4. Survey results

4.2 Direction of measures

4.2.1 Ideal state in research, development and clinical practice

- In terms of research and development, there were hopes for the development of a research environment for new modalities, the training and promotion of human resources, and the development of treatment methods through collaborative research with companies.
- In clinical practice, it was expected that the speed and accuracy of testing and diagnosis would improve, and that treatment options would be expanded for patients.

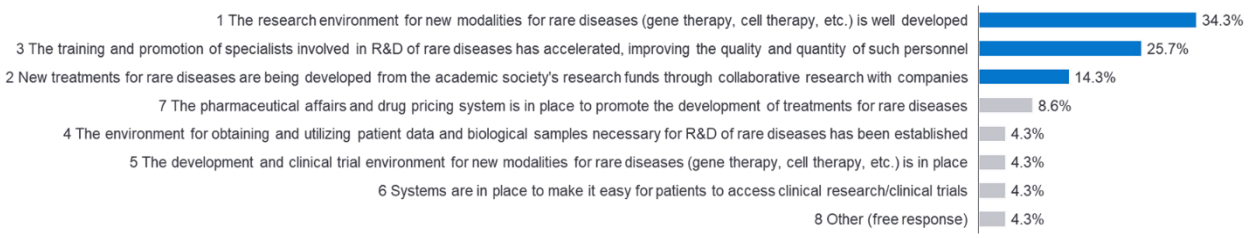
The development of a research environment for new modalities was the most anticipated outcome for both clinical researchers (basic and applied) and clinical researchers (development), followed by the development and promotion of human resources and collaborative research with companies (Figure 4.2.1-1).

Both reaffirm that there are high expectations for accelerating drug discovery and for developing and securing the necessary human resources which were mentioned as challenges in the previous chapter.

Similarly, in actual clinical practice, the challenges raised in the previous chapter include improving diagnostic accuracy and speed, expanding treatment options for patients and reducing the burden on patients associated with diagnosis and treatment, as well as improving access for clinical trials (Figures 4.2.1-2, 4.2.1-3).

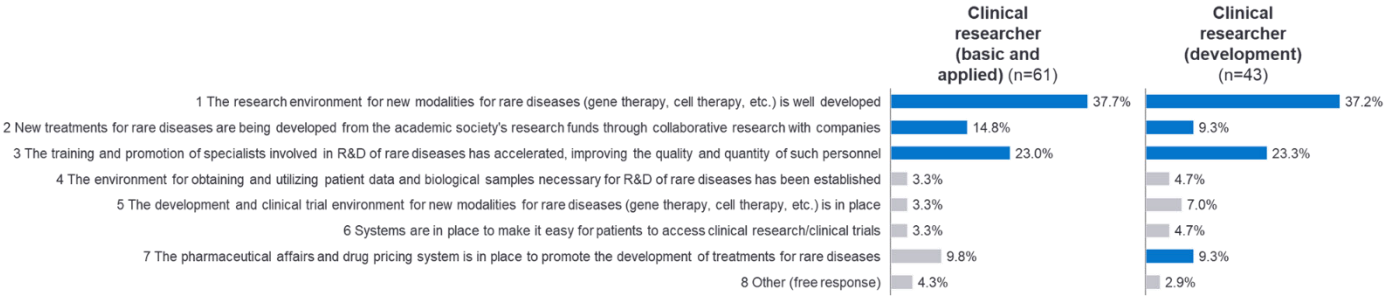
All these results are consistent with the challenges we have discussed so far and in the next section we will take up in detail the actions expected of each stakeholder.

Figure 4.2.1-1: What research and development should be like – Top selection result



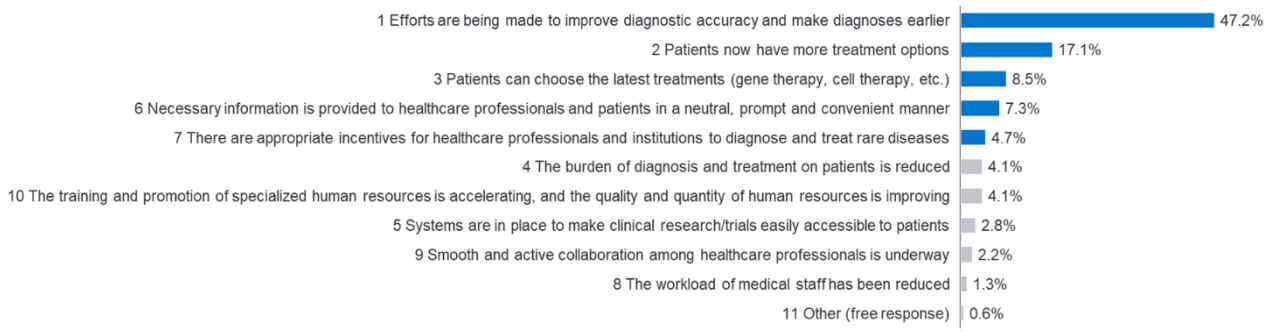
■Survey: Web survey
■Question: Based on the R&D challenges you have answered so far, please select top three answers that you agree are the way things should be (ranked)
■ Subjects: 70 clinical researchers (basic and applied), clinical researchers (development)

Figure 4.2.1-2: The Ideal State of Research and Development – Top Selection Results by Job Type



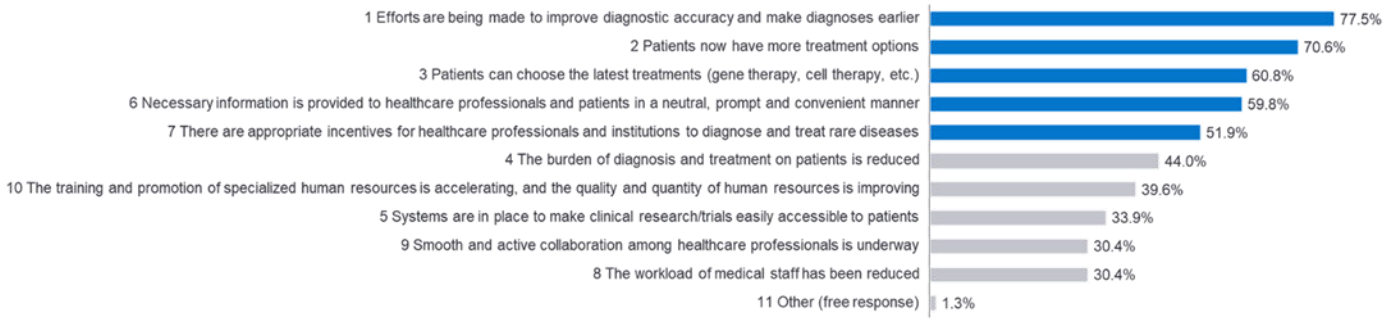
■Survey: Web survey
■Question: Based on the research and development challenges you have answered so far, please select top three answers that you agree are the way things should be (ranked)
■Subjects: 70 clinical researchers (basic and applied), clinical researchers (development)

Figure 4.2.1-3: What should be done in clinical practice – Top selection result



■Survey: Web survey
■Question: Based on the challenges you have answered so far in your clinical practice, please select the top 5 that you agree are the way things should be (ranked)
■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.2.1-4: What should happen in clinical practice – Top 5 selection results



■Survey: Web survey
■Question: Based on the challenges you have answered so far in your clinical practice, please select the top 5 that you agree are the way things should be (ranked)
■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

4.2.2 Expectations for the pharmaceutical industry

- The pharmaceutical industry was expected to accelerate the discovery and development of new modalities and build an ecosystem for this purpose, improve access to information on medical institutions, healthcare professionals and pharmaceuticals / development products involved in testing and treatment and contribute to the formation of rules and public opinion toward the realization of a 'society in which people can live comfortably with illness.'
- Specifically, there is a need to accelerate R&D by incorporating funds from both within Japan and overseas, by collaborating across industries, by creating opportunities for such collaboration to ensure the quality of information related to testing, treatment, pharmaceuticals and clinical trials, to strengthen the standardization and dissemination of such information and to disseminate information on the necessity and value of rare disease medical care and drug discovery in Japan.

To realize the ideal state, expectations regarding R&D for pharmaceutical companies (Figures 4.2.2-1, 4.2.2-2) included support for both research and manufacturing of new modalities such as gene therapy and cell therapy.

