Rakuten Medical

Our Innovation to Help Conquer Cancer

J.P. Morgan Healthcare Conference 2022

Hiroshi “Mickey” Mikitani
CEO, Rakuten Medical, Inc.

Image provided by Rush University Medical Center

Forward Looking Statements

This presentation contains forward-looking statements made pursuant to the safe harbor provisions of the (United States) Private Securities Litigation Reform Act of 1995 that involve risks, uncertainties, and assumptions that could cause Rakuten Medical's actual results and experience to differ materially from anticipated results and expectations expressed in these forward-looking statements. These forward-looking statements include information concerning Rakuten Medical's proprietary research platform known as Illuminox™ and the commercialization of services related to Rakuten Medical products such as ASP-1929 and other initiatives toward regulatory approval for products to be sold and marketed., including RM-1995. These products may not be granted regulatory approval to be sold and marketed nor may they commercially successful. Forward-looking statements suggest potential profitability, efficacy and safety, and the status of the application for approval. Rakuten Medical has in some cases identified forward-looking statements by using words such as "anticipates," "believes," "hopes," "estimates," "looks," "expects," "intends," "potential," "may," "suggest," "plans," "strategizes," "likely", "will", and similar expressions. Such forward-looking statements are based upon Rakuten Medical's current beliefs. Moreover, this presentation states an opinion related to clinical research data, hence the use of expressions such as "important," "notable" and "abnormal." Ongoing clinical studies involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including uncertainty of success in regulatory approval or commercialization of ASP-1929 which may be impacted by, among other things, problems with the manufacturing process for ASP-1929, the occurrence of adverse safety events, failure to demonstrate therapeutic benefit, and the other risks and uncertainties, both reasonable and unreasonable. Rakuten Medical undertakes no obligation to release publicly the results of any revisions to any such forward-looking statements that may be made to reflect new information obtained, events or circumstances after the date of this press release or to reflect the occurrence of unanticipated events, except as required by applicable law or regulation. In the event of one or more revisions to Rakuten Medical's forward-looking statement, it should not be inferred that such revisions or other forward-looking statements will be further revised.

Rakuten Medical's Illuminox™ Platform

Transforming Surgery

From "cut" to

ILLUMINATE

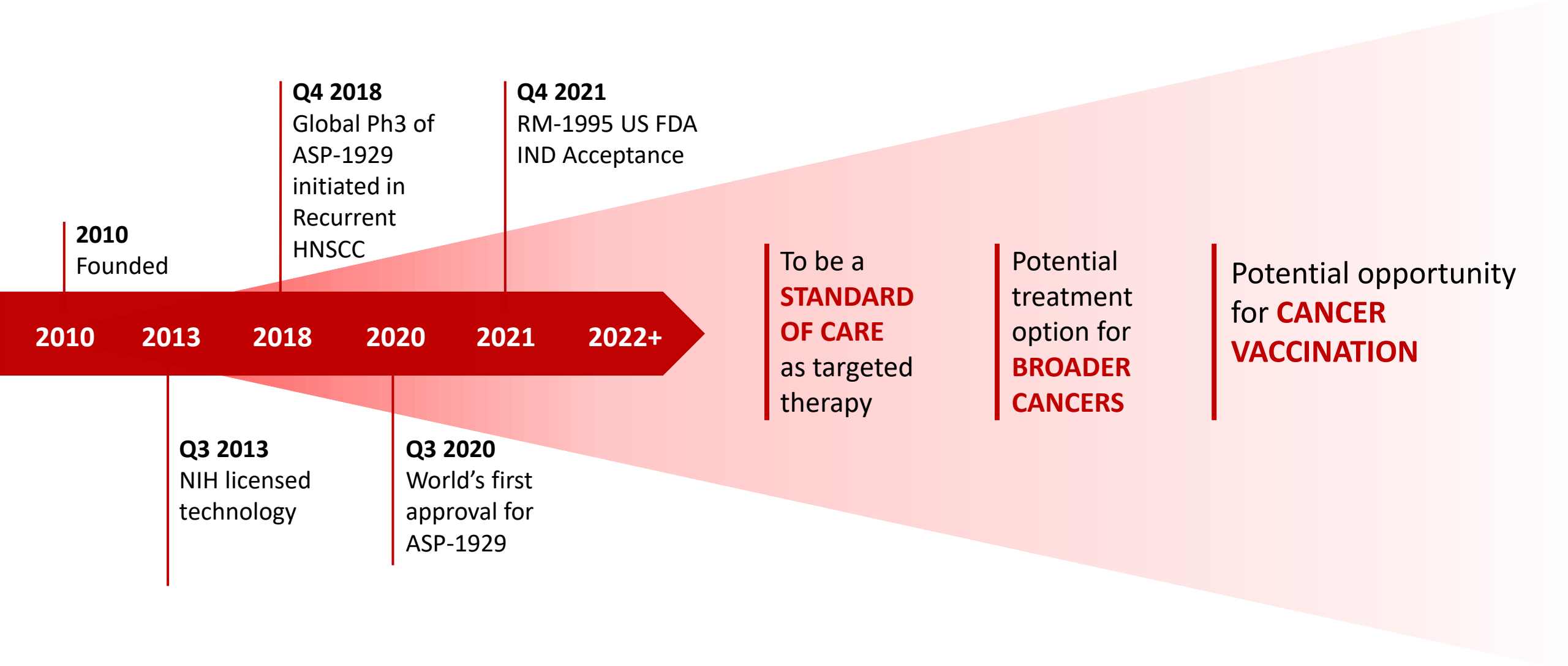
Rakuten Medical

A Potential 5th Pillar of Cancer Treatment

By illuminating the targeted cells with non-thermal light, it activates the rapid and selective necrosis with minimal effects on surrounding tissue.

