The second deal gives KHK worldwide rights to therapeutics using Dicerna's Dicer Substrate siRNA (DsiRNA) technology against a cancer target from KHK. In December 2010, KHK exercised an option to add immunology and inflammation indications.

"There's nothing yet in the clinic, but the research is going along very well," Hanai said. "We bring our internal liposome delivery technology — delivery is an issue for RNA. Having patience is important."

Indeed, a look at the deals KHK has done indicates it is heavy with early stage partnerships: eight of the 13 deals done since 2010 are research/technology deals *(see "Kyowa's Deal Flow").*

Unlike Japanese pharmas such as **Astellas Pharma Inc.**, which has moved its R&D core to the U.S., KHK plans to keep major hubs in both Japan and the U.S.

"For us, the Japanese market is still very important, so the center of development is in Tokyo," Hanai said. "It is possible that in the future we would move our center of development to the U.S. It depends on the stage of the company — which market is most important to us."

He added: "You need face-to-face communication. If we want to get good discoveries from academics, we need to be here. We also have a research force in California. So we need research in Japan and the U.S."

KHK also is focusing on improving manufacturing — though mostly for biosimilars, since changing the manufacturing process for existing drugs would likely require new clinical trials. The company has 200 scientists at its Bioproduction Research Technology Institute, which is focused on bioprocessing.

"The biosimilars business is a highly competitive area," Hanai said. "But we already have experience with the production of biologics and we can continue to make new technology. I think only limited companies can develop high-quality biosimilars."

Steady growth

KHK, which has a market cap of $6.3 billion, does not have M&A as a centerpiece of its growth strategy.

"Kyowa Hakko Kirin is different than Takeda," Hanai said. "Their strategy is M&A. We did M&A with ProStrakan, but they're a small company."

Kyowa's top five drugs

The top five drugs from **Kyowa Hakko Kirin Co. Ltd**. (Tokyo:4151) accounted for ¥135.9 billion ($1.7 billion) in sales, or about 54% of total net sales from the pharmaceuticals segment. *Source: Kyowa Hakko Kirin*

Product	2012 sales Yen B	2012 sales $M	Chg from 2011
Nesp darbepoetin alfa/Espo epoetin alfa	¥62.0	$775.0	0%
Allelock olopatadine	¥29.9	$373.8	3%
Coniel benidipine	¥17.1	$213.8	-13%
Gran filgrastim	¥13.5	$168.8	-9%
Regpara cinacalcet	¥13.4	$167.5	17%
Total	**¥135.9**	**$1,698.8**	

This translates into a build-it-yourself mentality.

"Our basic strategy for globalization is based on our technology and pipeline. This is different from a strategy of M&A. I don't think this is a time for that. We need to integrate ProStrakan and Kyowa Hakko Kirin first," said Hanai.

He added: "We don't buy sales just for making our financials better. We want to grow organically — sell products we created ourselves. There should be steady growth, not a risky jump ahead."

The company also is protecting itself against the pressures on pharmaceutical pricing via a two-pronged drug development strategy.

"In the future [the industry] may not have the high returns of the past," Hanai said. "Our strategy is, one, to keep our technology innovative — that's the high return strategy. And, two, we started a biosimilar business — it's not high return, but it is a certain, i.e., a sure, return. A mixed strategy is very important for the new era of the pharma business."

Hanai is banking on biosimilars to cover revenues gaps in product approvals.

The company currently has plans for four biosimilars, and expects to put one per year into the clinic. In 1H13 it plans to begin European trials of a biosimilar of Humira adalimumab, an anti-TNF from **AbbVie Inc.** that goes off patent in Europe in 2018.

"We want to be one of the first players when the patent expires," said Hanai.

"We want to meet European and Japanese guidelines," he added, noting "the U.S. pathway isn't clear yet."

The company plans to put a biosimilar of **Genentech Inc.**'s Avastin bevacizumab into the clinic in 2014 and hasn't disclosed the other two molecules. Avastin goes off patent in the U.S. in 2019 and around the same time in Europe, according to Genentech.

KHK plans to focus its biosimilars business in the mature markets because it doesn't believe it can compete against what it sees as lower-quality competition in emerging markets.