In relation to this, it is hoped that collaboration with academia with an eye toward exit strategies, consultation services on R&D related systems such as pharmaceutical affairs, sharing of know-how, provision of research funds and sharing of clinical trial information will all be necessary to accelerate drug discovery.

In terms of human resource development and exchange, in addition to creating opportunities / space for the dispatch of personnel and joint research to enable closer collaboration between the private sector and academia, there was also hope for companies to clearly disclose information on focus areas to facilitate smoother negotiations on licensing and other matters aimed at the social implementation of drug discovery funds.

In actual clinical practice (figures 4.2.2-3, 4.2.2-4), there are high expectations for the development of new treatments, elimination of drug lag and development of diagnostic methods. In addition, an attitude that contributes to eliminating the perception gap between stakeholders and accelerating collaboration by increasing awareness and understanding of rare diseases among healthcare professionals, patients, and their families through efforts to disseminate information about pharmaceuticals and products under development in a more neutral and centralized manner, is needed.

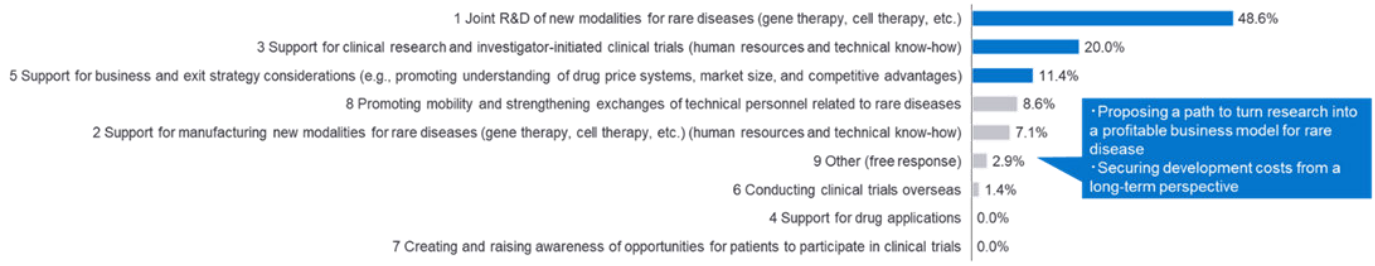
It was expected that the project would accelerate R&D through the incorporation of funds from both within Japan and overseas, collaboration across industries and the creation of similar opportunities, ensure the quality and standardization of information related to testing, treatment, pharmaceuticals and clinical trials and strengthen rare disease medical care and drug discovery in Japan (Figure 4.2.2-5).

> *I would like to see more efforts put into drug discovery for rare diseases and efforts to improve the accuracy of testing and diagnosis. Specifically, I would like to see continued visualization and update of progress of rare disease research, improved accessibility, creation of a system for accumulating genetic analysis data in Japan and the development of domestic drugs.*
> (Clinical researcher (basic and applied) / neuromuscular disease)

> *I hope to create collaborative opportunities with academia and build closer ties. I believe that an environment in which academia, pharmaceutical companies, and Patient Advocacy Groups can naturally interact daily, such as by sending researchers from pharmaceutical companies to academia or creating joint research spaces, will become an important ecosystem for the development of new drugs.*
> (Clinical researcher (basic and applied) / neuromuscular disease)

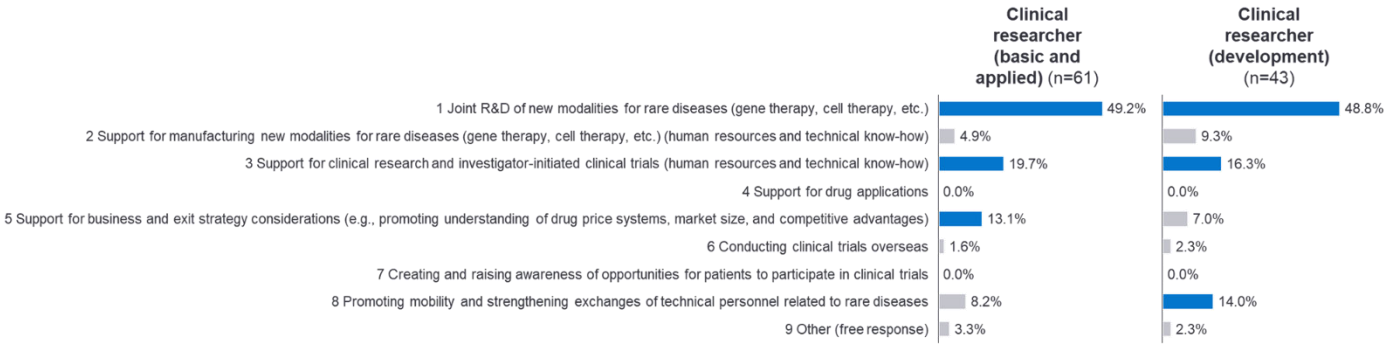
> *We hope to be able to communicate clinical trial information to patients and healthcare professionals in an easy-to-understand manner, and to lead to the development of new drugs.*
> (Specialist / Pediatrics)

Figure 4.2.2-1: Expectations for the pharmaceutical industry in research and development – Top selection results



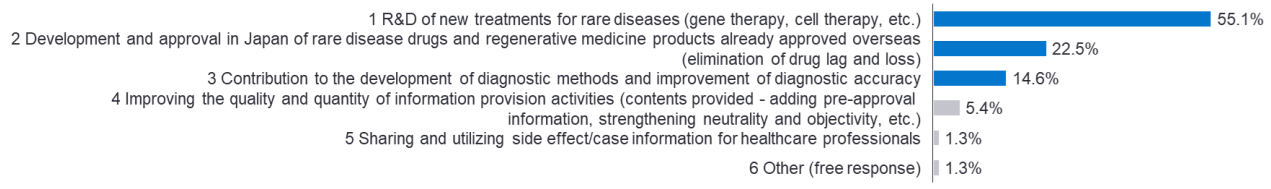
■Survey: Web survey
■Question: Please list your top three expectations for the pharmaceutical industry to achieve the ideal state (ranked)
■ Subjects: 70 clinical researchers (basic and applied), clinical researchers (development)

Figure 4.2.2-2: Expectations for the pharmaceutical industry in R&D – Top selection results by job type



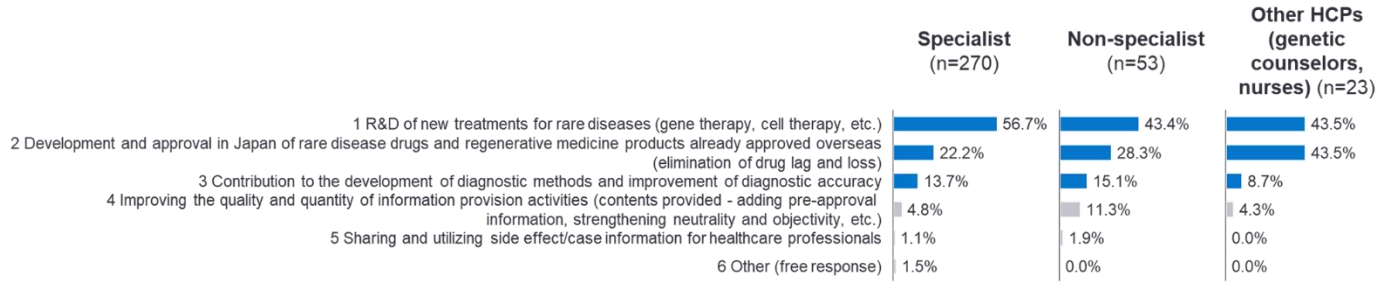
■Survey: Web survey
■Question: Please list your top three expectations for the pharmaceutical industry to achieve the ideal state (ranked)
■ Subjects: 70 clinical researchers (basic and applied), clinical researchers (development)

Figure 4.2.2-3: Expectations for the pharmaceutical industry in clinical practice – Top selection results