Rakuten Medical

Accelerating our Innovative Platform & Pipeline to Reach More Patients Around the World



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DISCLAIMER: Outside of Japan, ASP-1929 photoimmunotherapy is investigational. Pending FDA Approval

Co-creating Innovation With Global Partners

Rakuten Medical Office
Partner

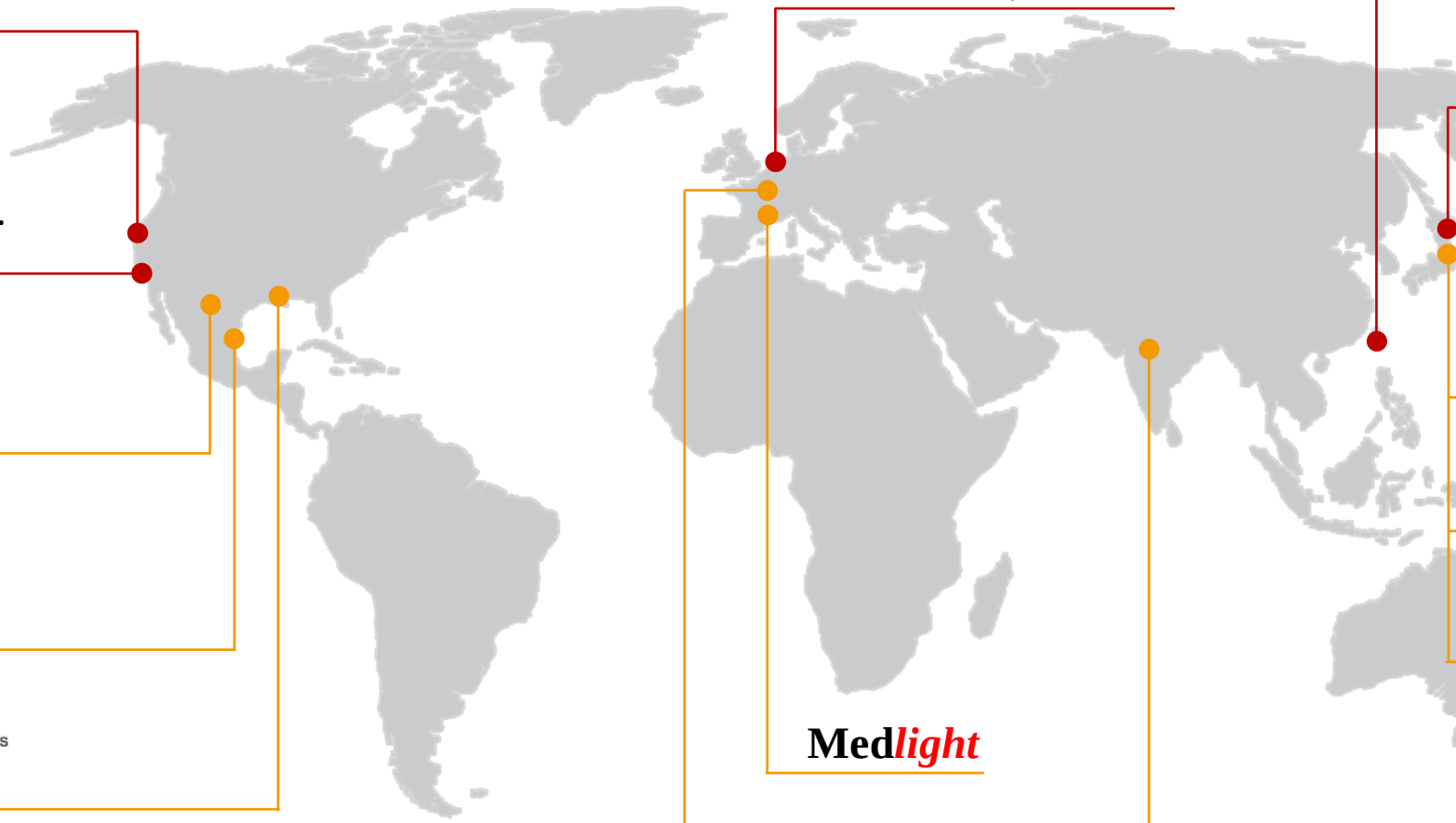
Rakuten Medical, Inc.
San Mateo, USA

Rakuten Medical, Inc.
San Diego, USA

Rakuten Medical Europe B.V.
Amsterdam, Netherlands

Rakuten Medical Taiwan, Inc.

Rakuten Medical K.K.