"Our strategy for biosimilars is the U.S., Europe and Japan," Hanai said. "Currently we don't think we will sell our biosimilars in emerging markets because we guarantee very high quality and that means some cost."

KHK's due diligence on data for biosimilars in emerging markets led to Hanai's conclusion. "We checked their quality — and that would not be able to be sold in the U.S., Japan or Europe," he said. "We can't compete in emerging markets where there are low-quality biosimilars."

Outside of these geographies, the company will make decisions compound by compound.

"We sell in China, Taiwan, Korea, but we have no plan to expand our territory," Hanai said. "We will not expand into Africa or the Islamic countries without a partner. ProStrakan may be able to handle Eastern Europe, but they're not there yet."

Inside Japan

KHK launched two new products in Japan in 2012: Poteligeo and Parkinson's drug Apokyn apomorphine, which it licensed from **Stada Arzneimittel AG** in 2006.

The company hopes to launch three new products in Japan this year: Abstral (KW-2246) for breakthrough cancer pain, istradefylline (KW-6002) for PD and saxagliptin for Type II diabetes.

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KHK filed last year for both Japanese and U.S. approval of istradefylline. Also last year, it refiled for Japanese approval of Abstral after the regulators asked for more data. The company has Japanese rights to Abstral from Orexo and will co-market it with **Hisamitsu Pharmaceutical Co. Inc.**

Partner **Otsuka Pharmaceutical Co. Ltd.** last year filed for Japanese approval of saxagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor developed by BMS. Otsuka granted marketing rights to KHK last year.

In addition, KHK plans a Japanese regulatory submission this year for pegfilgrastim long-acting G-CSF (KRN125) for chemotherapy-induced febrile neutropenia. And by 2015 it hopes to launch a fifth product in Japan, recombinant antithrombin (KW-3357).

Meanwhile, the company will hold down costs by not increasing the size of its sales force. Thus, KHK doesn't plan to add to its 1,400 sales reps in Japan even if it launches two or three products this year.

"In the past we would have increased the number of reps," said Hanai.

Moving forward, KHK wants to strengthen its Japanese presence in four disease areas: nephrology, which includes diabetes and hypertension; oncology; CNS; and immunology and allergy.

In the nephrology space, the company is enhancing its presence in chronic kidney disease (CKD) and maintaining its leading share in the renal anemia therapy market where its NESP erythropoiesis stimulating agent (ESA) has the leading market share; expanding the market for Regpara cinacalcet to treat secondary hyperparathyroidism; and launching saxagliptin. KHK has rights to Regpara from **NPS Pharmaceuticals Inc.**

In oncology, KHK wants to build out its position in hematology, primarily by establishing Poteligeo, accelerating development of tivantinib (ARQ-197) from **ArQule Inc.**, and enhancing its presence in cancer support therapies through the launch of pegfilgrastim.

Tivantinib is a c-Met inhibitor in Phase II in Japan for EGFR-receptor mutated lung cancer and in Japan and Korea for gastric cancer.

ArQule is developing it elsewhere with **Daiichi Sankyo Co. Ltd.** The partners just started Phase III testing in hepatocellular carcinoma (HCC). The compound has failed trials in combination with Tarceva erlotinib in non-small cell lung cancer (NSCLC) and in combination with Erbitux cetuximab in metastatic colorectal cancer.

In CNS, KHK wants to expand products for PD and quickly launch Apokyn, as well as develop KHK6188, an agonist of cannabinoid CB2 receptor (CNR2) that is in Phase II trials for neuropathic pain.

In immunology and allergy, KHK wants to enhance its presence in dermatology/otorhinology. This includes accelerating development of benralizumab and KHK4827, an anti-IL-17 antibody in Phase II trials in psoriasis.

However, immunology/allergy is the only one of the four disease areas in which KHK is projecting lower sales in 2015 than in 2012, based on the entry of generic competition for the company's core allergy product, the antihistamine Allelock, in December 2012.

> ***"I will fight for a late-stage or mid-stage compound, but I want to keep the research pipeline full. That's essential for Kyowa Hakko Kirin to survive for the future."***
>
> **Tamao Watanabe, KHK**

Meanwhile, KHK is looking for some cushion from its amino acids business, using logic similar to its expectations for biosimilars.

"It's not high return, but we are expanding our share," said Hanai.

The amino acids business did ¥20.2 billion ($252.5 million) in sales last year and KHK is forecasting ¥22.6 billion this year. The company estimates it had a 30% share of the 30,000-ton global amino acids business in 2010. By 2020 it wants to increase that share to 40% of what it estimates will be a global market of more than 50,000 tons.

"We get over 20% gross margins from a new drug, and 10% for the biosimilar and amino acid businesses," Hanai noted. "Operating profit on sales of pharma is about 20%."

As part of its strategy for confronting the growth challenges of the mature markets, KHK also is looking at new combinations of players and new ways of pricing drugs.

"We can't stay with the original pharma model," said Hanai. "KHK's partners may not always be typical pharma companies or biotechs. We may need to invite other companies that have advanced technology in different fields such as medical devices, chemicals and nanotech — it will be a new page of pharma R&D. We need to think differently than in the past to create a new paradigm."

He added: "Pricing will be very important. Payment based on patient outcomes is probably core for the future. Package pricing [bundling] — how to get profit from it — is the new challenge."

COMPANIES AND INSTITUTIONS MENTIONED

AbbVie Inc. (NYSE:ABBV), Chicago, Ill.
Alnylam Pharmaceuticals Inc. (NASDAQ:ALNY), Cambridge, Mass.
Amgen Inc. (NASDAQ:AMGN), Thousand Oaks, Calif.
ArQule Inc. (NASDAQ:ARQL), Woburn, Mass.
Astellas Pharma Inc. (Tokyo:4503), Tokyo, Japan
AstraZeneca plc (LSE:AZN; NYSE:AZN), London, U.K.
Bristol-Myers Squibb Co. (NYSE:BMY), Princeton, N.J.
Daiichi Sankyo Co. Ltd. (Tokyo:4568; Osaka:4568), Tokyo, Japan
Dicerna Pharmaceuticals Inc., Watertown, Mass.
Fred Hutchinson Cancer Research Center, Seattle, Wash.
Fujifilm Corp., (Tokyo:4901), Tokyo, Japan
Fujifilm Kyowa Kirin Biologics Co. Ltd., Tokyo, Japan
Genentech Inc., South San Francisco, Calif.
Hisamitsu Pharmaceutical Co. Inc. (Tokyo:4530; Osaka:4530), Tosu, Japan
Kyowa Hakko Kirin Co. Ltd. (Tokyo:4151), Tokyo, Japan
La Jolla Institute for Allergy & Immunology, La Jolla, Calif.
Life Science Pharmaceuticals Inc., Greenwich, Conn.
MedImmune LLC, Gaithersburg, Md.
NPS Pharmaceuticals Inc. (NASDAQ: NPSP), Parsippany, N.J.
Orexo AB (SSE:ORX), Uppsala, Sweden
Otsuka Pharmaceutical Co. Ltd., Tokyo, Japan
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Sanofi (Euronext:SAN; NYSE:SNY), Paris, France
Stada Arzneimittel AG (Xetra:SAZ), Bad Vilbel, Germany
University of Tokyo, Tokyo, Japan

Kyowa's deal flow

Since 2010, **Kyowa Hakko Kirin Co. Ltd.** (Tokyo:4151) has done at least 13 pipeline building deals. Nine were discovery or preclinical stage. Most recent deals at top. (A) JV between Kyowa and **Amgen Inc.** (NASDAQ:AMGN); *Sources: BCIQ: BioCentury Online Intelligence; Kyowa Hakko Kirin*

Partner/ acquisition	Deal type	Description	Financials	Status at time of deal	Date
Adimab LLC	Research collaboration	Identify antibodies against two targets selected by Kyowa; initial focus on an undisclosed membrane protein target	Undisclosed research fees and technical milestones; Adimab eligible for undisclosed clinical milestones and royalties on antibodies licensed by Kyowa	Discovery/ Preclin	Jan-13
NovAliX S.A.S.	Research collaboration	Use NovAliX's Graffinity fragment-based screening technology to discover and develop small molecules against undisclosed protein-protein interaction targets chosen by Kyowa	Undisclosed technology access fee, research funding, milestones	Discovery/ Preclin	Jan-13
Shionogi & Co. Ltd. (Tokyo:4507; Osaka:4507)	Research collaboration	Use GlycanMap technology from Shionogi's Ezose Sciences Inc. subsidiary to conduct glycomics studies	ND	Discovery/ Preclin	Jan-13
Genmab A/S (CSE:GEN)	Research collaboration	Use Genmab's DuoBody technology to create bispecific antibodies against undisclosed target from Kyowa	Undisclosed up front plus research funding	Discovery/ Preclin	Dec-12
Activiomics Ltd.	Research collaboration	Use Activiomics' Targeted In-depth Quantification of Cell Signaling (TIQUAS) mass spectrometry technology to identify signaling mechanisms of lead compounds from Kyowa	ND	Discovery/ Preclin	Nov-12
Anchor Therapeutics Inc.	Research collaboration	Use Anchor's pepducin technology to advance Kyowa's GPCR drug discovery portfolio; partners also will develop pepducin therapeutics and use the pepducin technology to co-develop research tools	Undisclosed up front, research funding, milestones	Discovery/ Preclin	Jul-12
Fujifilm Holdings Corp. (Tokyo:4901)	JV	50/50 JV to develop biosimilars	ND	Discovery/ Preclin [now plan to start clinical testing 1H13]	Mar-12
ImmunoCellular Therapeutics Ltd. (NYSE-M:IMUC)	Newco	Launches newco **Caerus Discovery LLC** with Kyowa's BioWa Inc. subsidiary; Caerus uses combinations of adjuvants, high zone tolerance and subtractive immunization to identify targets for cancer, autoimmune, inflammatory and infectious diseases	ImmunoCellular gets undisclosed equity stake in Caerus for contributing antibody technologies; BioWa, which provides program support, gets rights to technologies developed by the newco	Discovery/ Preclin	Jun-11

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Kyowa's Deal Flow,
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Partner/ acquisition	Deal type	Description	Financials	Status at time of deal	Date
ProStrakan Group plc	M&A	Gains EU and U.S. sales force and ProStrakan's specialty pharmaceutical products, including pain drug Abstral fentanyl	£292M ($474M) in cash	Mkt	Feb-2011 (prop); Apr-2011 (compl)
Kirin-Amgen Inc. (A)	In-license	Exclusive rights to AMG 827 (KHK4827) in Japan and certain countries in Asia, including China; AMG 827 is a human mAb against IL-17 receptor to treat autoimmune diseases	ND	Ph I in Japan [now Ph II in Japan]	Jan-11
Solasia Pharma K.K.	In-license	Exclusive rights in Taiwan, Hong Kong, Singapore and Malaysia to market Sancuso granisetron patch (SP-01), which is approved in the U.S. to treat chemotherapy-induced nausea and vomiting (CINV); Solasia received rights from ProStrakan Group under a 2008 deal	Undisclosed up front, milestones	Preparing filing [now filed in Asia]	Mar-10
Dicerna Pharmaceuticals	Research collaboration	Exclusive, worldwide rights to therapeutics using Dicerna's RNA (DsiRNA) technology against an undisclosed cancer target; Kyowa exercises option in December 2010 to add immunology and inflammation indications to deal; Kyowa exercises option in December 2011 to add undisclosed oncology target to deal	$4M up front, $120M in research funding and has right to add 11 undisclosed targets, for which Dicerna is eligible for $120M per target; Dicerna has option to co-promote compounds against the initial target in the U.S. and is eligible to share profits	Discovery/ Preclin	**Jan-10**
Reata Pharmaceuticals Inc.	In-license	Exclusive rights in Japan, China, Taiwan, Korea and Southeast Asia to Reata's bardoxolone for cardiovascular, renal or metabolic diseases; the small molecule activator of nuclear factor (erythroid-derived 2)-like 2 (NFE2L2; NRF2) is in development to treat chronic kidney disease (CKD) in patients with Type II diabetes; additional indications in the licensed territories will be co-developed	$35M up front, $237M in milestones, plus double-digit royalties	Ph I in Japan [now Ph II in Japan]	Jan-10