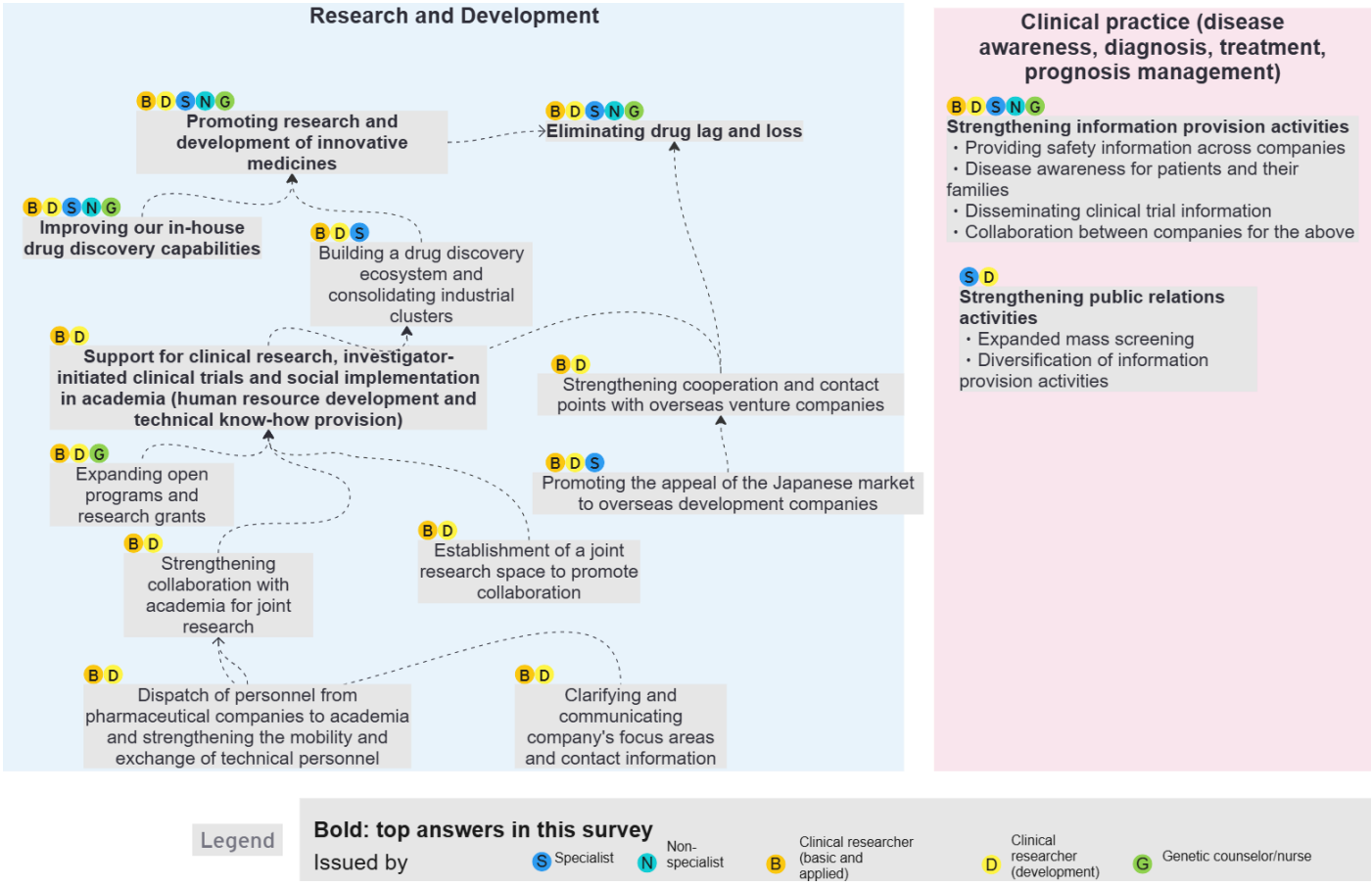
■Survey: Web survey
■Question: Please list your top three expectations for the pharmaceutical industry to achieve the ideal state (ranked)
■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.2.2-4: Expectations for the pharmaceutical industry in clinical practice – Top choice results by occupation



■Survey: Web survey
■Question: Please list your top three expectations for the pharmaceutical industry to achieve the ideal state (ranked)
■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.2.2-5: Overall expectations for the pharmaceutical industry



4.2.3 Expectations for academic societies

- The academic societies were expected to contribute to improving access to information on medical institutions, healthcare professionals, and pharmaceuticals / products under development involved in testing and treatment, expanding opportunities for training specialists and ensuring sustainability, and contributing to the formation of rules and public opinion toward the realization of a 'society in which people can live comfortably with their illnesses.'
- Specifically, there is a need to consolidate and network functions between medical institutions and healthcare professionals, speed up testing, create an attractive career development environment, disseminate role models and success stories, minimize barriers to participation, improve programs in specialized education courses and accelerate the mobility of human resources, and disseminate information about the necessity and value of rare disease medical care and drug development in Japan.

To realize the ideal status, clinical researchers (basic and applied) suggested that academic societies should provide incentives to secure human resources, while clinical researchers (development) suggested industry-government-academia collaboration (e.g., establishment of a consortium to develop treatments for rare diseases) (Figures 4.2.3-1, 4.2.3-2).

In actual clinical practice, the top priorities were the development of guidelines, the creation of educational opportunities, and the sharing of information overseas (Figures 4.2.3-3, 4.2.3-4). Specifically, to provide and expand educational opportunities related to rare diseases, it was necessary to increase the number of specialists and candidates involved in rare diseases by clarifying role models and career paths. To achieve this, it is necessary to build a system that contributes to more sustainable human resource development within the academic community, such as an appropriate evaluation and compensation system and improvements to the working environment, as well as to secure a budget to expand employment opportunities.

In addition, it was hoped that academic societies would take advantage of their neutrality and personal network to engage in proactive activities, such as eliminating vertical organizational silos and promoting collaboration among medical researchers, expanding reach to overseas companies by serving as a liaison office connecting with overseas bio ventures, and establishing and supporting a clinical trial framework that covers the entire country (Figure 4.2.3-5).

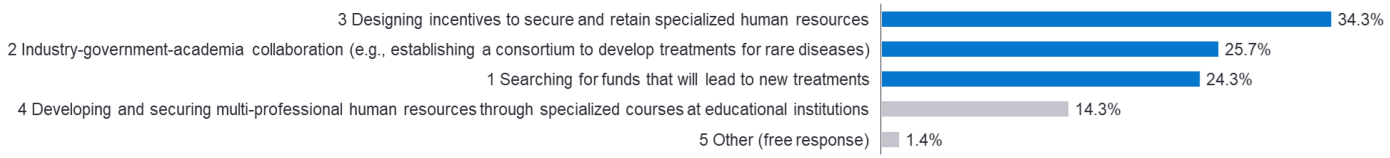
> *I would like them to compile and disseminate accurate information regarding treatment and diagnostic needs, etc.*
> (Non-specialist / Pediatrics)

> *Many of the patients who come to our hospital are referred from other hospitals, but some doctors are unsure of which patients they can refer to the hospital, so we feel it is necessary to strengthen awareness of referral criteria for each medical institution. We need to clarify which medical institutions have what expertise and the referral criteria for specialized facilities for each disease to accelerate cooperation between medical institutions.*
> (Specialist / Pediatrics)

> *We hope to see coordination of referrals from non-specialists to specialists to create an environment where referral sources can feel confident in referring patients in a timely manner.*
> (Non-specialist / Neurology)

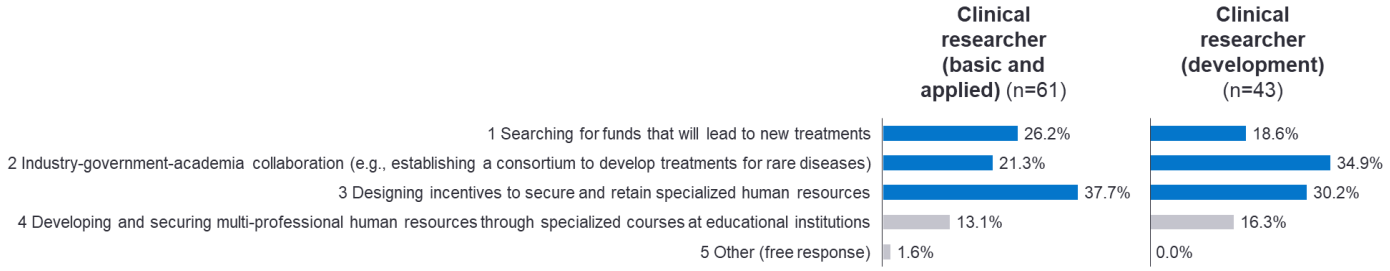
> *I want the unified voices of patients to be backed by academic evidence, that individual patients are not able to convey to the government. I believe that academic societies could complement the validity and importance of individual patients' claims. Internet has improved access to information, but erroneous understandings and different interpretations have increased as well. I want the academic society to clearly communicate what information is correct and what is incorrect.*
> (Clinical researcher (development) / All other hereditary disease)