LI-COR

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

NIH National Institutes of Health

神戸大学

国立研究開発法人 国立がん研究センター National Cancer Center Japan

SHIMADZU Excellence in Science

Medlight

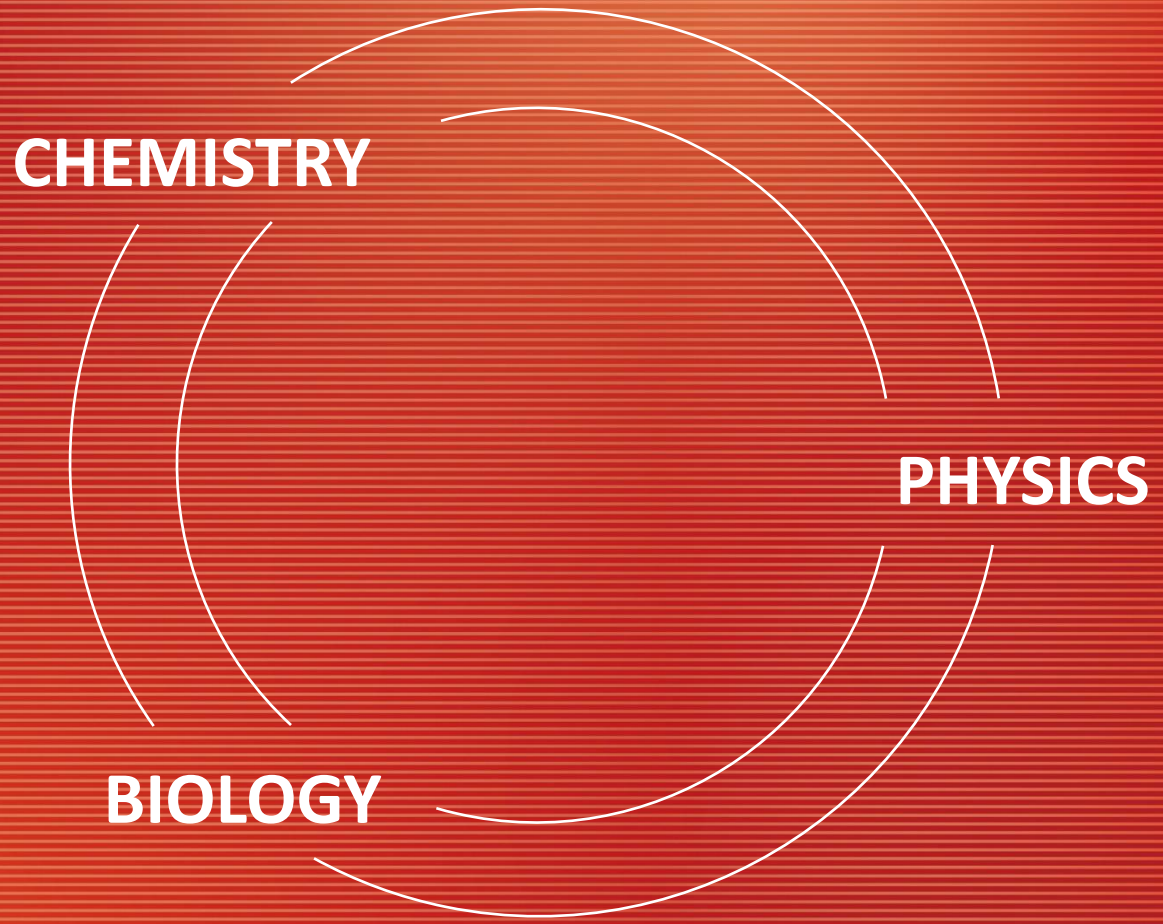
Merck KGaA

KARKINOS

Rakuten Medical

Our Mission is to

Conquer Cancer Through Innovation



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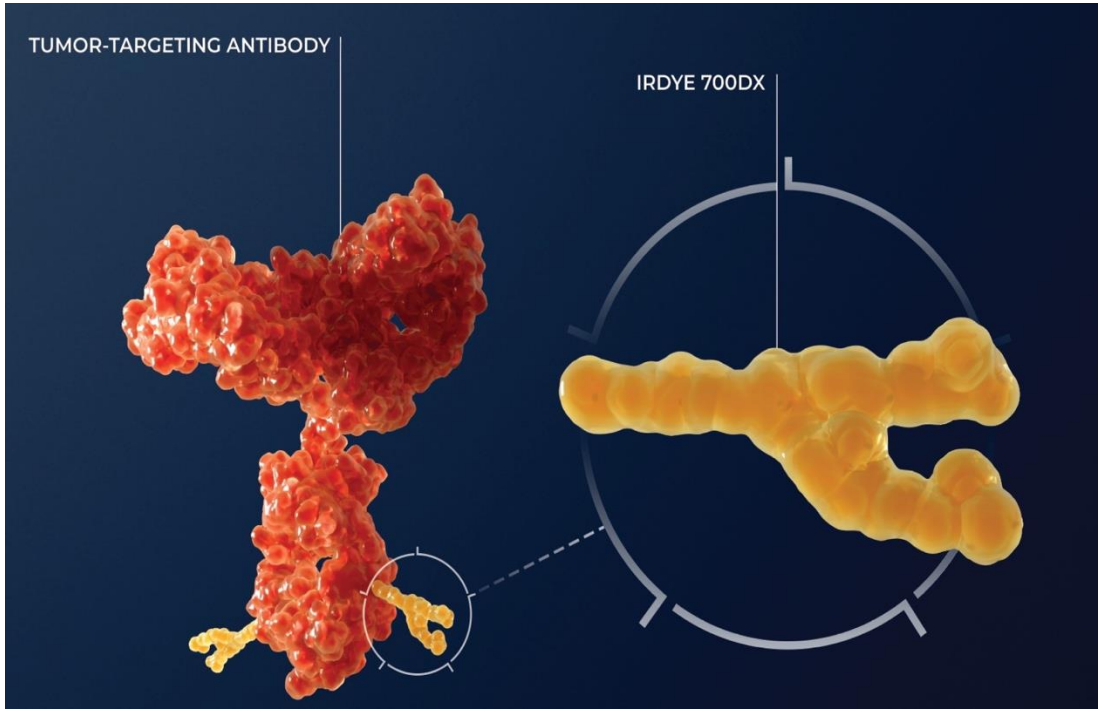
Our Innovative Technology

Drug & Device Combination

DRUG:

mAb-IRDye700DX conjugate

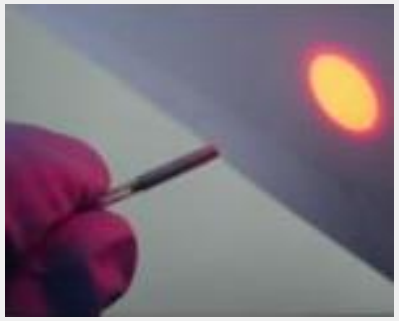


Cetuximab: Supplied by Merck KGaA
IR700 dye: Acquired rights from Li-Cor

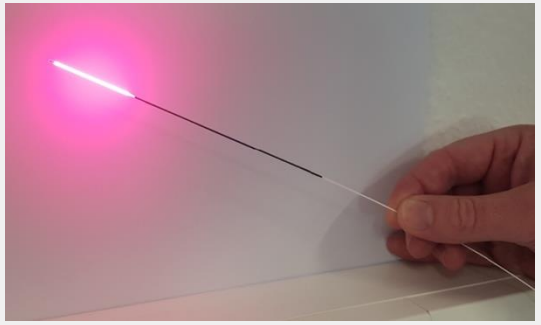
DEVICE:

