Unlocking the Secrets to Successful Japan Market Entry

FEB 10, 2022

HEADLAND STRATEGY GROUP

Photo by Nicki Eliza Schinow- Unsplash

Today's Speakers

ANDREW
MCKEE

MD,
Founder,
CEO

- Based in the SF Bay Area
- Ex-Genentech, McKinsey, Google
- Passionate about creativity, teams, learning, inclusivity, and high-quality solutions
- Japanese: intermediate

KEN
SHIMOKAWA

PhD,
BD/M&A
Expert, Sr. EM

- Based in the SF Bay Area
- 25+ years' experience (BD/M&A, VC, R&D, consulting)
- Ex-Santen, Astellas
- 23 VC or Partnering-stage deals
- Japanese: native fluency

AKIHIKO (AKI)
WATANABE

PhD,
Senior
Consultant

- Based in Japan
- 35+ years' experience (BD/Open Innovation, R&D, Commercial, Consulting)
- Ex-Teva Japan, Kyowa Kirin, Bayer, NapaJen
- Japanese: native fluency

LUDWIG
KANZLER

PhD,
CEO of Hanegi
Solutions

- Based in Japan
- 25 years' experience
- Japan regulatory, pricing, marketing & sales expert
- Longtime Headland collaborator
- Former Partner, McKinsey & Company (Tokyo office)
- Japanese: fluent

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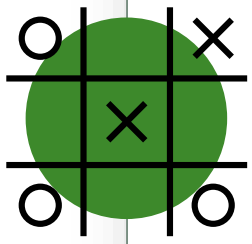
Typical questions we hear from our clients about Japan



Commercial and market planning

- ❑ How big is the overall opportunity?
- ❑ How do the patient journey, prescriber behavior differ from other markets?
- ❑ What reimbursement price can we get?
- ❑ When should we sequence a Japan launch?

BD/M&A and partnering

- ❑ Do we need a partner? If yes, at which stage?
- ❑ What are the pitfalls of partnering vs. going alone? How would we manage them?
- ❑ Who would be the best partner? How do we get the best potential partners interested in us?
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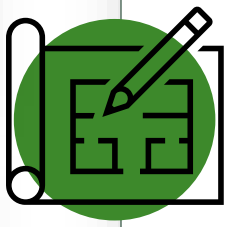

Trial design and PMDA

- ❑ Can we include Japan in a global Phase III trial and go for simultaneous submission?
- ❑ Do we need to do a PK/PD bridging study? If yes, how and where?
- ❑ How do we achieve fast and effective alignment on our approach with the PMDA?
- ❑ What are the pros/cons of pre-consultation vs. full consultation with PMDA?
- ❑ How quickly can we enter the market with a regenerative medicine program?
- ❑ How do we navigate the Japanese business culture and/or language?

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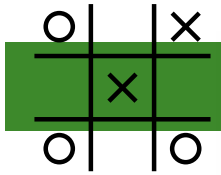
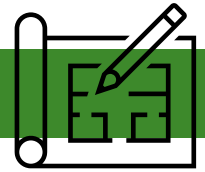
For Japan, our clients have 4 key needs



Commercial planning

- ❑ Revenue forecasting
- ❑ Primary market research (qualitative, quantitative) – MDs, patients, etc.
- ❑ Patient journey mapping
- ❑ TPP testing
- ❑ Launch pricing, market access



Trial design ± PMDA engagement

- ❑ Global trial program strategy including Japanese patients
- ❑ Trial design vetting with KOLs
- ❑ PMDA engagement, strategy (pre-consultation, full consultation)

BD/M&A, Partnering

- ❑ Cross-border partnering
- ❑ Pitch deck overhaul
- ❑ Due diligence support (e.g., aNPVs, revenue forecasts, benchmarking, scenario analysis)
- ❑ Negotiation strategy and/or facilitation

End-to-end Japan entry support

- ❑ 2-year or longer support duration
- ❑ Team composition flexibly shifts as functional needs, deliverables shift over time

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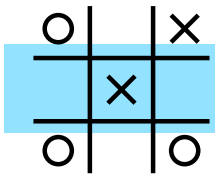
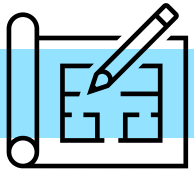
Preview of secrets we'll unlock today



Commercial planning

- ✓ Epidemiology, patient journey, and prescriber behavior can differ significantly vs. outside Japan
- ✓ MHLW pricing algorithms need to be carefully navigated
- ✓ Distributors have much more influence and broader capabilities vs. outside Japan



Trial design ± PMDA engagement

- ✓ It's possible to negotiate strategically with PMDA regarding global trial plans
- ✓ A well-prepared pre-consultation may prevent a full consultation
- ✓ You'll need help from an agency physically in Japan for PMDA interactions

BD/M&A, Partnering

- ✓ The business culture may seem impenetrable, but patience, respect, and sensitivity pay off
- ✓ Partners highly value long-term relationships and quality in their interactions and plans
- ✓ "Going alone" in Japan is becoming increasingly common

The Japanese market may seem like a black box. But the right consultancies and partners can ensure your success

HEADLAND STRATEGY GROUP

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Headland Strategy Group: Brief intro

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Japan: The opportunity

.03

Overcoming challenges of entry

.04

Going alone: wholesaler insights

.05

Q&A, wrap up

Agenda

.01

Headland Strategy Group: Brief intro

At Headland Strategy Group, **we empower growth strategy for therapeutics and diagnostics innovators**

Photo by Robert Gomez - Unsplash

We help our clients answer 3 fundamental growth questions

COMMERCIAL STRATEGY

How to commercialize innovative new products?