Figure 4.2.3-1: Expectations for academic societies in research and development – Top selection results



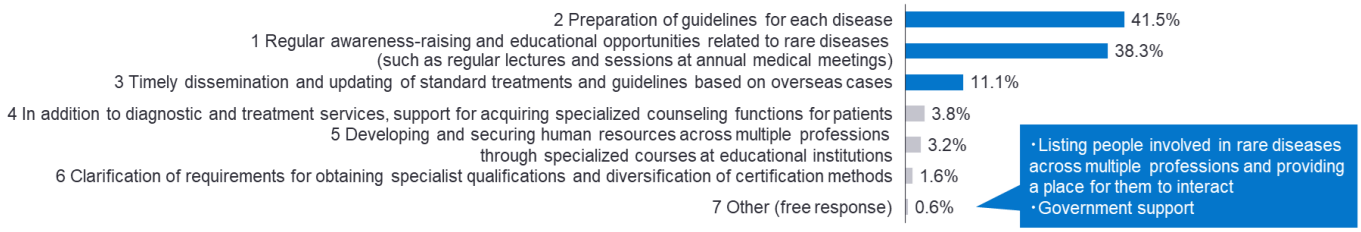
■Survey: Web survey
■Question: Please list your top three expectations from academic societies to realize your ideal state (ranked)
■ Subjects: 70 clinical researchers (basic and applied), clinical researchers (development)

Figure 4.2.3-2: Expectations for academic societies in research and development – Top selection results, by occupation



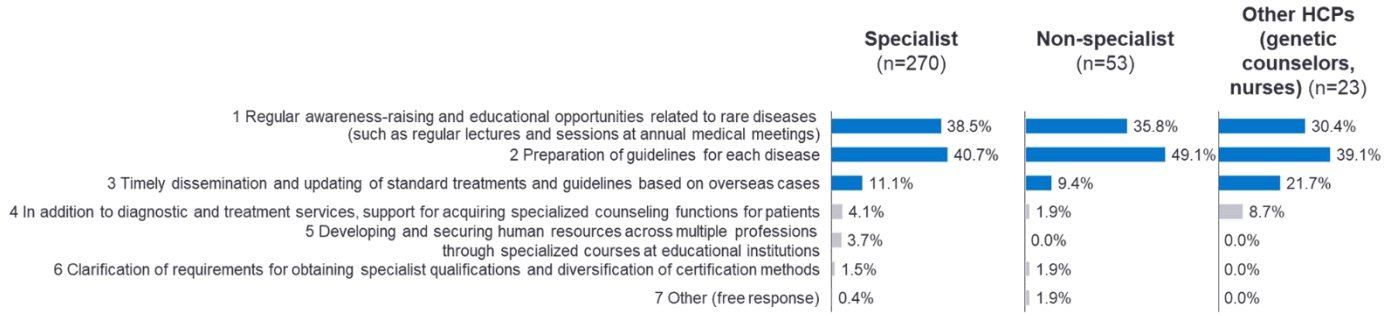
■Survey: Web survey
■Question: Please list your top three expectations from academic society to realize your ideal state (ranked)
■ Subjects: 70 clinical researchers (basic and applied), clinical researchers (development)

Figure 4.2.3-3: Expectations for academic societies in clinical practice – Top selection results



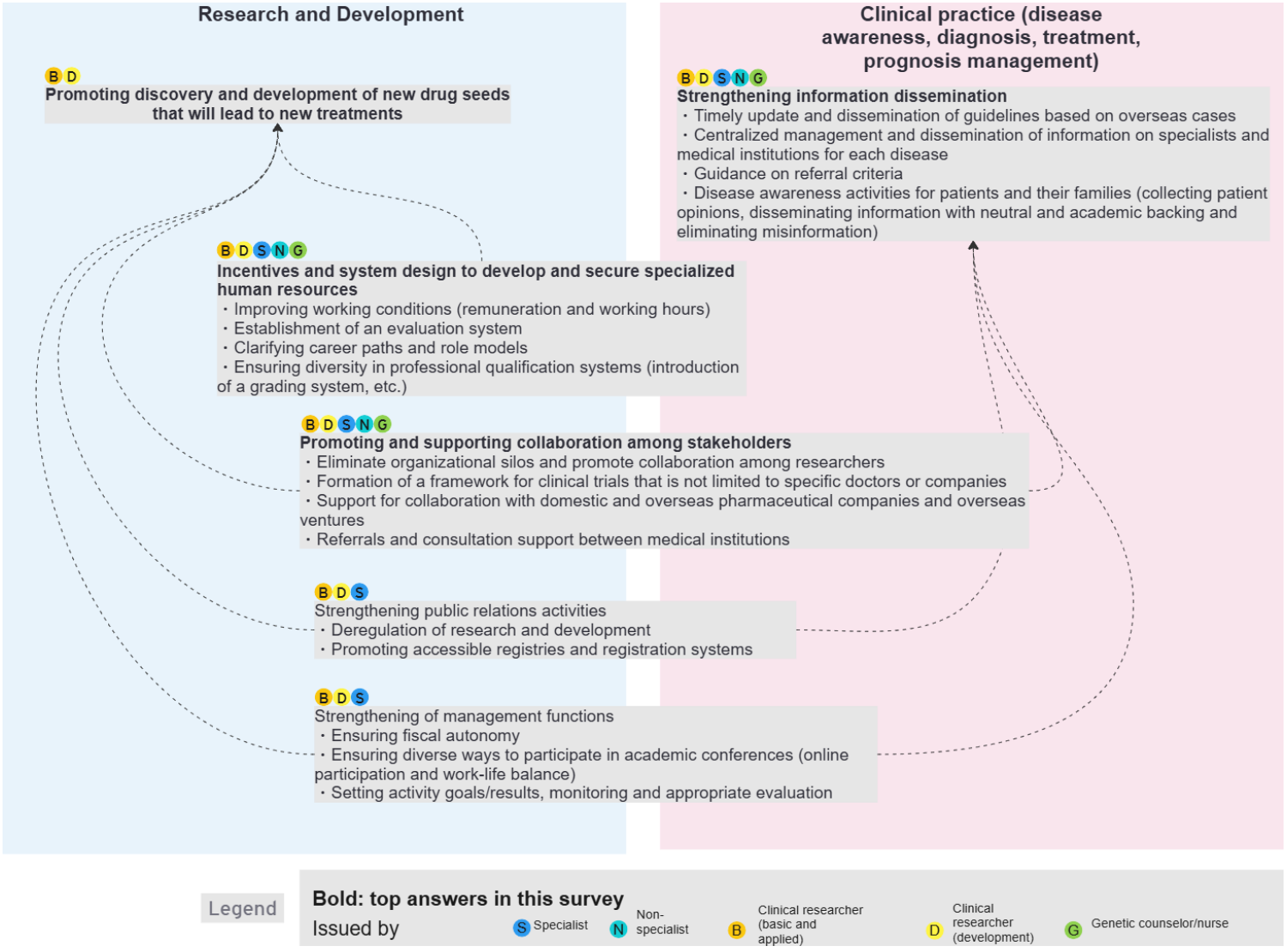
■Survey: Web survey
■Question: Please list your top three expectations from academic society to realize your ideal state (ranked)
■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.2.3-4: Expectations for academic societies in clinical practice – Top selection results by occupation



■Survey: Web survey
■Question: Please list your top three expectations from academic society to realize your ideal state (ranked)
■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.2.3-5: Expectations for academic society



4.2.4 Expectations for patient advocacy groups

- Patient advocacy groups were expected to accelerate the discovery and development of new modalities through collaboration with others and build ecosystems and systems for this purpose, improve access to information on medical institutions, healthcare professionals, and pharmaceuticals / products in development involved in testing and treatment, ensure diversification and flexibility in fund-raising and utilization methods, and participate in forming rules and public opinion to realize a 'society in which people can live comfortably with their illnesses.'
- Specifically, there is a need to strengthen organizational functions, advance PPI through inter-organizational collaboration, communicate needs, cooperate in registry construction, diversify activities and disseminate information to expand fundraising methods and strengthen organizational functions, and disseminate information about the necessity and value of rare disease medical care and drug discovery in Japan.