Illumination system developed by Rakuten Medical

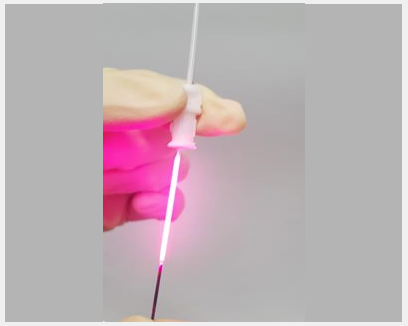
Benchtop laser



Light diffusers (frontal)



Light diffusers (cylindrical)



Catheters to position diffusers for interstitial illumination

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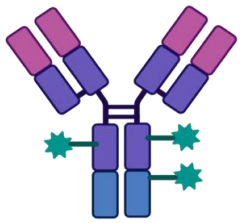
Our Innovative Technology

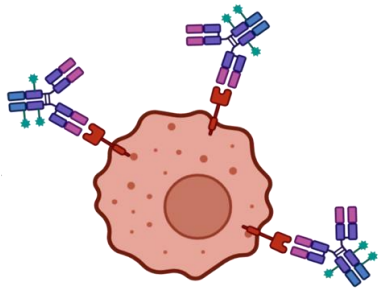
Treatment Procedure



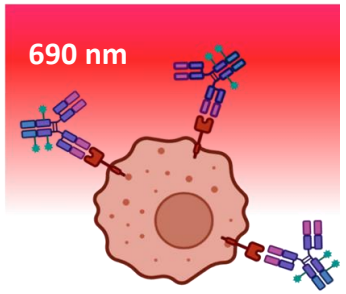
Antibody Conjugate

Light activatable dye

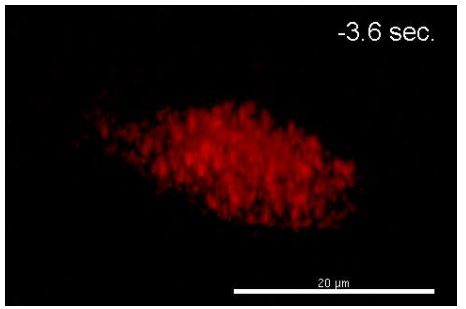
INFUSION



Antibody conjugate binds to cancer antigens

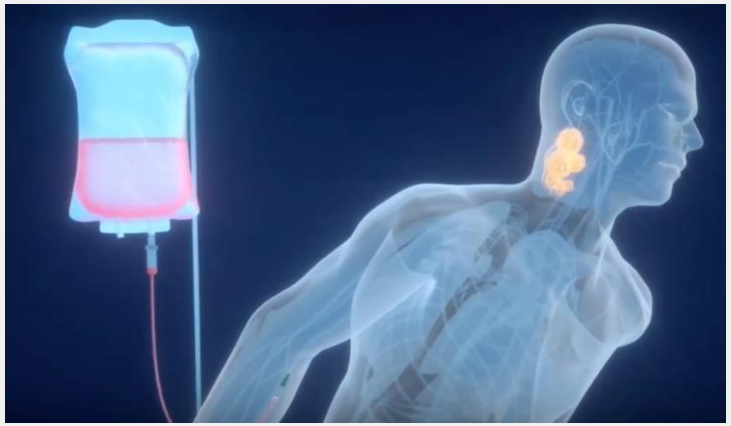


Tumor illumination with red light



Cell membrane permeability disrupted

Intravenous Infusion over 2 hours

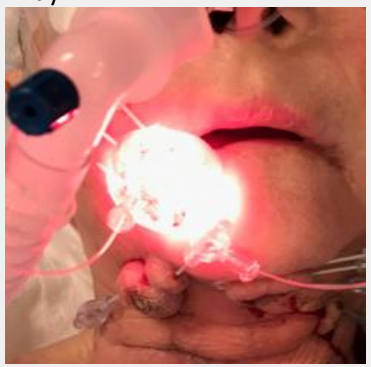


Illumination and tumor necrosis [1,2]

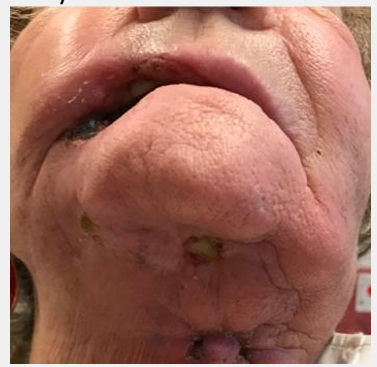
~ 5 min light illumination for each treated region

Pre-treatment

Day 1



Day 28



1. Mitsunaga M. et al. BMC Cancer. 2012;12:345.; 2. Ogawa M. et al. Oncotarget 8(6):10425-10436. 3. Hsu M. et al. AACR Annual Meeting Proceedings; 2019 Mar 29 - Apr 3; Atlanta, GA: AACR; 2019. Abstract 3734.

Japan's Inventive Approval System Helped us Commercialize with Sustainable Prices

Akalux IV infusion 250mg & BioBlade Laser System:

Received **our first approval** in Japan in Sep 2020, just 6 months after application under the "SAKIGAKE (fast track) designation" and "Conditional Early Approval System".

Early approval enables us to provide our treatment for **~ $53K** in Japan.