CORPORATE DEVELOPMENT

How to grow through deals (BD/M&A) and fundraising?

PORTFOLIO, R&D STRATEGY

How to invest in creative, compelling R&D strategies?

HEADLAND STRATEGY GROUP

We serve some of the most innovative firms on the planet

United States / Europe

Japan / Asia

Note: if/as needed, Headland Strategy Group uses an ethical screen ("firewall") policy, effective January 1 2020, to separate staff and information serving two different clients.

HEADLAND STRATEGY GROUP

Our Japan credentials: Local office, seasoned team, extensive relationships, and excellent track record

Shonan iPark, Japan

*OFFICE**

iPark Shonan

LINK-J

YEARS **65+**

Combined experience working for and consulting to **Japan-based** life science companies

5 TEAM MEMBERS

Fluent in **Japanese and English**, including for BD/M&A, PMDA meetings, and commercial primary market research

OUR PERFORMANCE:

100%

success rate for Japan-related projects **since our founding** (2017)

10

Ongoing/recent clients based in Japan

$950M

cumulative deal value creation involving Japanese life science companies

8

Total deals supported involving Japanese life science companies

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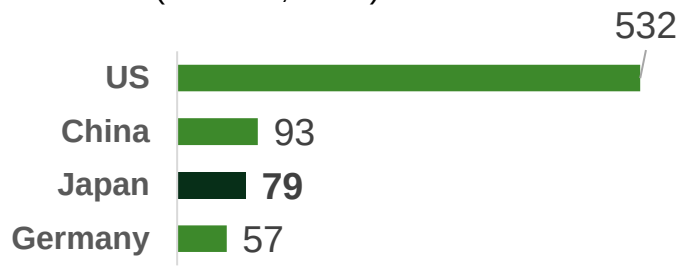
Japan:
The opportunity

Japan is the 3rd largest global pharma market, driven by fundamentals and despite recent slow economic growth

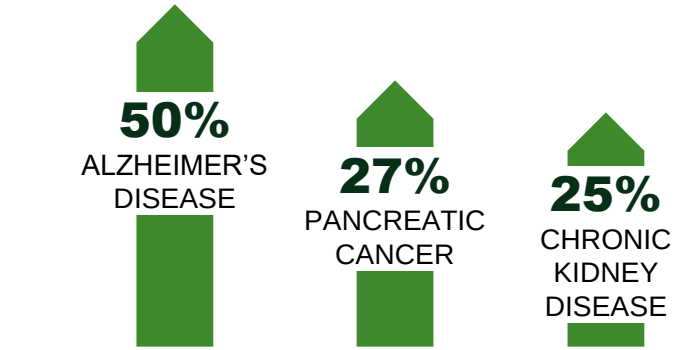
LARGE HEALTHCARE MARKET OPPORTUNITY

3rd Largest Pharma Market[1]
($B USD, 2020)



STRONG MEDICAL AND DEMOGRAPHIC DRIVERS

Aging population[2] (28% over 65)



Rising prevalence, select diseases[3] (2009-2019)

Pricing is usually **similar to or higher than EU**

Typically, fast uptake; highly receptive to **innovative new drugs**

Generally, coverage is widespread for any MHLW-approved medicine*

Various financial protections to **limit patient co-pay / out-of-pocket exposure**

* The Pharmaceutical and Medical Device Agency (PMDA) is an independent agency that makes recommendations for approval by Japan's Ministry of Health, Labor and Welfare (MHLW)

1. July 2021 IQVIA Survey - Market share of top 10 national pharmaceutical markets worldwide in 2020
2. "Statistical Handbook of Japan 2020" published by the Statistics Bureau of Japan
3. Japan Institute for Health Metrics & Evaluation

Examples of companies that have entered Japan skillfully and driven growth

ultragenyx	**Key strategic partnerships** to advance clinical and commercial operations in Japan; now, **plans to open a Japan affiliate**	**$65M** initial equity investment from Takeda to combat rare diseases in 2016	**$200M** deal granting Daiichi Sankyo access to gene therapy manufacturing platform	At JPM 2022, announced plans to open a commercial presence in Japan
Incyte	**Since 2017, has operated independently in Japan** with numerous regulatory approvals	**4 PMDA approvals** since 2017. Including Pemazyre for Biliary Tract Cancer (BTC, 2021) and Tabrecta (NSCLC, 2020)	Received **$20M** milestone payment with the PMDA's approval of Tabrecta	Received **$40M** in milestones for PMDA approvals (Jakavi, MF; Olumiant, RA)
Amicus Therapeutics	**Since 2016, has operated independently in Japan,** launched Galafold in 2018, with ongoing revenue growth	**First and only oral therapy approved** to treat Fabry Disease in Japan	**43% YoY revenue growth** in 2020 due in-part to strong patient demand in Japan	**17% YoY revenue increase** in 2021, plus double-digit guidance for 2022

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Overcoming challenges of entry

Japan: numerous challenges to overcome

Pricing, market access

- MHLW's pricing/reimbursement algorithms require expertise to navigate
- MHLW requires annual price erosions for branded drugs

PMDA interactions

- PMDA can seem intimidating to non-Japanese
- PMDA interactions require expertise and native-level fluency
- Requires in-country presence and real-time interpretation

Commercial and development planning

Compared to other major markets:

- Addressable epidemiology can be much higher/lower
- Diagnosis and/or treatment patterns can differ significantly
- MD areas of focus and treatment settings can differ

Doing business in Japan

- Partnering can feel like a black box
- Unfamiliar language and business culture norms, mores

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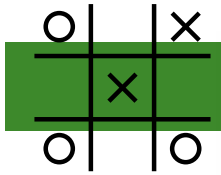

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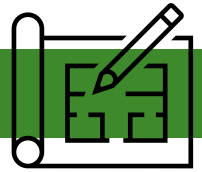

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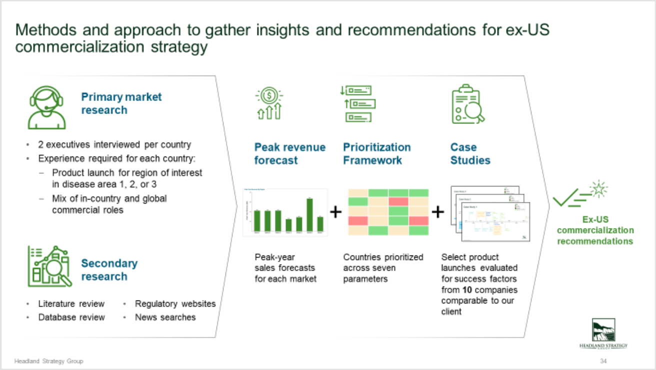
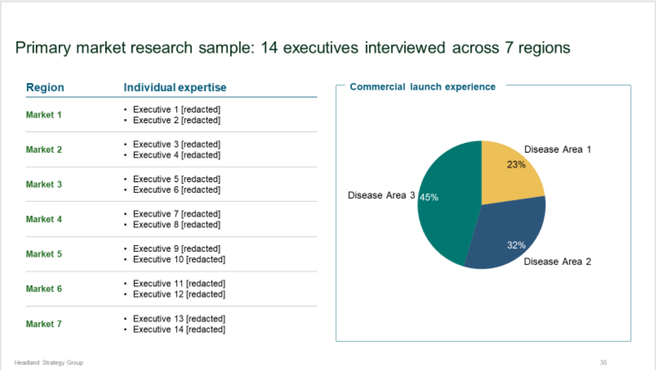
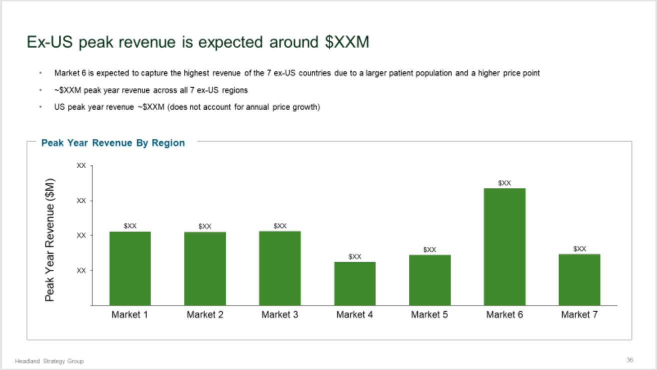
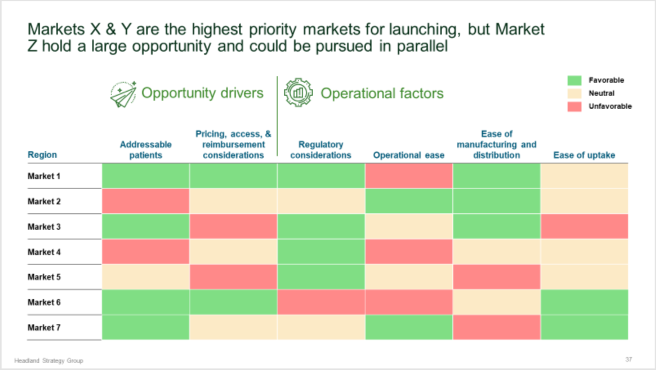
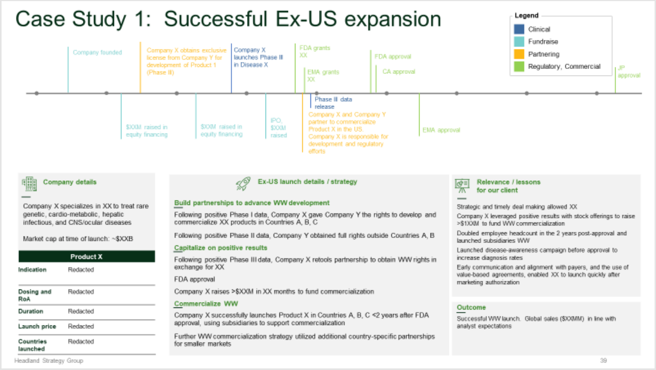
Case Study: Ex-US commercialization strategy for an oncology-focused US biotech