To realize this ideal state, there are high expectations that patient advocacy groups will increase their involvement in R&D, such as identifying needs in R&D, collaborating with academic societies and companies, and cooperating in building registries (Figures 4.2.4-1, 4.2.4-2).

To achieve this, there is a need to acquire the knowledge and skills to collaborate with each stakeholder, to become more involved in R&D that meets the needs of patients themselves, and to promote collaboration between patient advocacy groups as well as individual activities to raise resources (budgets and personnel) and societal interest.

In actual clinical practice, there was hope for strengthening information dissemination (Figures 4.2.4-3, 4.2.4-4). Specifically, in addition to the management activities of patient advocacy groups, there were hopes for fostering opportunities to involve more stakeholders and strengthening fundraising through external information dissemination activities such as charity and crowdfunding. These efforts would lead to awareness of organization and increase in activities in relevant disease field with expanded support by strengthening the organization and functions, patients' needs will be disseminated to the government and society and rare disease medical care will be considered proactively (Figure 4.2.4-5).

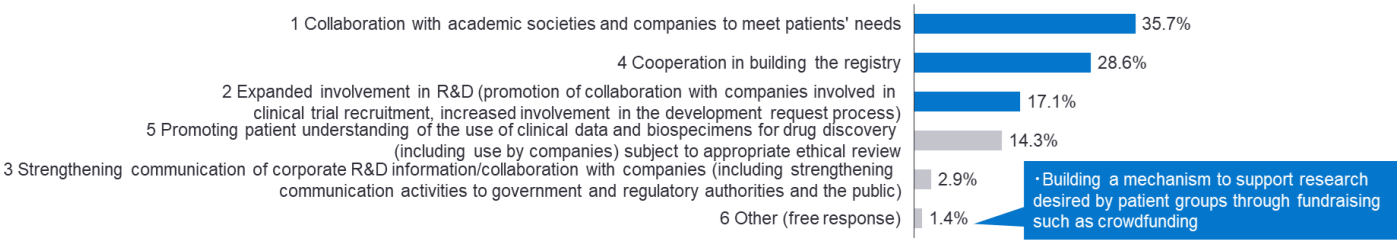
“*As a patient advocacy group, I would like to see the FDA actively involved in R&D and clinical activities. For example, while it is not easy for patients to register in the registry, without a foundation of patient data, further development is not possible, so I would like to see* Patient Advocacy Groups *actively cooperate with the FDA.*
(Clinical researcher (development) / All other hereditary disease)

“*Currently, the activities of each patient advocacy group vary, but regardless of the disease, patient advocacy groups are asked to improve peer support for patients and their families who cannot be supported by healthcare professionals.*
(Specialist / Pediatrics)

“*I believe that the existence and activities of patient advocacy groups have a major impact after a definitive diagnosis, and I hope that they will provide support to patients in terms of how to deal with the disease and in their daily lives mainly in terms of prognosis management.*
(Non-specialist / Neurology)

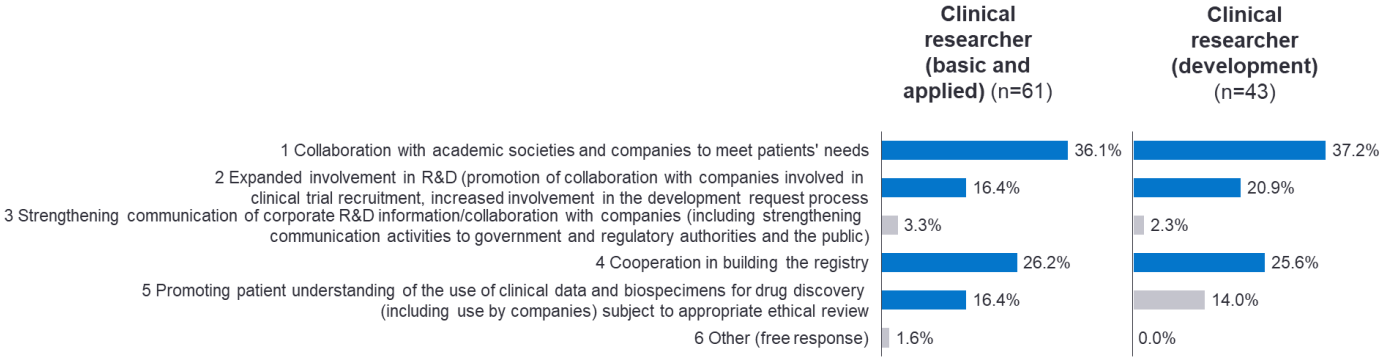
“*I would like them to strengthen their activities to raise awareness of themselves through media exposure, activities in the field of education, crowdfunding, etc. I think that by involving more stakeholders, creating contact points, and deepening mutual understanding, activities will accelerate.*
(Clinical researchers (basic and applied) / Other general hereditary disease)

Figure 4.2.4-1: Expectations for patient advocacy groups in research and development – Top selection results



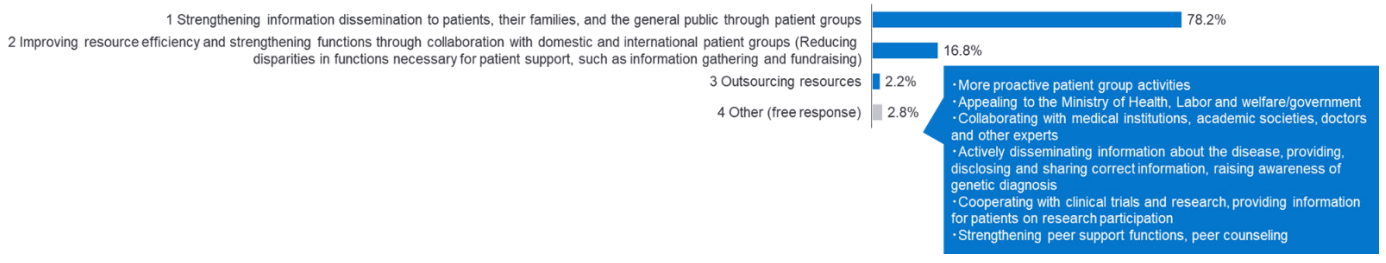
■Survey: Web survey
■Question: Please list your top three expectations of patient advocacy groups to achieve your vision (ranked)
■Subjects: 70 clinical researchers (basic and applied), clinical researchers (development)

Figure 4.2.4-2: Expectations for patient advocacy groups in R&D – Top choice results by occupation



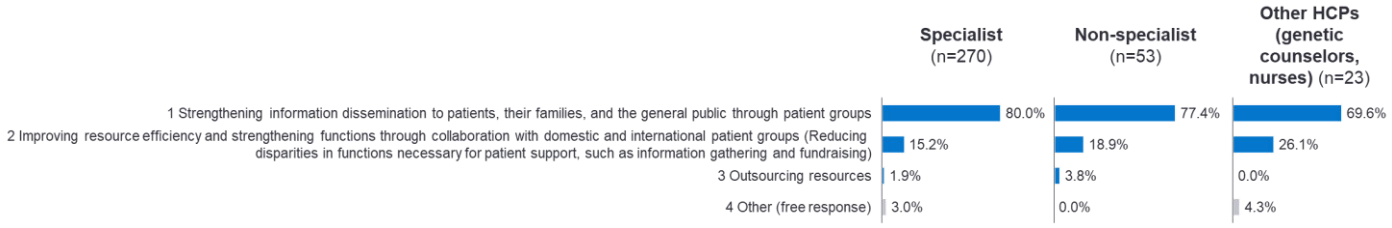
■Survey: Web survey
■Question: Please list your top three expectations of patient advocacy groups to achieve your vision (ranked)
■Subjects: 70 clinical researchers (basic and applied), clinical researchers (development)

Figure 4.2.4-3: Expectations for patient advocacy groups in clinical practice – Top choice results