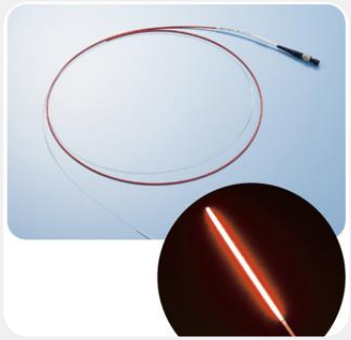
アキャルックス® 点滴静注 250mg

$35K / 4 vials

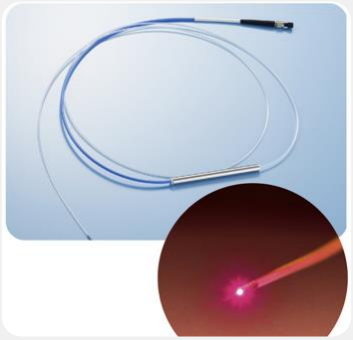
BioBlade® レーザシステム

$0.3K for rent
$35K for sale

BioBlade® シリンドリカル ディフューザー



BioBlade® フロンタル ディフューザー



$2K/diffuser
(# of diffusers required depends on patient)

BioBlade® ニードルカテーテル

$17/needle
(# of needles required depends on patient)

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DISCLAIMER: Outside of Japan, ASP-1929 photoimmunotherapy is investigational. Pending FDA Approval

In Japan, Illuminox Partner Hospitals will reach 60 sites with 200+ Illuminox Certified Doctors

38 Illuminox Partner Hospitals (As of Dec 2021)

Kansai Region
Kansai Medical University Hospital
Kobe University Hospital
Kyoto Prefecture University
Kyoto University Hospital
Osaka International Cancer Institute
Osaka University Hospital

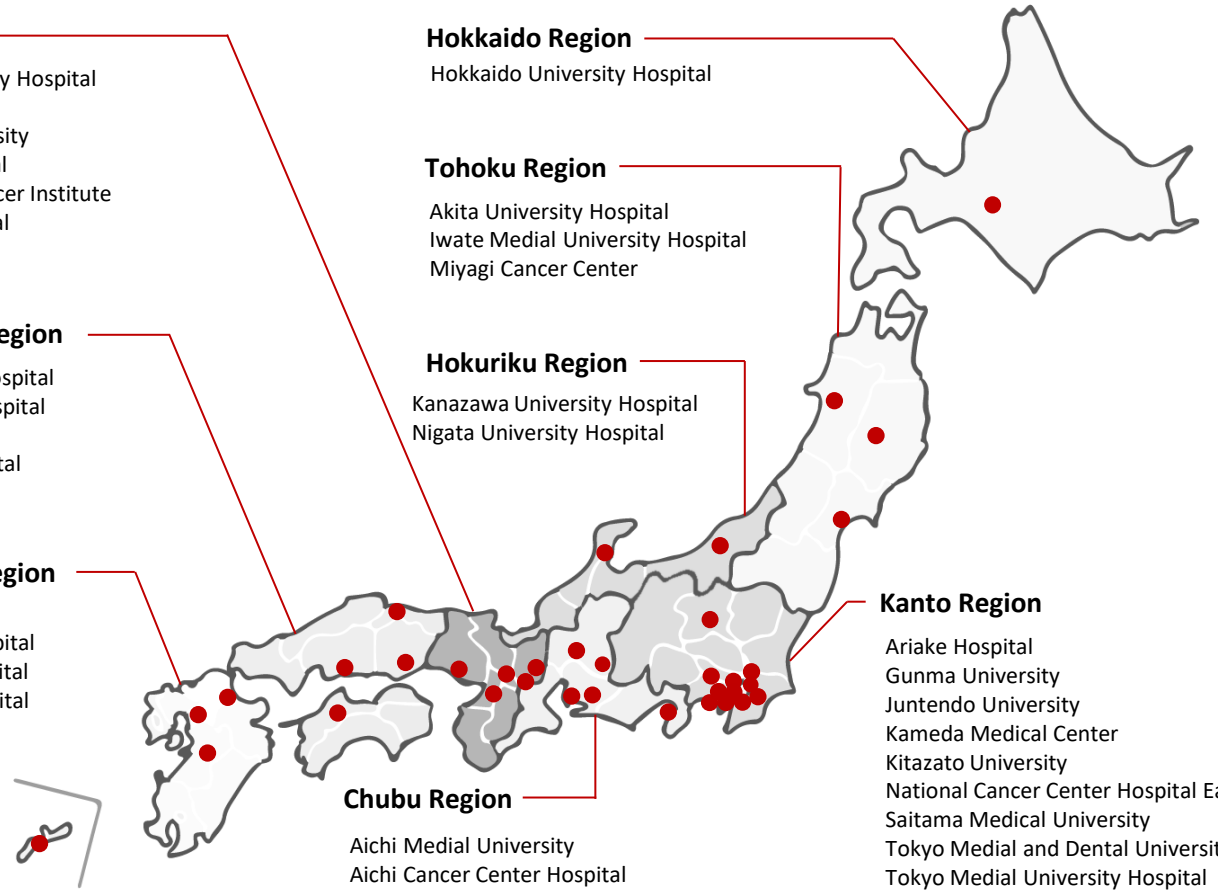
Hokkaido Region
Hokkaido University Hospital

Tohoku Region
Akita University Hospital
Iwate Medial University Hospital
Miyagi Cancer Center

Chugoku/Shikoku Region
Hiroshima University Hospital
Okayama University Hospital
Shikoku Cancer Center
Tottori University Hospital

Hokuriku Region
Kanazawa University Hospital
Nigata University Hospital

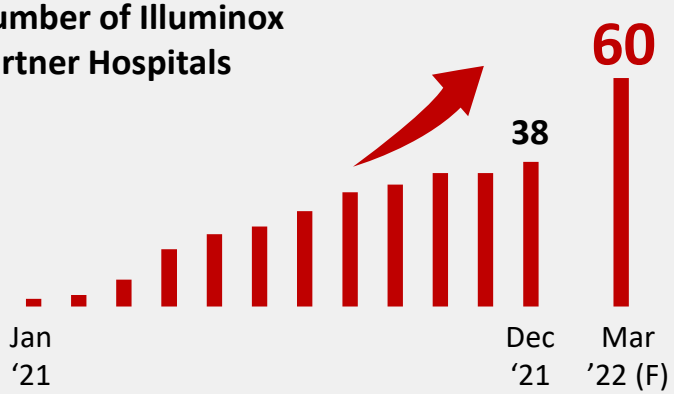
Kyushu/Okinawa Region
Kumamoto University
Kurume University Hospital
Kyushu University Hospital
Ryukyu University Hospital