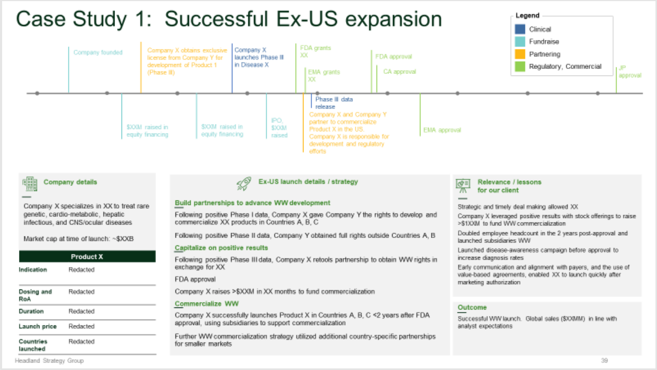


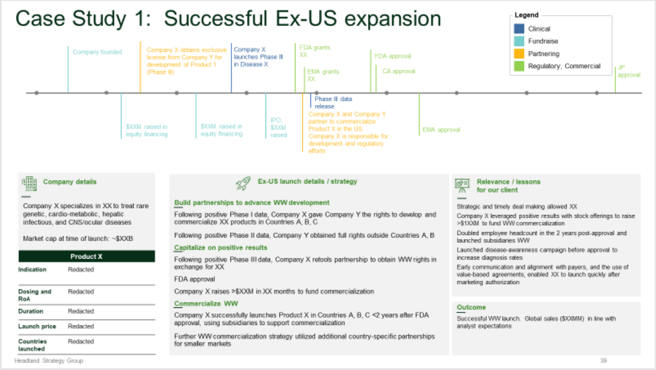












How was our work unique and important?

- We evaluated key commercialization elements in 7 markets (European and Asian) to inform ex-US commercialization strategy
- We used a multipronged approach to paint an exhaustive picture of the commercial investment and risks involved, plus potential benefits in each ex-US market
- Our findings informed launch order and partnering recommendations in each market, and the investment needed to pursue each strategic option

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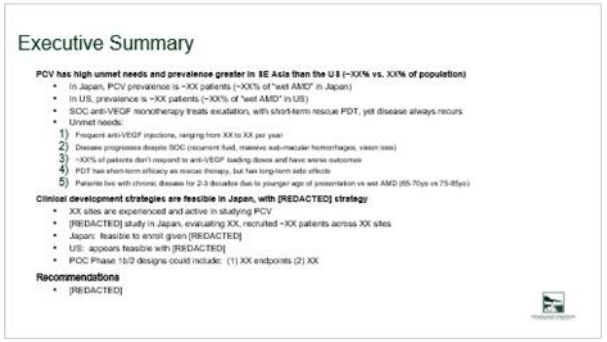
Case study: Primary market research to inform commercial and development planning in Japan

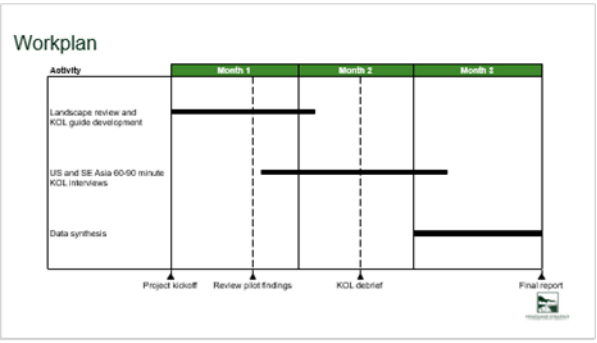
What was our impact?

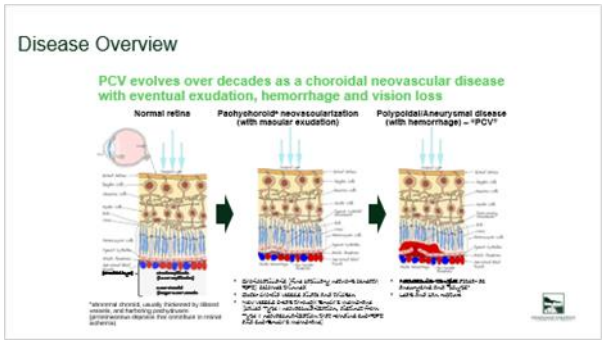
A US health care firm was seeking to conduct clinical trials for polypoidal choroidal vasculopathy (PCV in Japan). They needed help understanding the disease prevalence and patient journey to shape their clinical development strategy

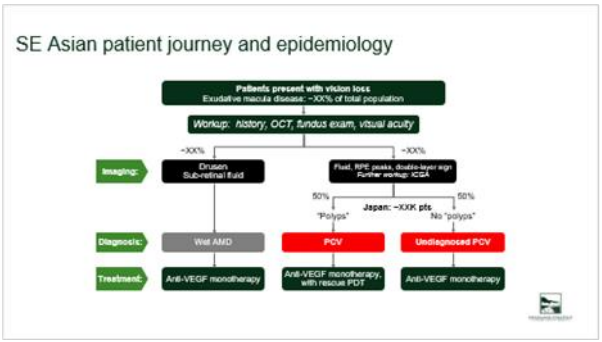
How we helped

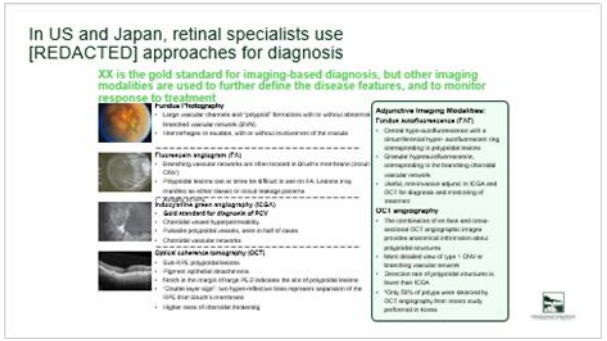
- ✔ Conducted research interviews with top key opinion leaders in South East Asia
- ✔ Evaluated key criteria to determine the quickest development path, leanest financials, and highest translatable proof of concept from early to late-stage development
- ✔ Analyzed difference in prevalence, treatment, and disease progression of PCV in Japan and the US
- ✔ Recommended top clinical development options to pursue Japanese CDP goals