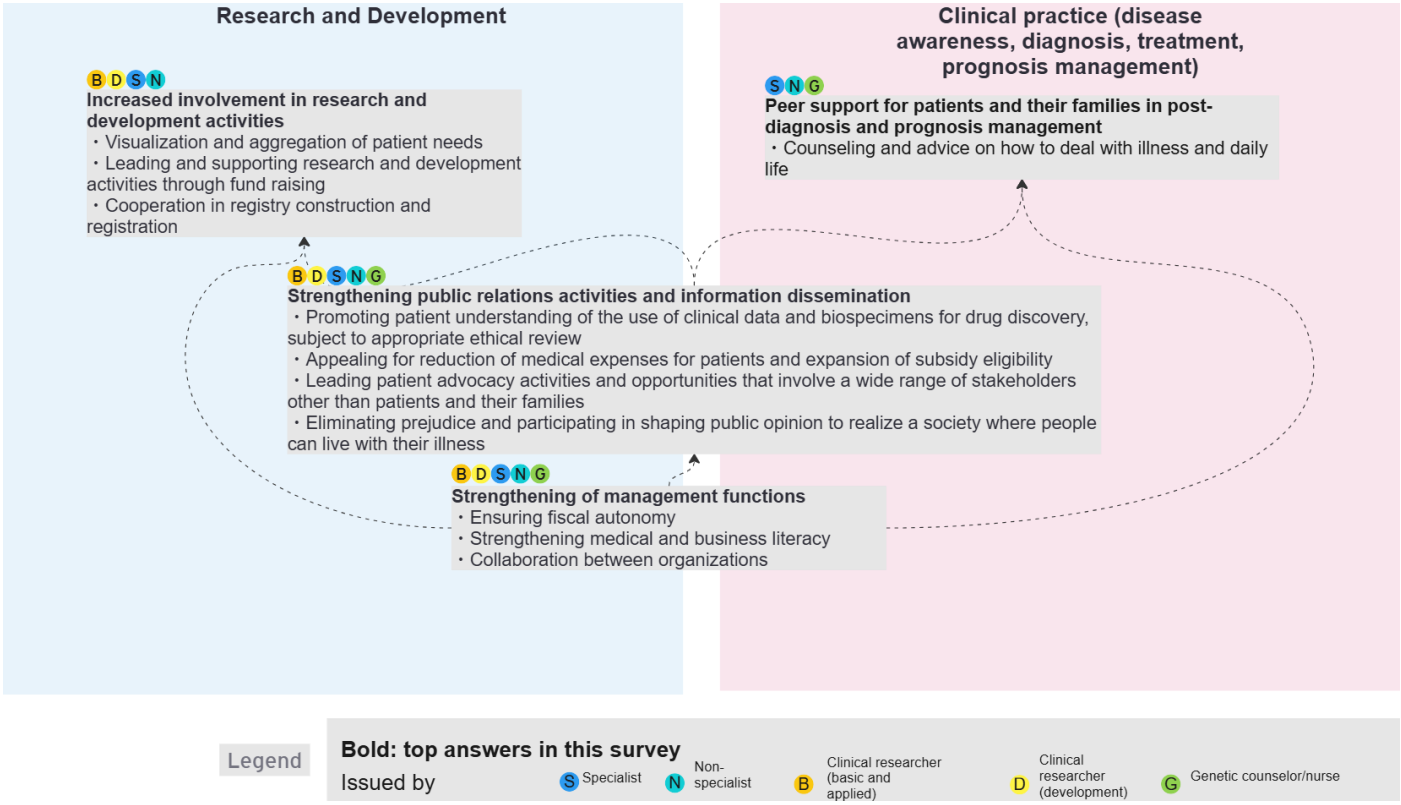
■Survey: Web survey
■Question: Please list your top three expectations of patient advocacy groups to achieve your vision (ranked)
■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.2.4-4: Expectations for patient advocacy groups in clinical practice – Top choice results by occupation



■Survey: Web survey
■Question: Please list your top three expectations of patient advocacy groups to achieve your vision (ranked)
■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.2.4-5: Overall Expectations of patient advocacy groups



4.2.5 Expectations for government and regulatory authorities

- Government and regulatory authorities were expected to support the promotion of R&D and policies related to the diagnosis of rare diseases; build ecosystems to accelerate drug discovery and development of new modalities; improve access to medical institutions and healthcare professionals who can perform testing and treatment and information on pharmaceuticals and products under development; expand opportunities to train specialized human resources and ensure sustainability; ensure diversification and flexibility in fund-raising and utilization methods; and contribute to the formation of rules and public opinion toward the realization of a 'society in which people can live comfortably with their illnesses.'
- Specifically, there is a demand to support the introduction of cutting-edge technology and infrastructure in drug discovery, such as GMP-compliant facilities and CPCs, promotion of drug pricing and pharmaceutical systems that will contribute to increasing the attractiveness of Japan's rare disease market, bold deregulation that will benefit patients, promotion of cooperation between medical institutions and the development of data infrastructure and systems to improve the efficiency of information transmission, improvement of the overall functionality of the medical system related to rare diseases through legislation, the development of registries, expansion of recipients and incentives for medical remuneration related to rare disease medical care, and policy discussions aimed at reducing the burden on patients and their families (such as the introduction of curricula on intractable and rare diseases in primary and secondary education, and special measures in research, development, and clinical practice).

To realize the ideal status, there are high expectations for government and regulatory authorities to support R&D related to the diagnosis of rare diseases. There are also high expectations for diversifying the means of fundraising for research, supporting R&D of new modalities, supporting the acceleration of animal model research and non-clinical trials, and establishing a drug price system that can properly evaluate the value of drugs for rare diseases (Figures 4.2.5-1, 4.2.5-2). Specifically, there were requests to lower the hurdles for R&D, simplify and ease the complex pharmaceutical system to eliminate drug lag and loss, establish a drug price system that can properly evaluate the value of drugs so that companies can recover their investments and promote drug discovery, and increase the budget necessary for training programs and employment of human resources who will be responsible for rare disease treatment in the future.

In addition, in actual clinical practice, there were expectations for support related to accelerating early diagnosis, disseminating the latest treatment methods, promoting collaboration between medical institutions and doctors, and strengthening expertise (Figures 4.2.5-3, 4.2.5-4). Specifically, in addition to involving various stakeholders, such as expanding mass screening, patient registries, promoting the use of medical data, consolidating and sharing functions in rare disease medical care (Center of Excellence, CoE [9]), and establishing rare disease-related programs in primary and secondary education and specialized education, administrative leadership through legal development was required. In relation to this, about human resource development, there were expectations for improving literacy and understanding not only in central government ministries and agencies but also in local government settings. These points were also mentioned in 4.1 Challenges, and concrete discussions are required to be promoted in the future.

> *"There are significantly fewer GMP-compliant facilities and CPC equipment related to new modalities compared to Europe and the United States, making securing materials a challenge.*
> (Clinical researcher (basic and applied) / Collagen Disease Department)

[9] To systematically create facilities and organizations that provide excellent treatment and research in specific medical fields

It is becoming more difficult to obtain funding from pharmaceutical companies, and the problem is that the government is not providing any budgetary support or alternatives to these situations. The current research grant system should be made more flexible, including reviewing the amount of funding and the selection criteria.
(Clinical researcher (basic and applied) / Pediatrics)

Clinical trial information is not being communicated to subjects sufficiently, making it extremely difficult to recruit appropriate subjects. If clinical trial information were centrally collected and there was a system that allowed users to narrow down clinical trial and subject information, it would be convenient for both healthcare professionals and subjects.
(Specialist / Pediatrics)

We hope that the government will aim to create a society in which 'patients can access the information and medicines they need' and 'patients and their families can live the same lives as healthy people' through a significant increase in budgets and personnel, relaxation of restrictions on the provision of information by the pharmaceutical industry and a review of genetics and diversity primary education.
(Clinical researcher (development) / All other hereditary disease)

I hope to see deregulation that will make it easier for industry-government-academia collaboration to proceed, genetic education for younger generations to help create a society free of prejudice and friction, and the development of mechanisms and systems that will allow people in rural areas to seamlessly receive medical care, such as testing and examinations, for rare diseases. I look forward to government leadership in the discussion of how to create a society that tolerates risk and failure.
(Clinical researcher (basic and applied) / All other hereditary disease)