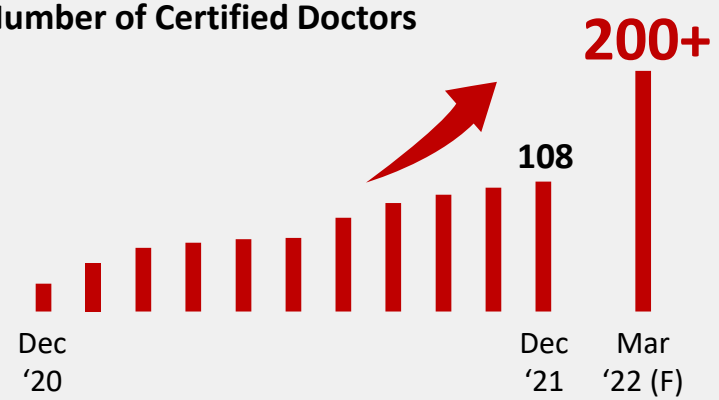
Kanto Region
Ariake Hospital
Gunma University
Juntendo University
Kameda Medical Center
Kitazato University
National Cancer Center Hospital East
Saitama Medical University
Tokyo Medial and Dental University Hospital
Tokyo Medial University Hospital
Tokyo Medical Center
Yokohama City University Hospital

Chubu Region
Aichi Medial University
Aichi Cancer Center Hospital
Fujita Medical University
Gifu University

Number of Illuminox Partner Hospitals



Number of Certified Doctors



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ADVANCED THROUGH ENGAGEMENT WITH ACADEMIC SOCIETIES

Illuminox™ Palette

A RANGE OF MAB-IR700 CONJUGATES TARGETING DIVERSE CANCERS

ONGOING CLINICAL & COMMERCIAL PROGRAMS

ASP-1929 targets EGFR (cancer cell selective necrosis)

- Approved, Phase 3, Phase 2
- Many solid tumors express EGFR: **HNSCC, cSCC, esophageal, premalignant dysplasia**, GBM, thyroid, lung SCC, prostate, penile, vulval, anal, renal, cBCC, cervical etc.

[New] **RM-1995 targets CD25** (TME)

- IND to Phase 1
- **Tumor microenvironment:** potential application to many solid tumors, based on suitability of light application

AND IN THE FUTURE

HER2 / MUC-1 / CEA / PSMA….

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New Rakuten Medical Program: RM-1995

Targeting to Tumor Microenvironment

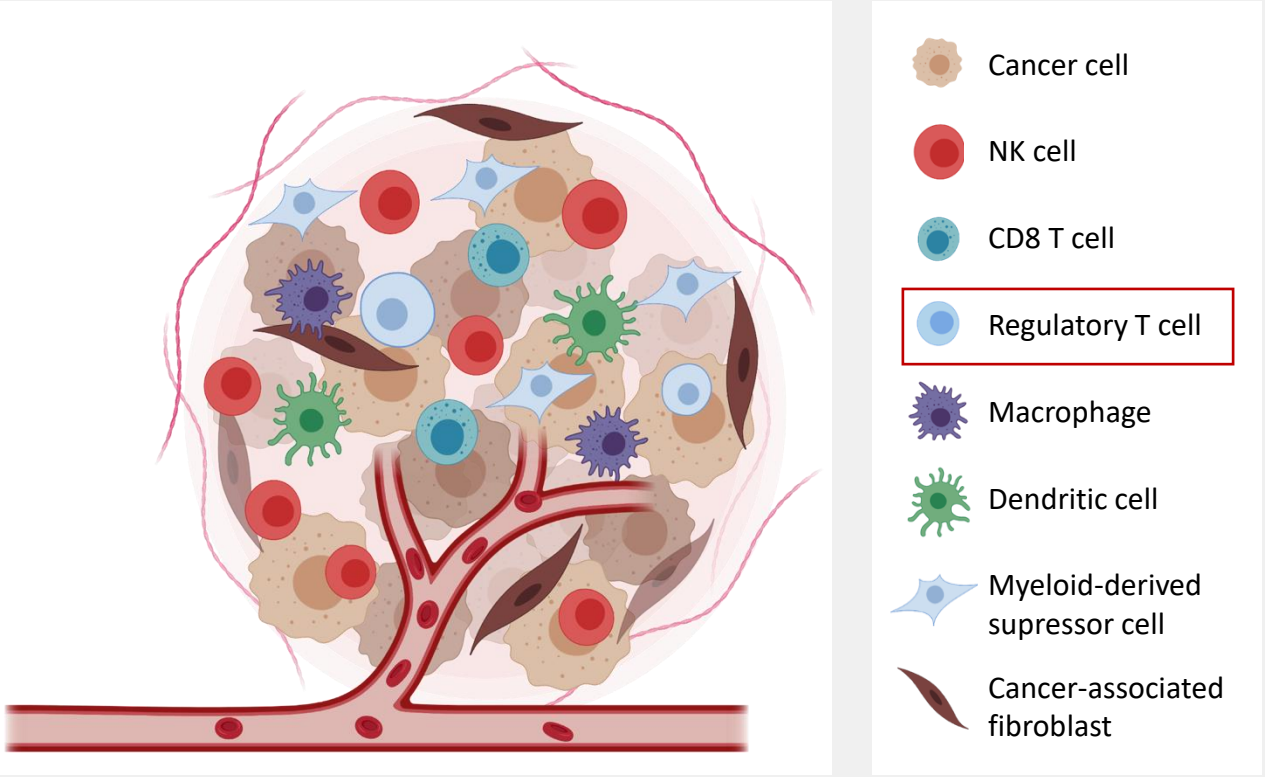
Potential Cellular immunosuppression with potential locoregional and systemic activity on many tumor types.