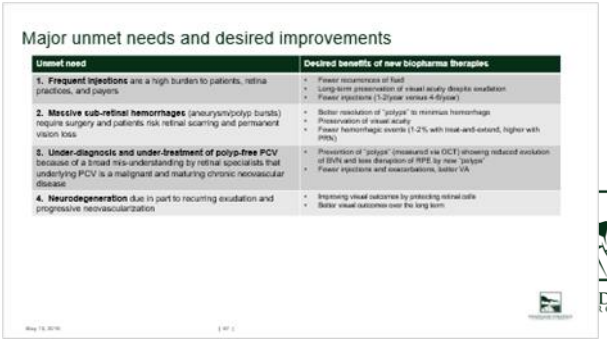












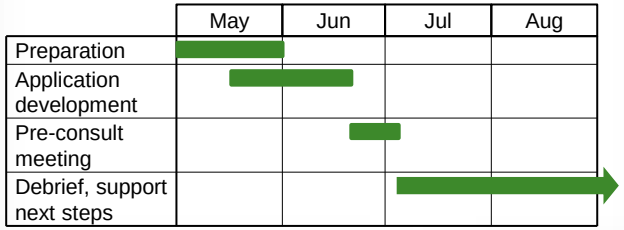
Case study: Supporting PMDA pre-consultations for a client with evolving, nuanced development strategy needs

Context

- A US biotech with a novel drug for a GI disease needed help engaging with PMDA about Japanese patients in a global Phase III study
- The company had previously retained another consultancy, but had received very conservative answers about how to approach the PMDA

Workplan

We designed a thoughtful approach with sufficient time for strategic discussions, planning, and iterations



Credentials

- ✓ We leveraged our extensive experience, having supported numerous PMDA consultations for wide range of biopharma companies across company size and specialty
- ✓ We have the industry experience, business culture, and linguistic know-how to understand what is said vs. implied, and how to confirm with PMDA (in Japanese)
- ✓ Our extensive R&D strategy and commercialization credentials helps us understand our client's development strategy and evaluate strategic options

Considerations

We used the following considerations to best help our client approach the PMDA

Category	Consideration
Disease and unmet need	How well do the SOC and pipeline competition perform on efficacy, safety, and other parameters?
	What is the addressable epi? In Japan, in what settings will diagnosis & treatment occur?
Program-specific	What preclinical and clinical data have been shown to date?
	How many Japanese patients and trial sites are included in the current global development plan?
	Has a PK or bridging study been planned or conducted yet?
Client-specific	What resource constraints to do you have?
	What is your risk tolerance?
	How important is launching in Japan? What is your commercialization plan?

Outcome

- ✓ We successfully steered our client through 2 successful pre-consultations as the data for their program, and strategic plans, evolved
- ✓ As a result of our work, a full-consultation with the PMDA was not needed
- ✓ We were able to complete everything on time or ahead of schedule, and with extremely positive feedback from the client about our strategic thought partnership and facilitation of the PMDA process

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Example: To overcome challenges with Japan market entry, Headland has strong connections to Japan executives

Company		Headland personal contacts (selection of senior executives)
alfresa	**Alfresa Holdings Inc. (including Alfresa Pharma)**	C level, VP level
astellas	**Astellas Pharma, Inc.**	C level, VP level
CHUGAI	**Chugai Pharmaceutical Co., Ltd.**	C level, VP level
Daiichi-Sankyo	**Daiichi Sankyo Co., Ltd. Sankyo Co., Ltd.**	VP in Research; Some BD contacts
Eisai	**Eisai Co., Ltd.**	VP level
KYOWA KIRIN	**Kyowa Kirin Co., Ltd.**	C level, VP level, Director level
meiji	**Meiji Seika Pharma Co., Ltd**	VP level
Mitsubishi Tanabe Pharma	**Mitsubishi Tanabe Pharma Corporation**	VP level
ono	**Ono Pharmaceutical Company, Ltd.**	VP level
Otsuka	**Otsuka Holdings Co., Ltd.**	VP level
SHIONOGI	**Shionogi & Co. Ltd.**	C level, VP level
Sumitomo Dainippon Pharma	**Sumitomo Dainippon Pharma Co., Ltd.**	Ex. Officer level, Senior Director level
Takeda	**Takeda Pharmaceutical Co. Ltd.**	VP level

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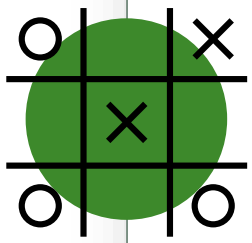
Going alone in Japan:
Increasingly common practice, but with its own challenges



Commercial and market planning

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- ❑ Do we need a partner? If yes, at which stage?
- ❑ What are the pitfalls of partnering vs. going alone? How would we manage them?
- ❑ Who would be the best partner? How do we get the best potential partners interested in us?
- ❑ What are the most important deal terms to ensure long-term success?

Extra considerations, going alone

- ❑ Are addressable patients concentrated by geography/setting and highly diagnosed, making commercialization easier?
- ❑ What CROs should we work with?
- ❑ Which wholesaler should we work with?
- ❑ How are wholesalers different from outside Japan?

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Agenda

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Going alone: wholesaler insights

Wholesaler functions in Japan are different from other markets

DISTRIBUTION

- Order Processing / Handling
- Procurement
- Packaging and Shipping
- Delivery

PROMOTION

- **Promotion** to Pharmacies
- **Promotion** to Prescribers

FINANCE (ACCOUNT MANAGEMENT)

- **Price Negotiations/Pricing**
- **Price maintenance**
- Credit Management / Debt Collection

INFORMATION

- **Provision/Collection** of Safety Information
- Provision of Regional Prescribing / Stock Information
- Provide support (information & feedback) to drug buyers
- Consulting services
- Post Marketing surveys

Items in bold above may seem unusual for those not familiar with the Japanese market

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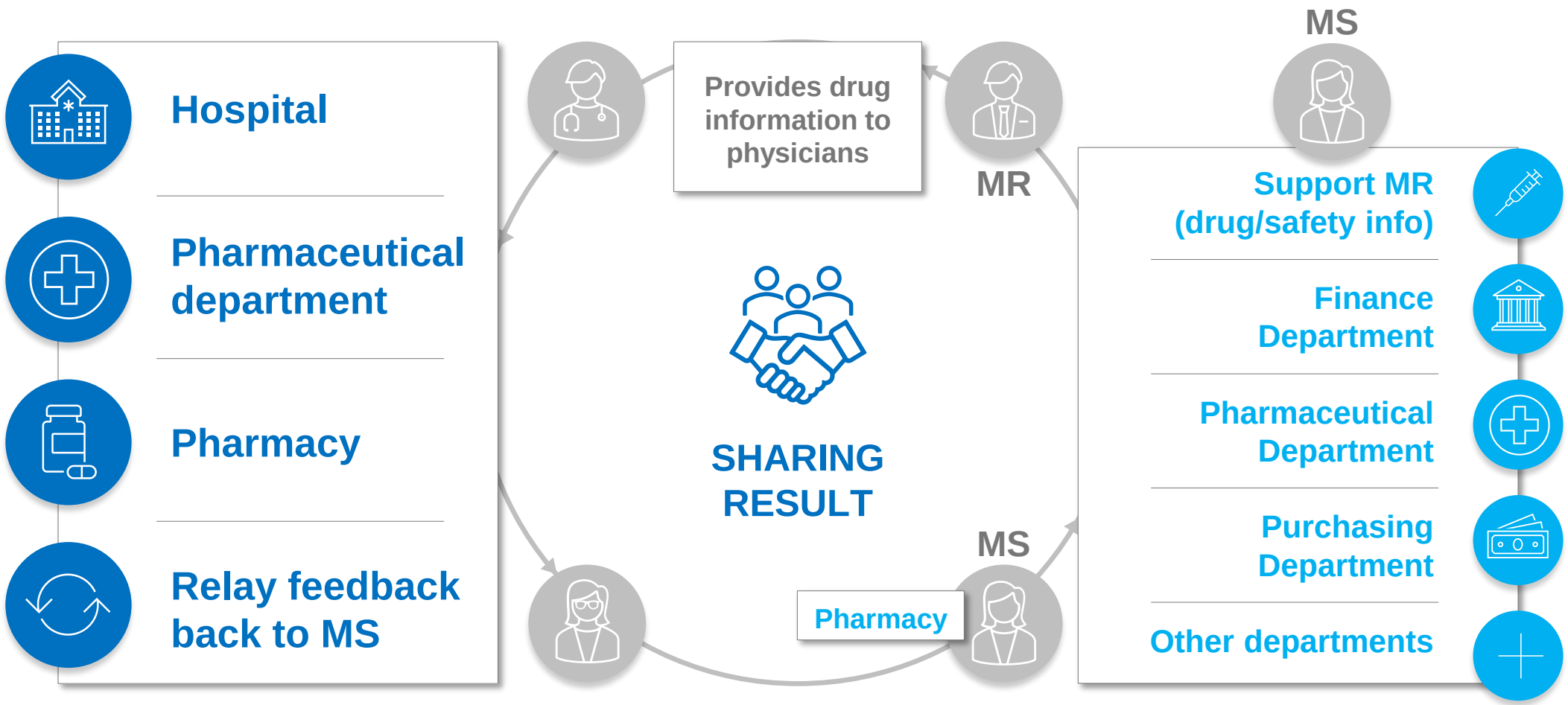
Wholesaler MSs: gaining importance vs. pharma MRs



1. Medical Representative
2. Marketing Specialist

Alfresa SMD is a “one-stop-shop” for Japan market entry

Model of Integration Supply Chain (Manufacture - Distribution – Patients for rare disease)

OVERSEAS	JAPAN			
Manufacturer	**Alfresa Group**			**Client**
	SMD			
Foreign Manufacturer	**Alfresa Pharma Okayama Plant** Labeling Packaging Storage Shipping decision	**Alfresa Distribution Center** Inventory management Distribution	**SMD** **Primary wholesaler** **Secondary wholesaler** For an overview of key functions, see later slides	



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Alfresa SMD Can Maximize Your Commercial Value in Japan

Options for Commercializing in Japan

	Typical approach: Out license in Japan	Partner in Japan, with SMD as your preferred distributor	Commercialize alone in Japan with SMD support
COMMERCIAL VALUE CAPTURED (*ILLUSTRATIVE*)			
SCENARIO			
AUTONOMY			
INVESTMENT COST			
BEST WHEN…	• Japan is not a priority	• Japan is a priority • Diseases are highly prevalent	• Japan is a priority • Diseases have orphan or ultra-rare prevalence

Partner Commercial Value Your Commercial Value

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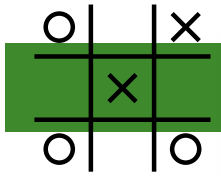
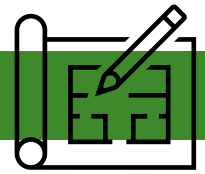
Q&A, wrap up

Summary: 4 ways we can help with Japan market entry



Commercial planning



Trial design ± PMDA engagement

BD/M&A, Partnering

End-to-end Japan entry support

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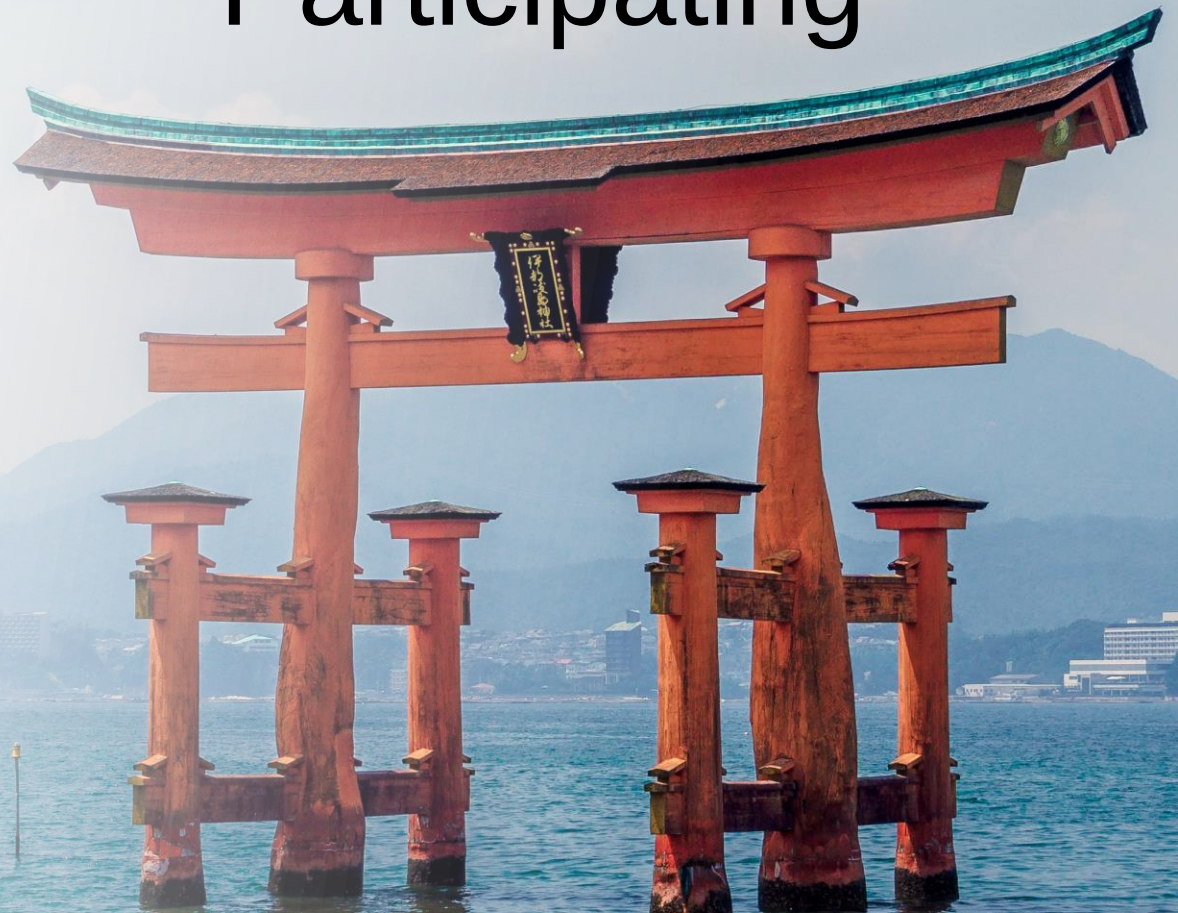
Next steps

- Please fill out our short survey (email forthcoming)
- We'll send you these slides and the recording
- Email Andrew McKee (andrew@headlandstrategy.com) for a complimentary consultation

Thank you for Participating



Thank you to our team!

Ken Shimokawa	*Content creation, editing, presenting*
Colin Waycott	*Content creation, logistics*
Bobby Brown III	*Content creation, logistics*
Celine Teoh	*Marketing lead, editing, coaching*
Akihiko Watanabe	*Content creation, editing, presenting*
Ludwig Kanzler	*Content creation, editing, presenting*
Diane Wallick	*Scheduling, communications*
Tak Yamaguchi	*Editing*
Andrew McKee	*Content creation, editing, presenting*

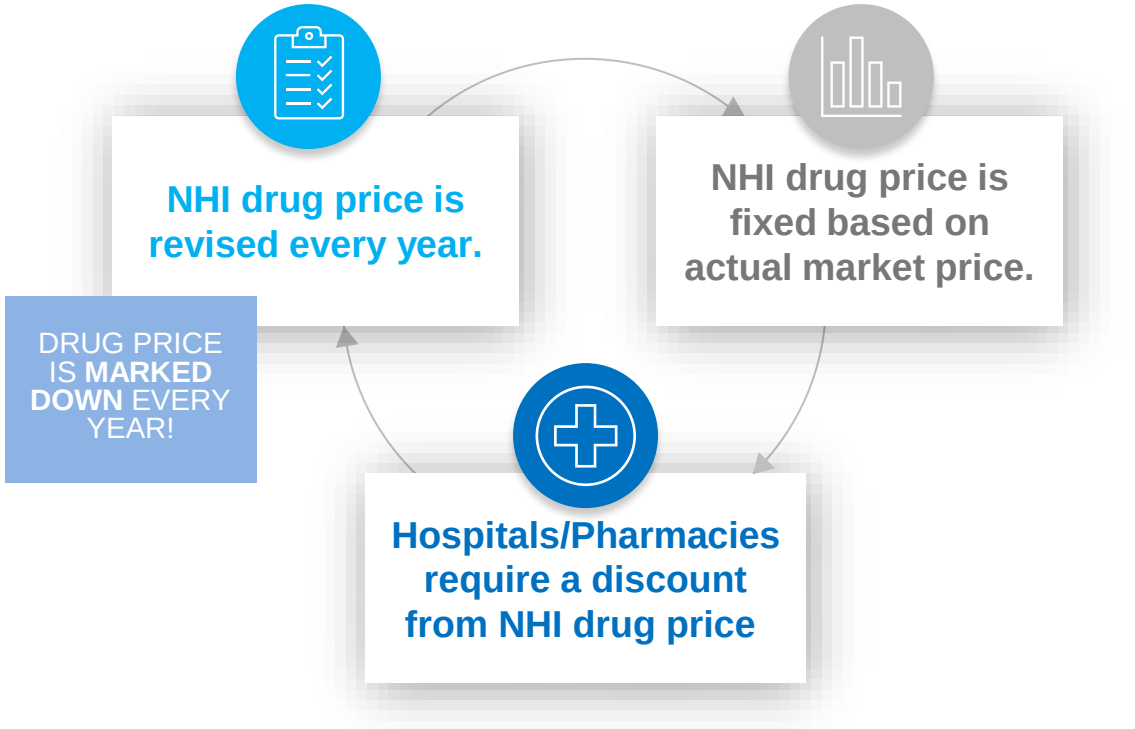
Photo by Robert Gomez - Unsplash

Agenda

Alfresa SMD case studies

Photo by Robert Gomez - Unsplash

Drug Pricing System in Japan



NHI price system has a built-in depreciation mechanism.

	Drug Pricing system	Market Price Negotiator
JAPAN	Free and open competition	Wholesaler
EUROPE	Official margin	Official margin
US	Free and open competition	Brand: Pharma Generic: Wholesaler (GPO, PBM)

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Transportation tools and compatible temperature zones

We have developed and introduced transportation tools for various temperature ranges

Compatible with temperature range from -150 ℃ to 40 ℃

We also provide dedicated transportation tools for specific product characteristics

<-150℃

-80℃

-25℃～-15℃

2℃～8℃

alf-GDP-Shipper

15℃～25℃

2℃～40℃

Standards for proper distribution of pharmaceuticals:
Realizing safe and secure distribution of medicines by refrigerated boxes compliant with PIC / S GDP

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Levodopa / Carbidopa (Duodopa) Distribution

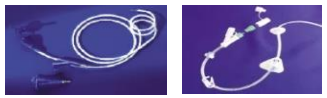
Manufacture & sales: AbbVie

15 weeks' storage life with cold temperatures (2-8 ° C)

STORAGE LIFE:

2 years when frozen, 15 weeks in refrigeration

Our manufacturing and sales timeline is dependent on proper drug storage

OUTSIDE OF JAPAN	INSIDE OF JAPAN			
Duodopa	**Osaka AP**	Thawing / Packaging Manufacturer **Alfresa Pharma** (Okayama)	**Alfresa** Aichi D.C. Saitama D.C. Osaka D.C.	**Medical institution**
 Duodopa Dedicated Tubes (Medical device)	**Narita AP**	Shipping decision / Packaging Manufacturing and sales **Alfresa Pharma** (Chiba)		

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Case Study: rare disease questionnaires to help with patient diagnosis, treatment, and/or compliance

Disease examples: spinal muscular atrophy, muscular dystrophy, congenital myopathy, Pompe disease, Prader-Willi syndrome

Questionnaire responses reveal

36 patients diagnosed with spinal muscular atrophy.

15 patients had been treated with Spinraza

Pediatric

Target facility	Implemented facility	Facilities where patients may exist	Number of patients who have been treated
10,000	7,590	360	15

Adult

∗1,726 neurology departments nationwide

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