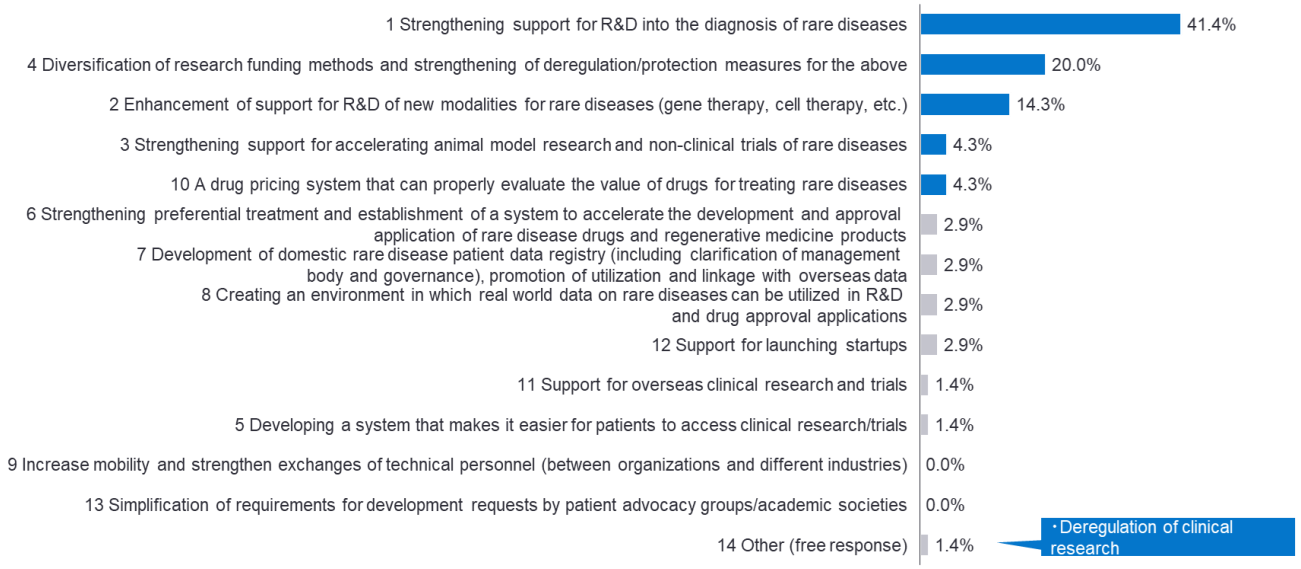
To resolve the shortage of human resources at medical institutions, we need to secure the necessary budgets for hiring and training full-time staff, make it easier to startup ventures on campus, and design incentives within academia through a review of personnel evaluation and rules on part-time work.
(Specialist / Collagen Disease Department)

Currently, registries are left to the discretion of individual organizations and individuals, but it would be ideal to have a registry system established as infrastructure by the government, like that for cancer, so that it can be used for research leading to the resolution of rare disease challenges. It would also be necessary to link this to the designated intractable disease system, and to relax regulations to promote the use of data.
(Specialist / Pediatrics)

The information provided by the government is often needed later, and the information itself is complicated and difficult to understand, which may result in delayed adoption of the system. I would like to see the system itself, such as medical fees, made easier to understand, and effectively communicated to healthcare professionals and facilities at the time they need it. I would also like to see the government strengthen its consultation function, which allows for frequent consultations, rather than simply communicating information one-way.
(Non-specialist / Neurology)

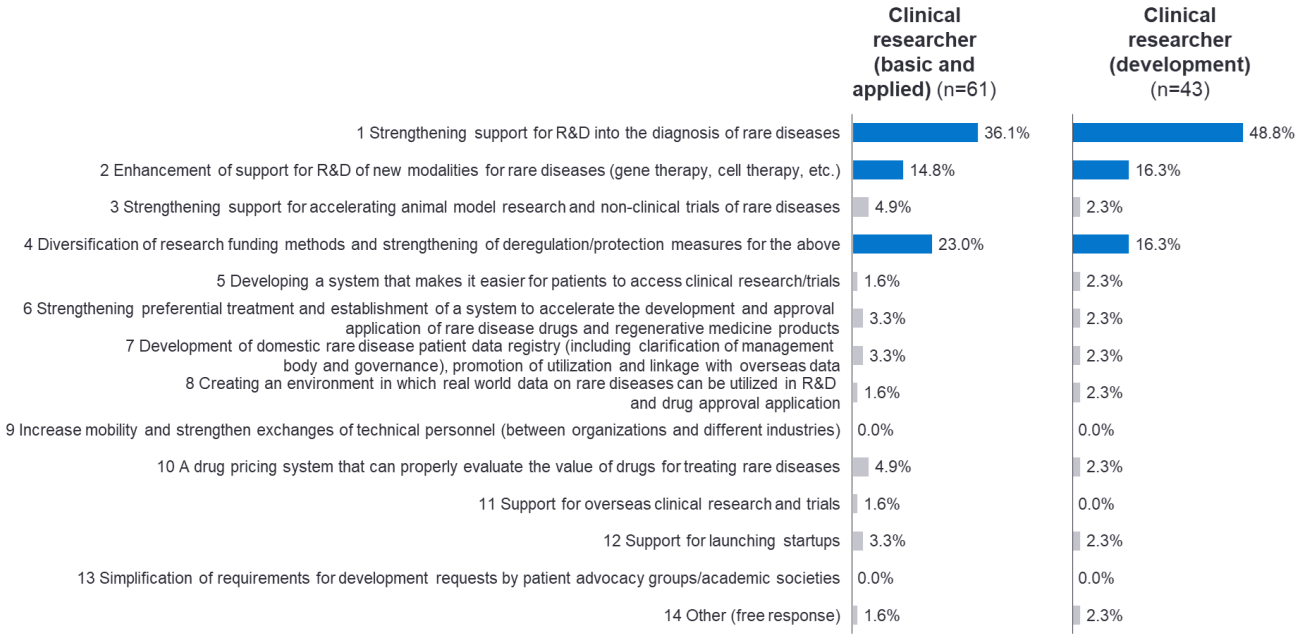
There is a large gap in understanding and response to rare disease medical care among local government officials, and policies are not unified. It is necessary to secure opportunities to deepen awareness and understanding.
(Clinical researcher (development) / Endocrinology and Metabolic Disease)

Figure 4.2.5-1: Expectations for government and regulatory authorities in R&D – Top selection results



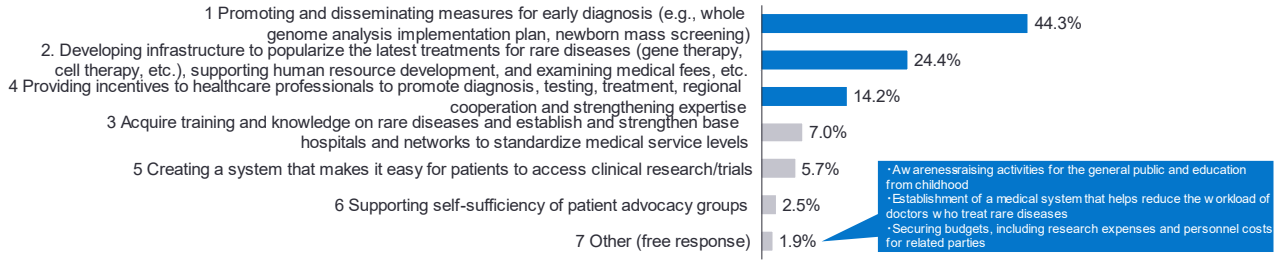
■Survey: Web survey
■Question: Please select the top five options that you expect from government and regulatory authorities to achieve the ideal state (ranked)
■Subjects: 70 clinical researchers (basic and applied), clinical researchers (development)

Figure 4.2.5-2: Expectations for government and regulatory authorities in R&D – Top selection results by occupation



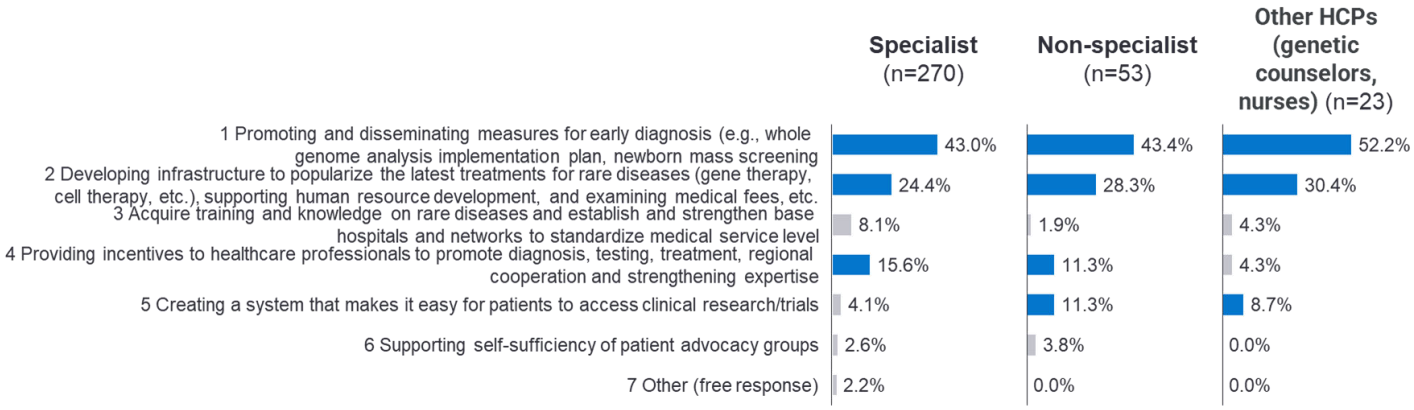
■Survey: Web survey
■Question: Please select your top five expectations of government and regulatory authorities to achieve the ideal state (ranking format)
■Subjects: 70 clinical researchers (basic and applied), clinical researchers (development)

Figure 4.2.5-3: Expectations for government and regulatory authorities in clinical practice – Top choice results



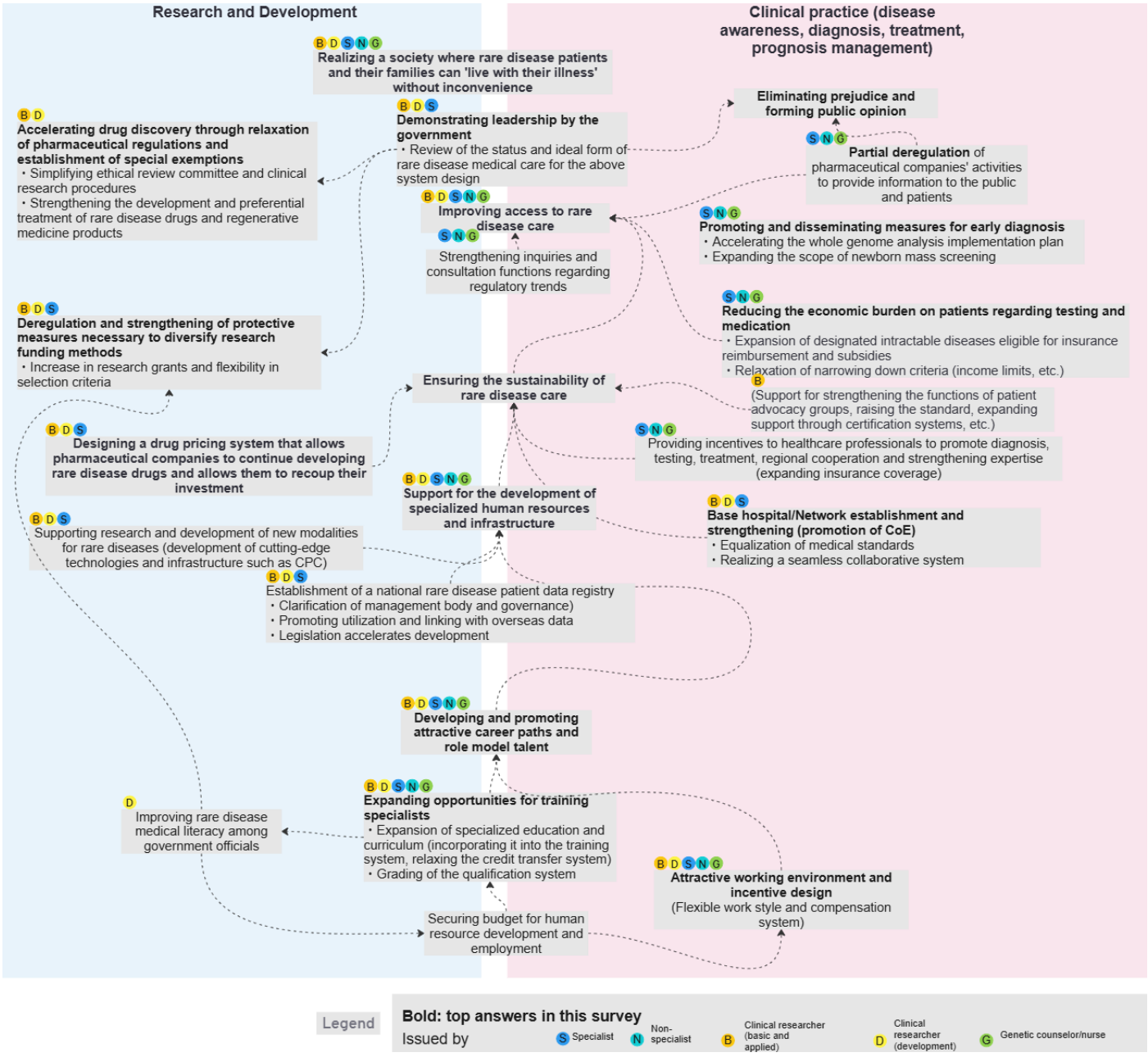
■Survey: Web survey
■Question: Please list your top three expectations of government and regulatory authorities to achieve the ideal state (ranked)
■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.2.5-4: Expectations for government and regulatory authorities in clinical practice – Top results by occupation



■Survey: Web survey
■Question: Please list your top three expectations of government and regulatory authorities to achieve the ideal state (ranked)
■Subjects: 316 specialists, non-specialists, and other HCPs (genetic counselors and nurses)

Figure 4.2.5-5: Overall expectations of government and regulatory authorities



4.2.6 Column: Future expectations for rare disease medicine

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On this occasion, Initiative on Rare and Undiagnosed Diseases (IRUD), Rare Disease Consortium Japan, and Japan Pharmaceutical Manufacturers Association have joined forces to carry out this comprehensive survey. We are delighted to share the findings and, simultaneously, outline strategic directions for addressing the identified challenges. IRUD has garnered support from a multitude of researchers, physicians, and healthcare professionals, marking this survey as unprecedented in its scope, and effectively bringing to light the myriad challenges faced by stakeholders daily. The challenges have been systematically cataloged and scrutinized from multiple angles, offering a holistic overview as well as detailed insights into diagnosis, treatment, and research and development. Moreover, we have synthesized and evaluated potential solutions, segmenting them by domain for ease of reference for those in search of domain-specific information.

Rare and intractable diseases are often mired in diagnostic uncertainty due to their scarcity and complexity, which in turn hampers the progress of therapeutic advancements, resulting in a substantial quandary. Since its establishment as a flagship initiative by Japan Agency for Medical Research and Development (AMED) in 2015, IRUD celebrates its tenth anniversary, having registered 9,046 families, completed analyses for 7,316, and identified causative factors in 3,521 cases, accounting for 48% of the total. Notably, this includes instances where novel genetic variants have been discovered, leading to the recognition of new disease entities and the initiation of therapeutic development, as well as cases where a diagnosis was finally secured after a prolonged diagnostic odyssey, with some patients fortuitously having access to existing treatments that led to recovery. The feedback from patients has been overwhelmingly positive, yet there have also been instances of bewilderment, underscoring the realities of genomic medicine in our nation.

In a serendipitous alignment, the "Act on the comprehensive and planned promotion of measures to ensure that the public can receive high-quality and appropriate genomic medicine with peace of mind," also known as the Genome Medicine Promotion Act, came into effect in May 2023, with the foundational plan currently under development. The insights derived from this survey are anticipated to enhance the substance and practicality of this foundational plan. As the survey has unveiled, the landscape of rare and intractable diseases is fraught with formidable challenges. Nevertheless, the success of IRUD in pinpointing genetic variants in nearly half of the undiagnosed cases, coupled with the development of gene therapies that have enabled previously immobile infants to stand and walk, heralds an optimistic future for the realm of rare and intractable diseases. It is our sincere hope that this report will make a meaningful contribution to the realization of that promising future.