RM-1995

IND Accepted Q4 2021
Entering Phase 1

Potential elimination of intratumoral Tregs leads to antitumor immunity

- **CD25 / T-Reg**
- **Potential to induce systemic anticancer immunity in broad range of tumors (M0 and M1)**
- **Potential to synergize with aPD1 and mAbs-IRdye700Dx**



Cancer Cells and Tumor Microenvironment

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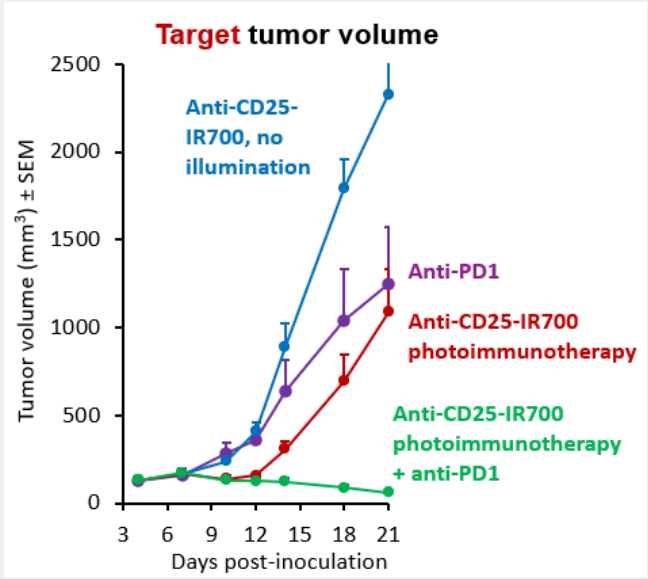
Anti-CD25-IR700 (RM-1995) Pre-Clinical Research

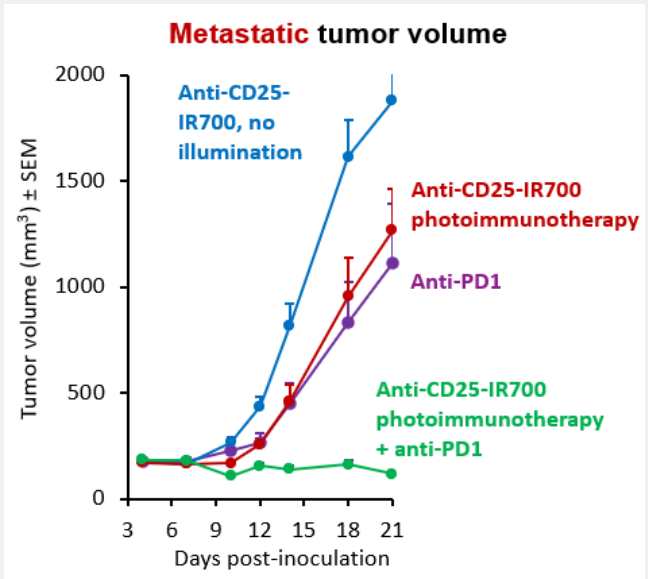
Pre-Clinical Research Indicates Anti-Cancer Activity in Target and Metastatic Cancers: Strong Synergy with Anti-PD-1.

RM-1995 photoimmunotherapy:
Elimination of intratumoral Tregs leads to antitumor immunity

Monotherapy (in mice):
Research indicated target and abscopal anticancer activity

Combination with anti-PD-1 (in mice):
Research indicated significant synergy in target and abscopal lesions





Treatment (in Mice)	# of CRs
Anti-CD25-IR700, no illumination	0/12 (0%)
Anti-CD25-IR700 photoimmunotherapy	7/20 (35%)
Anti-PD-1	1/12 (8%)
Anti-CD25-IR700 photoimmunotherapy + anti-PD-1	17/23 (74%)

Treatment (in Mice)	# of CRs on both sides
Anti-CD25-IR700, no illumination	0/15 (0%)
Anti-CD25-IR700 photoimmunotherapy	1/15 (6.7%)
Anti-PD-1	2/15 (12.5%)
Anti-CD25-IR700 photoimmunotherapy+ anti-PD-1	12/15 (80%)

Source: Company Materials.
DISCLAIMER: RM-1995 has not been approved by any regulatory authority.

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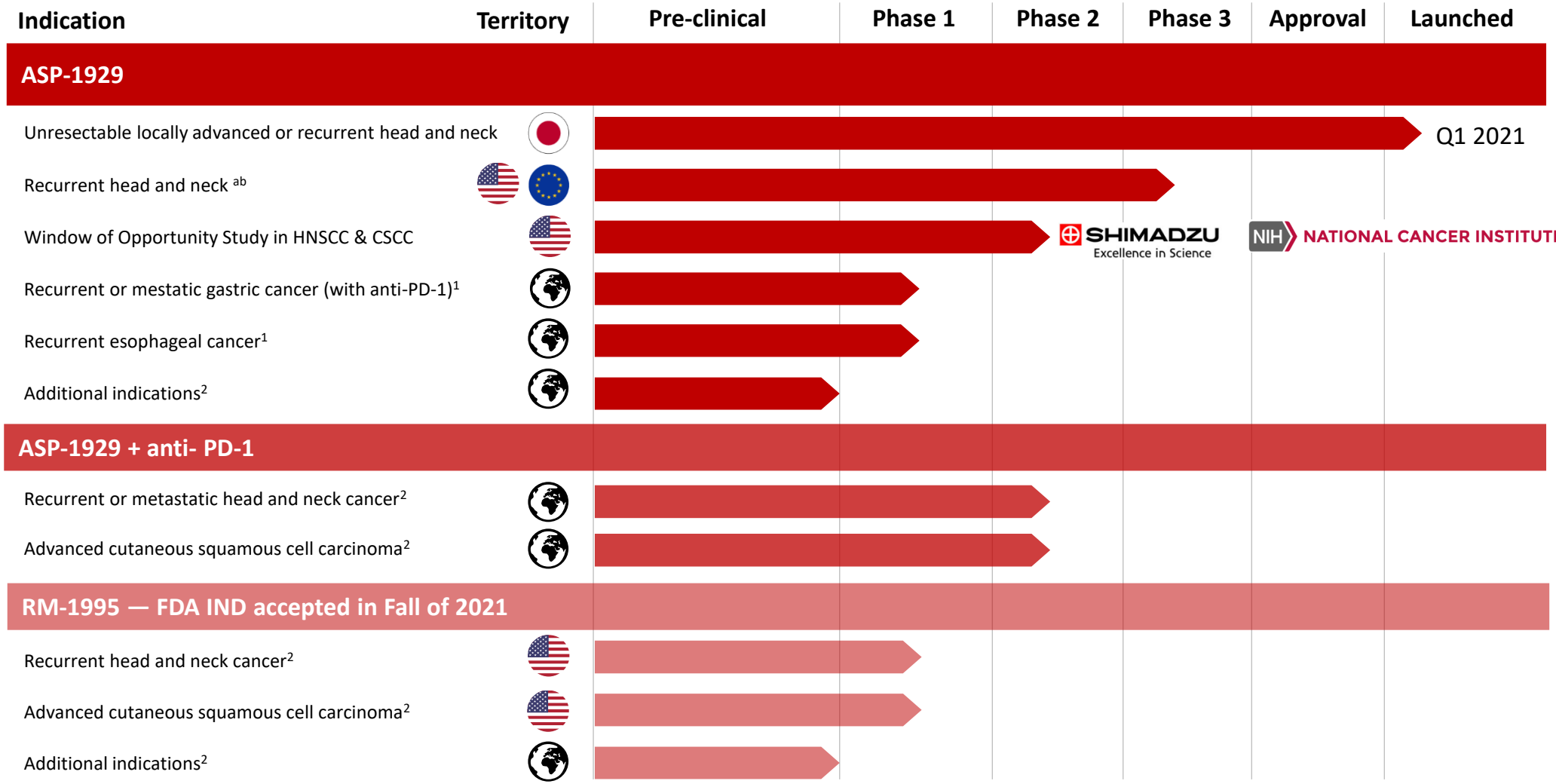
Strong Pipeline Utilizing Illuminox™ Platform Technology



(a) Encouraging results from a Phase 2a (part 2) study with RM-1929*** in patients with locoregional, recurrent HNSCC were announced at the 2019 ASCO conference. The overall response rate was 26.7 % and the median overall survival was 9.3 months. Treatment-related adverse events were generally manageable in those patients treated with RM-1929 who have failed prior therapies.

(b) Global Phase 3 study in patients with locoregional, recurrent HNSCC is ongoing to evaluate efficacy and safety of ASP-1929*** versus standard treatment.

Source: Company Materials; ClinicalTrials.gov
(1) Investigator-initiated trials
(2) Planned trials in 2022

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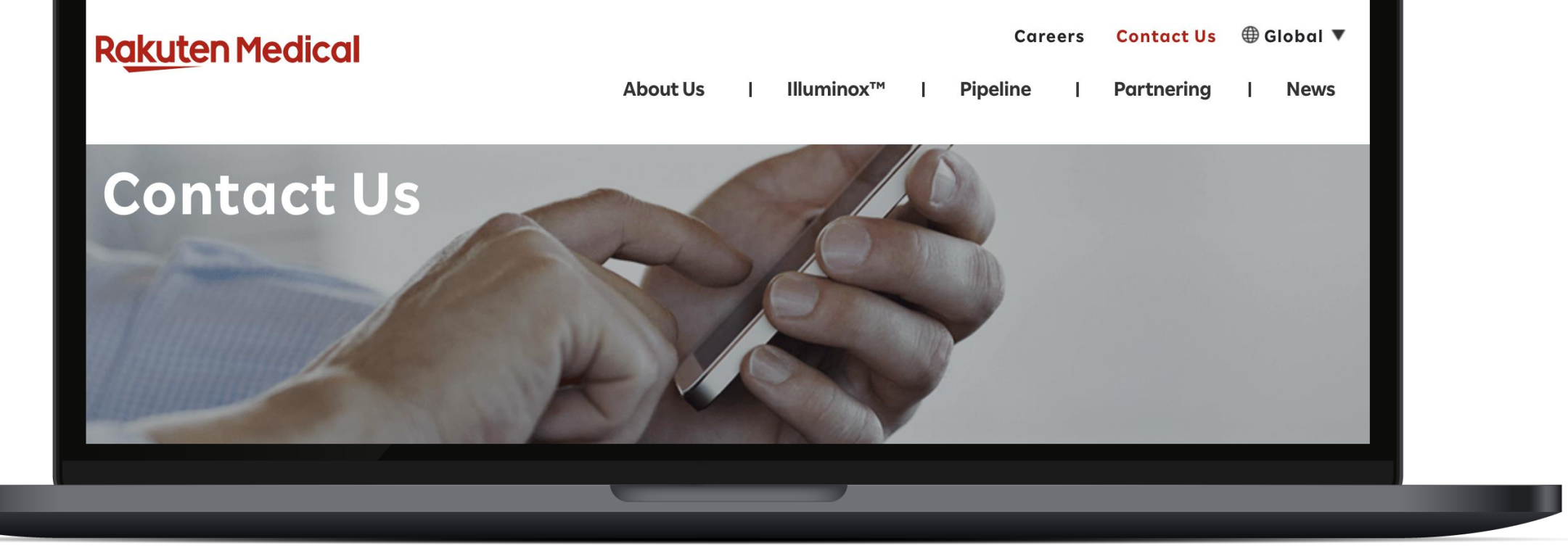

Partnership with Rakuten Medical

We are currently raising additional funds and are open to partnership opportunities.

CONTACT US Partnerships@rakuten-med.com

Scan the QR code to visit our website: