

### **REGISTRATION DOCUMENT**

This document constitutes the registration document of Celyad Oncology SA (hereinafter "Celyad" or "The Company") (the "Registration Document") within the meaning of Article 6 and Article 10 of the Prospectus Regulation 2017/1129. The date of this Registration Document is 30 June 2020.

This Registration Document is valid for a period of twelve months from its date of approval (until 30 June 2021). The obligation to supplement this Registration Document in the event of significant new factors, material mistakes or material inaccuracies does not apply when this Registration Document is no longer valid.

The Financial Services and Markets Authority ("FSMA") approved the English version of this Registration Document in accordance with Article 20 of the Prospectus Regulation 2017/1129. The FSMA only approves this Registration Document as meeting the standards of completeness, comprehensibility and consistency imposed by the Prospectus Regulation and such approval by the FSMA should not be considered as an endorsement of the issuer.

### **TABLE OF CONTENTS**

1. KIS	SK FACTORS	5
1.1.	RISKS RELATED TO COMPANY'S FINANCIAL POSITION AND CAPITAL REQUIREMENTS	)
1.1.1.	The Company may need substantial additional funding, which may not be available on acceptable terms when needed, if at all	)
1.1.2.	The Company has incurred net losses in each period since its inception and anticipates that it will continue to incur net losses in the future	)
1.2.	RISKS RELATED TO COMPANY'S BUSINESS ACTIVITIES AND INDUSTRY	l
1.2.1.	Our autologous drug product candidates CYAD-01 and CYAD-02 as well as our allogeneic drug candidate CYAD-101 are new approaches to cancer treatment that presents significant challenges.	1
1.2.2.	Its drug product candidates are biologics, which are complex to manufacture, and the Company may encounter difficulties in production	2
1.2.3.	The future commercial success of the Company's product candidates will depend on the degree of market acceptance of its products among physicians, patients, healthcare payers and the medical community	3
1.2.4.	The Company may face significant competition and technological change which could limit or eliminate the market opportunity for its product candidates	3
1.3.	RISKS RELATED TO CLINICAL DEVELOPMENT14	1
1.3.1.	The Company may encounter substantial delays in its clinical trials or may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities	1
1.3.2.	In previous clinical trials involving T cell-based immunotherapies, some patients experienced serious adverse events. Our autologous drug product candidates CYAD-01 and CYAD-02 as well as our allogeneic drug candidate CYAD-101 may demonstrate a similar effect	5
1.3.3.	THINK trial is ongoing and not complete. Initial success in its ongoing clinical trial may not be indicative of results obtained when this trial is completed.	5
1.4.	RISKS RELATED TO LEGAL AND REGULATORY RISKS	5
1.4.1.	The Company is heavily dependent on the regulatory approval of CYAD-01, CYAD-02 or CYAD-101 in the United States and Europe	5
1.4.2.	Nearly all aspects of the Company's activities are subject to substantial regulation. No assurance can be given that any of the Company's product candidates will fulfil regulatory compliance	5
1.5.	RISKS RELATED TO INTELLECTUAL PROPERTY	7
1.5.1.	The Company could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of its drug product candidates	7
	The Company could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of its drug product candidates	
1.5.2.	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes	3
1.5.2. 1.5.3.	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates	8 9
1.5.2. 1.5.3.	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates	3 9
<ol> <li>1.5.2.</li> <li>1.5.3.</li> <li>1.5.4.</li> <li>1.6.</li> </ol>	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates	3
<ol> <li>1.5.2.</li> <li>1.5.3.</li> <li>1.5.4.</li> <li>1.6.</li> </ol>	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates	3 9 1
<ol> <li>1.5.2.</li> <li>1.5.3.</li> <li>1.5.4.</li> <li>1.6.</li> <li>1.6.1.</li> <li>1.7.</li> </ol>	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates	3 9 1 1
<ol> <li>1.5.2.</li> <li>1.5.3.</li> <li>1.5.4.</li> <li>1.6.</li> <li>1.6.1.</li> <li>1.7.</li> <li>1.7.1.</li> </ol>	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates	3 9 1 1 1
<ol> <li>1.5.2.</li> <li>1.5.3.</li> <li>1.5.4.</li> <li>1.6.</li> <li>1.6.1.</li> <li>1.7.</li> <li>1.7.1.</li> <li>1.7.2.</li> </ol>	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates	3 9 1 1 1
<ol> <li>1.5.2.</li> <li>1.5.3.</li> <li>1.5.4.</li> <li>1.6.</li> <li>1.6.1.</li> <li>1.7.</li> <li>1.7.1.</li> <li>1.7.2.</li> <li>1.7.3.</li> </ol>	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates	
<ol> <li>1.5.2.</li> <li>1.5.3.</li> <li>1.5.4.</li> <li>1.6.</li> <li>1.6.1.</li> <li>1.7.</li> <li>1.7.1.</li> <li>1.7.2.</li> <li>1.7.3.</li> <li>2. GE</li> <li>2.1.</li> </ol>	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates	3 9 1 1 1 1 2 <b>4</b> 5
<ol> <li>1.5.2.</li> <li>1.5.3.</li> <li>1.5.4.</li> <li>1.6.</li> <li>1.7.</li> <li>1.7.1.</li> <li>1.7.2.</li> <li>1.7.3.</li> <li>2. GE</li> <li>2.1.</li> <li>2.1.1.</li> </ol>	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates	8 9 1 1 1 1 1 1 1 1 1 1 1 1 1
<ol> <li>1.5.2.</li> <li>1.5.3.</li> <li>1.5.4.</li> <li>1.6.</li> <li>1.6.1.</li> <li>1.7.1.</li> <li>1.7.2.</li> <li>1.7.3.</li> <li>2. GE</li> <li>2.1.1.</li> <li>2.1.2.</li> </ol>	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates	<pre>33 33 30 11 11 11 12 2 4 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5</pre>

2.1.4.	Statutory Auditor	
2.1.5.	Forward-looking statements	27
2.1.6.	Market and Industry Information	
2.1.7.	Other available information	
2.1.8.	Availability of this Registration Document	
2.1.9.	Information incorporated by reference	
3. FIN	VANCIAL INFORMATION	30
3.1.	FINANCIAL INFORMATION CONCERNING THE COMPANY'S ASSETS AND LIABILITIES, FINANCIAL POSITION, PROFITS LOSES	
3.2.	Securities issued by the Company	
3.3.	Legal proceedings	
3.4.	Significant change in the financial position of Celyad since 31 December 2019	
3.5.	Dividends and dividend policy	
3.6.	Financial commitments	
3.7.	OVERVIEW FUNDInG	
3.8.	CURRENT CASH POSITION	
4. INI	DUSTRY AND BUSINESS OVERVIEW	
4.1.	INDUSTRY AND BUSINESS OVERVIEW	
4.1.1.	Principal activities	
4.1.1.	1.0verview	
4.1.1.2	2.Pipeline and Approach	
4.1.2.	Principal markets on which the Company competes	50
4.1.3.	Strategy	50
4.1.4.	Licensing and Collaboration Agreements and Intellectual Property	52
4.1.4.	I.Licensing and Collaboration Agreements	52
4.1.4.2	2.Intellectual Property	56
4.1.5.	Competition	57
4.1.6.	Investments	58
4.1.7.	Government Regulation	58
5. MA	NAGEMENT AND CORPORATE GOVERNANCE	74
5.1.	General	
5.2.	Board of Directors	
5.2.1.	Composition of the Board of Directors	
5.2.2.	Board mandates	80
5.2.3.	Director Independence	82
5.2.4.	Role of the Board in Risk Oversight	83
5.2.5.	Committees within the Board of Directors	83
5.2.5.	l.General	83
5.2.5.2	2.Audit Committee	83
	3. Nomination and Remuneration Committee	
5.2.5.4	4.Strategy Committee	85
5.2.5.	5. Meetings of the Board and the committees	
5.3.	Executive Committee	
5.4.	Conflict of Interest of directors and members of the executive team and transactions with affiliated companies	
5.4.1.	General	

5.4.7.	Viarket abuse regulations
	Code of Business Conduct and Ethics
	Transactions with affiliates
	Related Party Transactions
5.4.3.	Existing conflicts of interest of members of the Board of Directors
5.4.2.	Conflicts of interest of directors

### **1. RISK FACTORS**

The risks and uncertainties that the Company believes are material are described below.

The risk factors are presented in seven categories, depending on their nature. In each category, the risk factor which in the assessment of the Company is the most material, taking into account the negative impact on the Company (including any relevant mitigation measures) and the probability of its occurrence, is mentioned first. The remaining risk factors within each category are not ranked in order to their materiality.

The table below summarises the material risk factors identified by the Company and provides, for each risk factor, their probability of occurrence (on three levels: low, moderate and high) and their negative impact on the Company (on three levels: low, moderate and high). In each of the seven categories, the risk factors have been ranked on the basis of these criteria.

А.	RISKS RELATED TO COMPANY'S FINANCIAL POSITION AND CAPITAL	Probability of occurrence	Negative impact on Celyad
	REQUIREMENTS	Low/moderate/high	Low/moderate/high
1.	The Company may need substantial additional funding, which may not be available on acceptable terms when needed, if at all.	Moderate	High
2.	The Company has incurred net losses in each period since its inception and anticipates that it will continue to incur net losses in the future.	Moderate	Low

B. 1.	RISKS RELATED TO COMPANY'S BUSINESS ACTIVITIES AND INDUSTRY The Company's drug product candidates are new approaches to cancer treatment that presents significant challenges.	Probability of occurrence Low/moderate/high High	Negative impact on Celyad Low/moderate/high High
2.	The Company's drug product candidates are biologics, which are complex to manufacture, and the Company may encounter difficulties in production, particularly with respect to process development or scaling-out of its manufacturing capabilities. If the Company or any of its third- party manufacturers encounters such difficulties, its ability to provide supply of its drug product candidates for clinical trials or its products for patients, if approved, could be delayed or stopped, or the Company may be unable to maintain a commercially viable cost structure.	Moderate	High
3.	The future commercial success of the Company's product candidates will depend on the degree of	Moderate	High

	market acceptance of its products among physicians, patients, healthcare payers and the medical community.		
4.	The Company may face significant competition and technological change which could limit or eliminate the market opportunity for its product candidates.	Moderate	Moderate

C.	RISKS RELATED TO CLINICAL DEVELOPMENT	Probability of occurrence Low/moderate/high	Negative impact on Celyad Low/moderate/high
1.	The Company may encounter substantial delays in its clinical trials or may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.	Moderate	High
2.	In previous clinical trials involving T cell-based immunotherapies, some patients experienced serious adverse events. The Company's drug product candidates may demonstrate a similar effect or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.	Low	High
3.	The Company'strials are ongoing and not complete. Initial success in its ongoing clinical trial may not be indicative of results obtained when this trial is completed. Furthermore, success in early clinical trials may not be indicative of results obtained in later trials.	Low	Low

D.	RISKS RELATED TO LEGAL AND REGULATORY RISKS	Probability of occurrence Low/moderate/high	Negative impact on Celyad Low/moderate/high
1.	The Company is heavily dependent on the regulatory approval of CYAD-01, CYAD-02 and CYAD-101 in the United States and Europe, and subsequent commercial success of CYAD-01, 02 or 101, both of which may never occur.		High
2.	Nearly all aspects of the Company's activities are subject to substantial regulation. No	Moderate	Moderate

assurance can be given that any of the	
Company's product candidates will fulfil	
regulatory compliance. Failure to comply with	
such regulations could result in delays,	
suspension, refusals, fines and withdrawal of	
approvals.	

E.	RISKS RELATED TO INTELLECTUAL PROPERTY	Probability of occurrence Low/moderate/high	Negative impact on Celyad Low/moderate/high
1.	The Company could be unsuccessful in obtaining, maintaining or protecting its intellectual property rights for one or more of its drug product candidates.	High	Moderate
2.	The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates, which may impede the Company's ability to compete effectively.	High	Moderate
3.	The Company depends on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm its business.	Low	Moderate
4.	The Company may infringe on the patents or intellectual property rights of others and may face patent litigation, which may be costly and time consuming.	Moderate	Low

F.	POST-AUTHORIZATION RISKS	Probability of occurrence Low/moderate/high	Negative impact on Celyad Low/moderate/high
1.	The Company has not yet finalized its clinical development program for CYAD-01 and CYAD-02 in AML and CYAD-101 in CRC. The FDA and comparable foreign regulators may not agree with its proposed protocols for these clinical trials, or may withdraw approvals, which could result in delays or cancellation of the programs.	Moderate	High

			1
G.	RISKS LINKED TO THE COMPANY'S RELIANCE ON THIRD PARTIES	Probability of occurrence Low/moderate/high	Negative impact on Celyad Low/moderate/high
1.	Cell-based therapies rely on the availability of specialty raw materials, which may not be available to the Company on acceptable terms or at all.	Moderate	High
2.	The Company relies on third parties to conduct, supervise and monitor its clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, the Company may not be able to obtain regulatory approval for or commercialize its drug product candidates and its business could be substantially harmed.	Moderate	High
3.	The Company relies and will continue to rely on collaborative partners regarding the development of its research programmes and product candidates.	Moderate	Moderate

### 1.1. RISKS RELATED TO COMPANY'S FINANCIAL POSITION AND CAPITAL REQUIREMENTS

### 1.1.1. The Company may need substantial additional funding, which may not be available on acceptable terms when needed, if at all.

The Company's operations have required substantial amounts of cash since inception. The Company expects to continue to spend substantial amounts to continue the clinical development of its drug product candidates, including its ongoing and planned clinical trials for CAR-T NKG2D and any future drug product candidates. If approved, the Company will require significant additional amounts in order to launch and commercialize our drug product candidates.

The Company ended first quarter 2020 with a treasury position of  $\in$ 33.8 million (\$37.3 million). Net cash burn over the first quarter of 2020 amounted to  $\in$ 5.5 million, which is in line with expectations. The Company confirms its previous guidance that its treasury position should be sufficient to fund operating expenses and capital expenditure requirements, based on the current scope of activities, into third quarter 2021. However, changing circumstances may cause it to increase its spending significantly faster than it currently anticipates, and the Company may need to spend more money than currently expected because of circumstances beyond its control. The Company may require additional capital for the further development and commercialization of its drug product candidates and may need to raise additional funds sooner if the Company chooses to expand more rapidly than it presently anticipates.

The achievement of milestones (R&D, scientific, clinical, regulatory, business) will trigger payment obligations towards Celdara, Dartmouth and Horizon, which will negatively impact Celyad's profitability and may require material additional funding (see Section 3.6).

The Company contracted over the past year numerous funding agreements with the Walloon Region to partially finance its research and development programs. Under the terms of the agreements, the Company would need to obtain the consent of the Walloon Region for any out-licensing agreement or sale to a third party of any or all of its products, prototypes or installations which may reduce the Company's ability to partner or sell part or all of its products. Furthermore, when the research and development programs partially financed by the Company enter in "exploitation phase", the Company has to start reimbursing the funding received (see Section 3.6).

The Company may not be able to reimburse such funding under the terms of the agreements or such reimbursement may jeopardize the funding of its clinical and scientific activities.

The Company's ability to raise additional funds will depend on financial, economic and market conditions and other factors, over which it may have no or limited control, and the Company cannot guarantee that additional funds will be available to it when necessary on commercially acceptable terms, if at all. If the necessary funds are not available, the Company may need to seek funds through collaborations and licensing arrangements, which may require it to reduce or relinquish significant rights to its research programmes and product candidates, to grant licences on its technologies to partners or third parties or enter into new collaboration agreements, the terms could be less favourable to the Company than those it might have obtained in a different context. If adequate funds are not available on commercially acceptable terms when needed, the Company may be forced to delay, reduce or terminate the development or commercialisation of all or part of its research programmes or product candidates or it may be unable to take advantage of future business opportunities.

### 1.1.2. The Company has incurred net losses in each period since its inception and anticipates that it will continue to incur net losses in the future.

The Company is not profitable and has incurred losses in each period since its inception. For the years ended December 31, 2019, 2018 and 2017, the Company incurred a loss for the year of  $\notin$ 28.6 million,  $\notin$ 37.4 million and  $\notin$ 56.4 million, respectively. As of December 31, 2019, the Company had a retained loss of  $\notin$ 74.4 million. The Company expects these losses to increase as it continues to incur significant research and development and other expenses related to its ongoing operations, continues to advance its drug product candidates through pre-clinical studies and clinical trials, seek regulatory approvals for its drug product candidates, scale-up manufacturing capabilities and hire additional personnel to support the development of its drug product candidates and to enhance its operational, financial and information management systems.

Even if the Company succeeds in commercializing one or more of its drug product candidates, it will continue to incur losses for the foreseeable future relating to its substantial research and development expenditures to develop its technologies.

The Company may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect its business. The size of its future net losses will depend, in part, on the rate of future growth of its expenses and its ability to generate revenue.

Its prior losses and expected future losses have had and will continue to have an adverse effect on its shareholders' equity and working capital. Further, the net losses the Company incurs may fluctuate significantly from quarter to quarter and year to year, such that a period to period comparison of its results of operations may not be a good indication of its future performance.

### **1.2.** RISKS RELATED TO COMPANY'S BUSINESS ACTIVITIES AND INDUSTRY

## 1.2.1. Our autologous drug product candidates CYAD-01 and CYAD-02 as well as our allogeneic drug candidate CYAD-101 are new approaches to cancer treatment that presents significant challenges.

The Company has concentrated its research and development efforts on cell-based immunotherapy technology, and its future success is highly dependent on the successful development of cell-based immunotherapies in general and in particular its approach using NKG2D receptor ligands, an activating receptor of NK cells. The Company cannot be sure that its T-cell immunotherapy technologies will yield satisfactory products that are safe and effective, scalable or profitable.

Its approach to cancer immunotherapy and cancer treatment generally poses a number of challenges, including:

- developing and deploying consistent and reliable processes for engineering a patient's T cells ex vivo and infusing the engineered T-cells back into the patient;
- educating medical personnel regarding the potential side effect profile of each of its drug product candidates, such as the potential adverse side effects related to cytokine release or neurotoxicity;
- developing processes for the safe administration of these drug product candidates, including long-term follow-up for all patients who receive its drug product candidates;
- developing therapies for types of cancers beyond those addressed by its current drug product candidates.

Additionally, because its technology involves the genetic modification of patient cells ex vivo using a virus, the Company is subject to many of the challenges and risks that gene therapies face, including:

• Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. To date, only one product that involves the genetic modification of patient cells has been approved in the United States and only

one has been approved in the European Union (for sake of clarity, said approvals relate to products form other companies than Celyad. Celyad has no such product approved yet);

- Although its viral vectors are not able to replicate, there is a risk with the use of retroviral or lentiviral vectors that they could lead to new or reactivated pathogenic strains of virus or other infectious diseases;
- The FDA recommends a 15-year follow-up observation period for all patients who receive treatment using gene therapies, and the Company may need to adopt such an observation period for its drug product candidates.

Moreover, public perception of therapy safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved, of physicians to subscribe to the novel treatment mechanics. Physicians may not be willing to undergo training to adopt this novel and personalized therapy, may decide the therapy is too complex to adopt without appropriate training and may choose not to administer the therapy. Based on these and other factors, hospitals and payors may decide that the benefits of this new therapy do not or will not outweigh its costs.

### 1.2.2. Its drug product candidates are biologics, which are complex to manufacture, and the Company may encounter difficulties in production

Its drug product candidates are biologics and the process of manufacturing its products is complex, highly-regulated and subject to multiple risks. The manufacture of its drug product candidates involves complex processes, including harvesting cells from patients, selecting and expanding certain cell types, engineering or reprogramming the cells in a certain manner to create CAR-T cells, expanding the cell population to obtain the desired dose, and ultimately infusing the cells back into a patient's body. As a result of the complexities, the cost to manufacture its drug product candidates, is higher than traditional small molecule chemical compounds, and the manufacturing process is less reliable and is more difficult to reproduce. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions.

Although the Company is working, or will be working, to develop commercially viable processes for the manufacture of its drug product candidates, doing so is a difficult and uncertain task, and there are risks associated with scaling to the level required for later-stage clinical trials and commercialization, including, among others, cost overruns, potential problems with process scale-out, process reproducibility, stability issues, lot consistency, and timely availability of reagents or raw materials. We may ultimately be unable to reduce the cost of goods for its drug product candidates to levels that will allow for an attractive return on investment if and when those drug product candidates are commercialized.

In addition, the manufacturing process that the Company develops for its drug product candidates is subject to regulatory authorities' approval process, and the Company will need to make sure that the Company or its contract manufacturers, or CMO's, if any, are able to meet all regulatory authorities requirements on an ongoing basis. If the Company or its CMO's are unable to reliably produce drug product candidates to specifications acceptable to the regulatory authorities, the Company may not obtain or maintain the approvals the Company needs to commercialize such drug product candidates. Even if the Company obtains regulatory approval for any of its drug product candidates, there is no assurance that either the Company or its CMO's will be able to manufacture the approved product to specifications acceptable to the regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could have an adverse effect on its business, financial condition, results of operations and growth prospects.

## 1.2.3. The future commercial success of the Company's product candidates will depend on the degree of market acceptance of its products among physicians, patients, healthcare payers and the medical community.

The Company's product candidates are at varying stages of development and the Company may never have a product that is commercially successful.

The Company does not expect to be able to market any of its products for a number of years. Furthermore, when available on the market physicians may not prescribe the Company's products, which would prevent the Company from generating significant revenues or becoming profitable. Market acceptance of the Company's future products by physicians, patients and healthcare payers will depend on a number of factors, many of which are beyond the Company's control, including, but not limited to:

- Acceptance by physicians, patients and healthcare payers of each product as safe, effective and cost-effective;
- Relative convenience, ease of use, ease of administration and other perceived advantages over alternative products;
- Prevalence and severity of adverse events;
- The extent to which products are approved for inclusion and reimbursed on formularies of hospitals and managed care organizations;

### 1.2.4. The Company may face significant competition and technological change which could limit or eliminate the market opportunity for its product candidates.

The market for pharmaceutical products is highly competitive. The Company's competitors include many established pharmaceutical, biotechnology, universities and other research or commercial institutions, many of which have substantially greater financial, research and development resources than the Company. The fields in which the Company operates are characterised by rapid technological change and innovation. There can be no assurance that competitors of the Company are not currently developing or will not in the future develop technologies and products that are equally or more effective and/or are more economical as any current or future technology or product of the Company. Competing products may gain faster or greater market acceptance than the Company's products and medical advances or rapid technological development by competitors may result in the Company's product candidates becoming non-competitive or obsolete before the Company is able to recover its research and development and commercialisation expenses. If the Company or its product candidates do not compete effectively, it may have a material adverse effect on the Company's business.

#### **1.3.** RISKS RELATED TO CLINICAL DEVELOPMENT

### 1.3.1. The Company may encounter substantial delays in its clinical trials or may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities

Before obtaining regulatory approval or marketing authorization from regulatory authorities for the sale of its drug product candidates, if at all, the Company must conduct extensive pre-clinical tests and clinical trials to demonstrate the safety and efficacy of the drug product candidates in humans. Preclinical tests and Clinical testing are expensive, time-consuming and uncertain as to outcome. The Company cannot guarantee that any pre-clinical tests and clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

- delays in obtaining required Investigational Review Board, or IRB, approval at each clinical trial site;
- imposition of a clinical hold by regulatory agencies, after an inspection of its clinical trial operations or trial sites;
- failure by its CRO's, other third parties or the Company to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's good clinical practices, or GCP's, or applicable regulatory guidelines in other countries;
- delays in the testing, validation, manufacturing and delivery of its drug product candidates to the clinical sites;
- occurrence of serious adverse events associated with the drug product candidate that are viewed to outweigh its potential benefits;

Furthermore, the timely completion of clinical trials in accordance with their protocols depends, among other things, on its ability to enrol a sufficient number of patients who remain in the trial until its conclusion. The Company may experience difficulties in patient enrolment in its clinical trials for a variety of reasons, including:

- the patient eligibility criteria defined in the protocol;
- its ability to recruit clinical trial investigators with the appropriate competencies and experience;
- competing clinical trials for similar therapies;
- the risk that patients enrolled in clinical trials will not complete a clinical trial.

Any inability to successfully complete pre-clinical and clinical development could result in additional costs to the Company or impair its ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Clinical trial delays could also shorten any periods during

which the Company may have the exclusive right to commercialize its drug product candidates or allow its competitors to bring products to market before the Company does, which could impair its ability to successfully commercialize its drug product candidates and may harm its business and results of operations.

Its drug product candidates could potentially cause other adverse events that have not yet been predicted. As described above, any of these events could prevent the Company from achieving or maintaining market acceptance of its drug product candidates and impair its ability to commercialize its products if they are ultimately approved by applicable regulatory authorities.

# 1.3.2. In previous clinical trials involving T cell-based immunotherapies, some patients experienced serious adverse events. Our autologous drug product candidates CYAD-01 and CYAD-02 as well as our allogeneic drug candidate CYAD-101 may demonstrate a similar effect.

In previous and ongoing clinical trials involving CAR-T cell products by other companies or academic researchers, many patients experienced side effects such as neurotoxicity and CRS, which have in some cases resulted in clinical holds in ongoing clinical trials of CAR-T drug product candidates. There have been life threatening events related to severe neurotoxicity and CRS, requiring intense medical intervention such as intubation or pressor support, and in several cases, resulted in death. Severe neurotoxicity is a condition that is currently defined clinically by cerebral edema, confusion, drowsiness, speech impairment, tremors, seizures, or other central nervous system side effects, when such side effects are serious enough to lead to intensive care. In some cases, severe neurotoxicity was thought to be associated with the use of certain lymphodepletion preconditioning regimens used prior to the administration of the CAR-T cell products.

Undesirable side effects caused by its drug product candidates could cause the Company or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA or other comparable foreign regulatory authorities. Results of its trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trials or result in potential product liability claims (the Company is insured to compensate for potential claims that would occur in each of its clinical trials). The Company expects to have to train medical personnel regarding its T-cell based immunotherapy drug product candidates to understand their side effects of to both its planned clinical trials and upon any commercialization of any T-cell based immunotherapy drug product candidates. Inadequate training in recognizing or managing the potential side effects of T-cell based immunotherapy drug product candidates could result in patient deaths. Any of these occurrences could have a material adverse effect on its business, financial condition and prospects.

### 1.3.3. THINK trial is ongoing and not complete. Initial success in its ongoing clinical trial may not be indicative of results obtained when this trial is completed.

Its clinical experience with its lead drug product candidate CYAD-01 is limited. The Company has treated a small number of patients as of the date of this report. In particular, the results of the CM-CS1 trial and the interim results of the THINK trial should not be relied upon as evidence that its ongoing or future clinical trials will succeed. There is limited data concerning long-term safety and efficacy following treatment with CYAD-01. Its drug product candidates may fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical trials.

Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development.

#### 1.4. RISKS RELATED TO LEGAL AND REGULATORY RISKS

### 1.4.1. The Company is heavily dependent on the regulatory approval of CYAD-01, CYAD-02 or CYAD-101 in the United States and Europe.

The Company is a clinical-stage biopharmaceutical company with no products approved by regulatory authorities or available for commercial sale. The Company may be unable to develop or commercialise a product, product candidate or research programme, or may cease some of its operations, which may have a material adverse effect on the Company's business.

The Company has generated limited revenue to date and does not expect to generate any revenue from product sales for the foreseeable future. The Company's ability to generate revenues in the near term will depend on its ability to obtain regulatory approval and successfully commercialize CYAD-01, CYAD-02 and CYAD-101 on its own in the United States, the first country in which the Company intends to seek approval for these candidates. The Company may experience delays in obtaining regulatory approval in the United States for these candidates, if it is approved at all, and the price of its ordinary shares and/or ADSs may be negatively impacted. Even if the Company receives regulatory approval, the timing of the commercial launch of these candidates in the United States is dependent upon a number of factors, including, but not limited to, hiring sales and marketing personnel, pricing and reimbursement timelines, the production of sufficient quantities of commercial drug product and implementation of marketing and distribution infrastructure.

## 1.4.2. Nearly all aspects of the Company's activities are subject to substantial regulation. No assurance can be given that any of the Company's product candidates will fulfil regulatory compliance.

The international pharmaceutical and medical technology industry is highly regulated by government bodies (hereinafter the "Competent Authorities") that impose substantial requirements covering nearly all aspects of the Company's activities notably on research and development, manufacturing, preclinical tests, clinical trials, labelling, marketing, sales, storage, record keeping, promotion and pricing of its research programmes and product candidates. Compliance with standards laid down by local Competent Authorities is required in each country where the Company, or any of its partners or licensees, conducts said activities in whole or in part. The Competent Authorities notably include the European Medicine Agency ("EMA") in the European Union and the Food and Drug Administration ("FDA") in the United States.

There can be no assurance that product candidates of the Company will fulfil the criteria required to obtain necessary regulatory clearance to access the market. Also, at this time, the Company cannot guarantee or know the exact nature, precise timing and detailed costs of the efforts that will be necessary to complete the remainder of the development of its research programmes and products candidates.

The specific regulations and laws, as well as the time required to obtain Competent Authorities approvals, may vary from country to country, but the general regulatory procedures are similar in the European Union and the United States of America. At any time Competent Authorities may require discontinuation or holding of clinical trials or require additional data prior to completing their review or may issue restricted authorisation or authorise products for clinical trials or marketing for narrower indications than requested or require further data or studies be conducted and submitted for their review. There can be no guarantee that such additional data or studies, if required, will corroborate earlier data.

#### **1.5. RISKS RELATED TO INTELLECTUAL PROPERTY**

### 1.5.1. The Company could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of its drug product candidates.

The patent application process is expensive and time-consuming, and the Company and its current or future licensors and licensees may not be able to apply for or prosecute patents on certain aspects of its drug product candidates or deliver technologies at a reasonable cost, in a timely fashion, or at all. It is also possible that the Company or its current licensors, or any future licensors or licensees, will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, its patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of its business. It is possible that defects of form in the preparation or filing of its patents or patent applications may exist, or may arise in the future, such as with respect to proper priority claims, inventorship, claim scope or patent term adjustments. Under its existing license agreements with the Trustees of Dartmouth College, the Company has the right, but not the obligation, to enforce its licensed patents. If its current licensors, or any future licensors or licensees, are not fully cooperative or disagree with the Company as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised and the Company might not be able to prevent third parties from making, using, and selling competing

products. If there are material defects in the form or preparation of its patents or patent applications, such patents or applications may be invalid and unenforceable.

Celyad currently has issued patents and patent applications directed to its drug product candidates and medical devices, and the Company anticipates that it will file additional patent applications in several jurisdictions, including several European Union countries and the United States, as appropriate.

Celyad cannot be certain, however, that the claims in its pending patent applications will be considered patentable by patent offices in various countries, or that the claims in any of its issued patents will be considered valid and enforceable by local courts.

The strength of patents in the biotechnology and pharmaceutical field can be uncertain, and evaluating the scope of such patents involves complex legal and scientific analyses. The patent applications that the Company owns or in-licenses may fail to result in issued patents with claims that cover its drug product candidates or uses thereof in the European Union, in the United States or in other jurisdictions. Even if the patents do successfully issue, third parties may challenge the validity, enforceability, or scope thereof, which may result in such patents being narrowed, invalidated, or held unenforceable. If the breadth or strength of protection provided by the patent applications the Company holds with respect to its drug product candidates is threatened, this could dissuade companies from collaborating with the Company to develop, and could threaten its ability to commercialize, its drug product candidates. Further, because patent applications in most countries are confidential for a period of time after filing, the Company cannot be certain that it was the first to file any patent application related to its drug product candidates.

Patents have a limited lifespan. Various extensions may be available; however the life of a patent, and the protection it affords, is limited. Further, the extensive period of time between patent filing and regulatory approval for a drug product candidate limits the time during which the Company can market a drug product candidate under patent protection, which may particularly affect the profitability of its early-stage drug product candidates. If the Company encounters delays in its clinical trials, the period of time during which the Company could market its drug product candidates under patent protection for its drug product candidates, the Company may be open to competition from biosimilar versions of its drug product candidates.

Filing, prosecuting and defending patents on drug product candidates in all countries throughout the world would be prohibitively expensive. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as laws in the European Union or the United States. Consequently, the Company may not be able to prevent third parties from practicing its inventions in all countries, or from selling or importing products made using its inventions in and into other jurisdictions.

## 1.5.2. The Company's patents and other intellectual property rights portfolio is relatively young and may not adequately protect its research programmes and product candidates.

The Company's success will depend in part on the ability of the Company to obtain, maintain and enforce its patents and other intellectual property rights. The Company's research programs and product candidates are covered by several patent application families, which are either licensed to the Company or owned by the Company. Out of the numerous patent applications controlled by the Company, eleven national patents have been granted in the US relating to the field of immuno-oncology. The Company cannot guarantee that it will be in a position in the future to develop new patentable inventions or that the Company or its licensors will be able to obtain or maintain these patent rights against patent offices and other third-party challenges to their validity, scope and/or enforceability. Moreover, we may have little or no control over its licensors abilities' to preventing the infringement of their patents or the misappropriation of their intellectual property. There can be no assurance that the technologies used in our research programs and product candidates are patentable. If the Company or its licensors do not obtain patents in respect of their technologies or if the patents of the Company or its licensors are invalidated, third parties may use the technologies without payment to the Company. A third party's ability to use unpatented technologies is enhanced by the fact that the published patent application contains a detailed description of the relevant technology.

The Company cannot guarantee that third parties, contract parties or employees will not claim ownership rights over the patents or other intellectual property rights owned or held by the Company.

The Company also relies on proprietary know-how to protect its research programmes and product candidates. Know-how is difficult to maintain and protect. The Company uses reasonable efforts to maintain its know-how, but it cannot assure that its partners, employees, consultants, advisors or other third parties will not wilfully or unintentionally disclose proprietary information to competitors.

As far as the Company is aware, its intellectual property has not been challenged otherwise than by patent offices in the normal course of examination of its patent applications or misappropriated.

## 1.5.3. The Company depends on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm its business.

The Company is dependent on patents, know-how, and proprietary technology, both its own and licensed from others. We license technology from the Trustees of Dartmouth College, or Dartmouth College. Dartmouth College may terminate our license, if we fail to meet a milestone within the specified time period, unless we pay the corresponding milestone payment. Dartmouth College may terminate either the license in the event we default or breach any of the provisions of the applicable license, subject to 30 days' prior notice and opportunity to cure. In addition, the license automatically terminates in the event we become insolvent, make an assignment for the benefit of creditors or file, or have filed against us, a petition in bankruptcy. Furthermore, Dartmouth College may terminate our license, after April 30, 2024, if we fail to meet the specified minimum net sales obligated to pay had we met such minimum net sales obligation. We also license technology from Horizon Discovery Limited, or Horizon Discovery.

Horizon Discovery may terminate our license in case of insolvency, material breach or force majeure. Any termination of these licenses or any of our other licenses could result in the loss of significant rights and could harm its ability to commercialize its drug product candidates. Disputes may also arise between the Company and its licensors regarding intellectual property subject to a license agreement, including those relating to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which its technology and processes infringe on intellectual property of the licensor that is not subject to the license agreement;
- its right to sublicense patent and other rights to third parties under collaborative development relationships;
- the amount and timing of milestone and royalty payments;
- whether the Company is complying with its diligence obligations with respect to the use of the licensed technology in relation to its development and commercialization of its drug product candidates;

If disputes over intellectual property that the Company has licensed prevent or impair its ability to maintain its current licensing arrangements on acceptable terms, the Company may be unable to successfully develop and commercialize the affected drug product candidates. If the Company or its licensors fail to adequately protect this intellectual property, the Company's ability to commercialize its products could suffer.

The licenses of the Company may be terminated if it is unable to meet the payment obligations under the agreements (notably if the Company is unable to obtain additional financing).

### 1.5.4. The Company may infringe on the patents or intellectual property rights of others and may face patent litigation, which may be costly and time consuming.

The Company's success will depend in part on its ability to operate without infringing on or misappropriating the intellectual property rights of others. The Company cannot guarantee that its activities, or those of its licensors, will not infringe on the patents or other intellectual property rights owned by others.

The Company may also be required to cease development, use or sale of the relevant research programme, product candidate or process or it may be required to obtain a licence on the disputed rights, which may not be available on commercially reasonable terms, if at all.

The Company may spend significant time and effort and may incur substantial costs if required to defend against any infringement claims or to assert its intellectual property rights against third parties. The risk of such a procedure by a third party may increase in view of the Company making public announcement regarding one or more of its research programmes and product candidates. The Company may not be

successful in defending its rights against such procedures or claims and may incur as a consequence thereof significant losses, costs or delays in its intended commercialisation plans as a result thereof.

#### 1.6. POST-AUTHORIZATION RISKS

### 1.6.1. The Company has not yet finalized its clinical development program for CYAD-01, CYAD-02 and CYAD-101 in AML and CRC. Regulators may not agree with its proposed protocols for these clinical trials, which could result in delays.

The Company is still considering the clinical development program for its product candidates in AML and CRC. Prior to initiating new clinical trials for its drug product candidates, The Company is required to submit clinical trial protocols for these trials to the FDA and comparable foreign regulators in other jurisdictions where the Company plans to undertake clinical trials. The Company may not reach agreement with these regulators, or there may be a delay in reaching agreement. These regulators may want to see additional clinical or preclinical data regarding its drug product candidates before the Company initiates new clinical trials. Any of these decisions could have a material adverse effect on its expected clinical and regulatory timelines, business, prospects, financial condition and results of operations.

#### 1.7. RISKS LINKED TO THE COMPLANY'S RELIANCE ON THIRD PARTIES

### 1.7.1. Cell-based therapies rely on the availability of specialty raw materials, which may not be available to the Company on acceptable terms or at all.

Engineered-cell therapies require many specialty raw materials, some of which are manufactured by small companies with limited resources and experience to support a commercial product. The suppliers may be ill-equipped to support the Company's needs, especially in non-routine circumstances like an FDA inspection or medical crisis, such as widespread contamination. The Company also does not have contracts with many of these suppliers and may not be able to contract with them on acceptable terms or at all. Accordingly, the Company may experience delays in receiving key raw materials to support clinical or commercial manufacturing.

In addition, some raw materials are currently available from a single supplier, or a small number of suppliers. The Company cannot be sure that these suppliers will remain in business, or that they will not be purchased by one of its competitors or another Company that is not interested in continuing to produce these materials for its intended purpose.

## 1.7.2. If third parties conducting clinical trials do not successfully carry out their contractual duties, the Company may not be able to obtain regulatory approval for or commercialize its drug product candidates.

The Company relies on clinical research organizations, or CRO's, and clinical trial sites to ensure its clinical trials are conducted properly and on time. While the Company will have agreements governing their activities, the Company will have limited influence over their actual performance. Nevertheless, the Company will be responsible for ensuring that each of its clinical trials is conducted in accordance

with the applicable protocol, legal, regulatory and scientific standards, and its reliance on the CRO's does not relieve the Company of its regulatory responsibilities.

The Company and its CRO's are required to comply with the GCP's (from both FDA and EMA) for conducting, recording and reporting the results of clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. If the Company or its CROs fail to comply with applicable GCP's, the clinical data generated in its future clinical trials may be deemed unreliable and the FDA, the EMA, or other foreign regulatory authorities may require the Company to perform additional clinical trials before approving any marketing applications. Upon inspection, the FDA or EMA may determine that its clinical trials did not comply with GCP's. In addition, its future clinical trials will require a sufficient number of test subjects to evaluate the safety and effectiveness of its drug product candidates. Accordingly, if its CRO's fail to comply with these regulations or fail to recruit a sufficient number of patients, the Company may be required to repeat such clinical trials, which would delay the regulatory approval process.

Its CRO's are not the Company's employees, and the Company is therefore unable to directly monitor whether or not they devote sufficient time and resources to its clinical and pre-clinical programs. These CRO's may also have relationships with other commercial entities, including its competitors, for whom they may also be conducting clinical trials or other product development activities that could harm the Company's competitive position. If its CRO's do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to the Company's clinical protocols or regulatory requirements, or for any other reasons, the Company's clinical trials may be extended, delayed or terminated, and the Company may not be able to obtain regulatory approval for, or successfully commercialize, its drug product candidates. If any such event were to occur, the Company's financial results and the commercial prospects for its drug product candidates would be harmed, its costs could increase, and its ability to generate revenues could be delayed.

If any of the Company's relationships with these third-party CRO's terminate, the Company may not be able to enter into arrangements with alternative CRO's or to do so on commercially reasonable terms. Further, switching or adding additional CRO's involves additional costs and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which could materially impact its ability to meet its desired clinical development timelines. Though the Company carefully manages its relationships with its CRO's, there can be no assurance that the Company will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on its business, financial condition and prospects.

### 1.7.3. The Company relies and will continue to rely on collaborative partners regarding the development of its research programmes and product candidates.

The Company is and expects to continue to be dependent on collaborations with partners relating to the development and commercialisation of its existing and future research programmes and product candidates. The Company had, has and will continue to have discussions on potential partnering opportunities with various pharmaceutical and medical device companies. If the Company fails to enter into or maintain collaborative agreements on reasonable terms or at all, the Company's ability to develop its existing or future research programmes and product candidates could be delayed, the commercial potential of its products could change and its costs of development and commercialisation could increase.

The Company's dependence on collaborative partners subjects it to a number of risks, including, but not limited to, the following:

- the Company may be required to relinquish significant rights, including intellectual property, marketing and distribution rights;
- the Company relies on the information and data received from third parties regarding its research programs and product candidates and will not have control of the process conducted by the third party in gathering and composing such data and information. The Company may not have formal or appropriate guarantees from its contract parties with respect to the quality and the completeness of such data;
- a collaborative partner may develop a competing product either by itself or in collaboration with others, including one or more of the Company's competitors;

### **2. GENERAL INFORMATION**

### 2.1. GENERAL INFORMATION

This Registration Document of Celyad Oncology SA (also referred to herein as the "**Company**") is a registration document within the meaning of Article 6 and Article 10 of the Prospectus Regulation 2017/1129 (the "**Prospectus Regulation**"). The English version of this report has been approved by the Financial Services and Markets Authority on 30 juin 2020 in accordance with Article 20 of the Prospectus Regulation. The FSMA's approval of this Registration Document does not imply any judgment on the situation of the Company. The FSMA only approves this Registration Document as meeting the standards of completeness, comprehensibility and consistency imposed by Prospectus Regulation.

This Registration Document has been drawn up as part of a simplified prospectus in accordance with Article 14 of Prospectus Regulation.

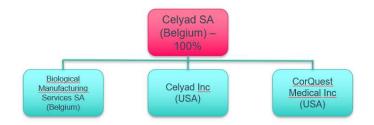
This Registration Document has not been submitted for approval to any supervisory body or governmental authority outside Belgium.

#### 2.1.1. Legal information

The legal and commercial name of the Company is Celyad Oncology SA. The legal name of the Company was adopted (from "Celyad" to "Celyad Oncology") by an extraordinary shareholders' meeting held on 8 June 2020. Celyad is registered with the legal entities register (Nivelles) under number 0891.118.115 and was incorporated in Belgium on 24 July 2007, under the name of Cardio3 BioSciences, for an indefinite period of time. The Company is a limited liability company incorporated in the form of a "société anonyme" under the laws of Belgium. The Company's registered office is located at rue Edouard Belin 2 at 1435 Mont-Saint-Guibert (Belgium). The legal entity identifier ("LEI") of the Company is 549300ORR0M8XF56OI64. The phone number of the Company is +32.10.39.41.00. Its website is <u>www.celyad.com</u>, the content of the website is not part of this Registration Document, except if it has been precisely incorporated by reference.

Name	Country of Incorporation and Place of Business	Nature of Business	Proportion of ordinary shares directly held by parent (%)	Proportion of ordinary shares held by the Company (%)	Proportion of ordinary shares held by non- controlling interests (%)
Celyad Oncology SA	BE	Biopharma	Parent company		
Celyad Inc	US	Biopharma	100%	100%	0%
CorQuest Medical Inc	US	Medical Device	100%	100%	0%
Biological Manufacturing Services SA	BE	Manufacturing	100%	100%	0%

The consolidation scope of the Company is as follows:



### 2.1.2. Language of this Registration Document

Celyad Oncology SA has established this Registration Document in English.

### 2.1.3. Persons responsible for the contents of the Registration Document

The Company, represented by its board of directors (see Section 5.2.1), assumes responsibility for the information contained in this Registration Document. To the best of the knowledge of the Company and its directors (having taken all reasonable care to ensure that such is the case), the information contained in this registration document is in accordance with the facts, is not misleading and is true, accurate and complete, and does not omit anything likely to affect the import of such information.

Any information from third parties identified in this Registration Document as such, has been accurately reproduced and as far as the Company is aware and is able to ascertain from the information published by a third party, does not omit any facts which would render the reproduced information inaccurate or misleading.

The contents of this Registration Document should not be construed as providing legal, business, accounting or tax advice. Each prospective investor should consult its own legal, business, accounting and tax advisers prior to making a decision to invest in the Shares.

### 2.1.4. Statutory Auditor

CVBA E&Y Bedrijfsrevisoren-Réviseurs d'Entreprises, having its registered office at De Kleetlaan 2, B – 1831 Diegem, Belgium, represented by Carlo-Sébastien d'Addario, has been appointed as Statutory Auditor of the Company on 5 May 2020 for a term of three years. Carlo-Sébastien d'Addario is a member of the Belgian Institute of Certified Auditors ("Institut des Réviseurs d'Entreprises").

The statutory financial statements as per 31 December 2019, 31 December 2018 and 31 December 2017 were prepared in accordance with Belgian GAAP. The 2019, 2018 and 2017 statutory financial statements in accordance with Belgian GAAP have been audited by BDO Reviseurs d'Entreprises scrl, represented by Bert Kegels, who delivered unqualified opinions.

The consolidated financial statements as of 31 December 2019, 31 December 2018 and 31 December 2017 have also been prepared in accordance with IFRS. The 2019, 2018 and 2017 consolidated annual

financial statements in accordance with IFRS have been audited by BDO Reviseurs d'Entreprises scrl, represented by Bert Kegels, who delivered unqualified opinions.

On 5 May 2020, the annual shareholder's meeting decided not to renew the independent public accounting firm mandate of BDO Reviseurs d'Entreprises scrl, organised and existing under the laws of Belgium, with registered office at The Corporate Village, Da Vincilaan 9, Box E.6, Elsinore Building, 1935 Zaventem, Belgium, represented by Bert Kegels. At the time of shareholders decision, BDO had been its auditor for three years.

#### 2.1.5. Forward-looking statements

This Registration Document contains forward-looking statements and estimates made by the Company with respect to the anticipated future performance of Celyad and the market in which it operates. Certain of these statements, forecasts and estimates can be recognized by the use of words such as, without limitation, "believes", "anticipates", "expects", "intends", "plans", "seeks", "estimates", "may", "will", "predicts", "projects" and "continue" and similar expressions. They include all matters that are not historical facts. Such statements, forecasts and estimates are based on various assumptions and assessments of known and unknown risks, uncertainties and other factors, which were deemed reasonable when made but may or may not prove to be correct. Actual events are difficult to predict and may depend upon factors that are beyond the Company's control. Therefore, actual results, the financial condition, performance or achievements of Celyad, or industry results, may turn out to be materially different from any future results, performance or achievements expressed or implied by such statements, forecasts and estimates such a difference include, but are not limited to, those discussed in the section "Risk Factors". Furthermore, forward-looking statements, forecasts and estimates only speak as of the date of the publication of this registration document.

All statements are made and all information is provided as of the date of this Registration Document, except when explicitly mentioned otherwise.

#### 2.1.6. Market and Industry Information

Information relating to markets and other industry data pertaining to the Company's business included in this Registration Document has been obtained from internal surveys, scientific publications, section association studies and government statistics. The Company accepts responsibility for having correctly reproduced information obtained from publications or public sources, and, in so far as the Company is aware and has been able to ascertain from information published by those industry publications or public sources, no facts have been omitted which would render the reproduced information inaccurate or misleading. However, the Company has not independently verified information obtained from industry and public sources. Certain other information in this registration document regarding the industry reflects the Company's best estimates based on information obtained from industry and public sources. Information from Company's internal estimates and surveys has not been verified by any independent sources.

#### 2.1.7. Other available information

The Company has filed its deed of incorporation and must file its restated Articles of Association and all other deeds and resolutions that are to be published in the Belgian Official Gazette (*Moniteur belge*) with the clerk's office of the commercial court of Nivelles (Belgium), where such documents are available to the public. A copy of the most recent restated Articles of Association, the reports of the Board of Directors and the minutes of the shareholders' meeting are also available on the Company's website (<u>www.celyad.com</u>).

The Company prepares annual audited and consolidated financial statements. All financial statements, together with the reports of the Board of Directors and the statutory auditors are filed with the National Bank of Belgium, where they are available to the public. Furthermore, as a company with shares listed and admitted to trading on Euronext Brussels and Paris, the Company published an annual financial report (including its financial statements and the reports of the Board of Directors and the statutory auditors) and an annual announcement prior to the publication of the annual financial report, as well as a half-yearly financial report on the first six months of its financial year and quarter business updates. Copies of these documents are available on the Company's website (www.celyad.com) and STORI, the Belgian central storage platform which is operated by the FSMA and can be accessed via its website (www.fsma.be).

The Company must also disclose price sensitive information and certain other information relating to the public. In accordance with the Belgian Royal Decree of 14 November 2007 relating to the obligations of issuers of financial instruments admitted to trading on a Belgian regulated market such information and documentation will be made available through the Company's website, press release and the communication channels of Euronext Brussels.

#### 2.1.8. Availability of this Registration Document

To obtain a copy of the Registration Document free of charge, please contact:

CELYAD ONCOLOGY SA Attn. Philippe Dechamps 2 rue Edouard Belin 1435 Mont-Saint-Guibert Phone : +32(0) 10 39 41 00 Fax : +32(0) 10 39 41 41 E-mail : investors@celyad.com

Pursuant to Article 21 of the Prospectus Regulation, an electronic version of this Registration Document is also available on the website of Celyad (<u>www.celyad.com</u>). The posting of this Registration Document on the internet does not constitute an offer to sell or a solicitation of an offer to buy any of the Shares to any person in any jurisdiction in which it is unlawful to make such offer or solicitation to such person.

The electronic version may not be copied, made available or printed for distribution. Other information on the website of the Company or on another website does not form part of the Registration Document.

Finally, in accordance with Article 21, §5 of the Prospectus Regulation, the FSMA will publish the approved version of the Registration Document on its website <u>www.fsma.be</u>.

#### 2.1.9. Information incorporated by reference

The Registration Document shall be read and construed in conjunction with the full 2019 annual report including the audited consolidated financial statements of the Company prepared in accordance with IFRS for the financial year ended 31 December 2019 together with the related audit report thereon, incorporated by reference.

Copies of the document incorporated by reference in this Registration Document may be obtained without charge- from the registered offices of the Company and the website of the Company (www.celyad.com). This document is also accessible on the following link: https://www.celyad.com/en/investors/regulated-information.

### **3. FINANCIAL INFORMATION**

### 3.1. FINANCIAL INFORMATION CONCERNING THE COMPANY'S ASSETS AND LIABILITIES, FINANCIAL POSITION, PROFITS AND LOSSES

The table below includes references to the relevant pages of the audited consolidated financial statements of the Company for the financial years ended 31 December 2019, as set out in the annual report of the Company.

Consolidated statement of financial position	p. 81	
Consolidated statement of comprehensive loss	p. 81	
Consolidated statement of changes in equity	p. 82	
Consolidated statement of cash flows	p. 83	
Notes to the consolidated financial statements	p. 84-137	
Current cash situation	p. 106	
Auditor's report	p. 75-80	

### 3.2. SECURITIES ISSUED BY THE COMPANY

At the date of this Registration Document, the Company's capital amounts to EUR 48,512,614.57 and is represented by 13,942,344 ordinary Shares without nominal value.

At the Date of this Registration Document, 1,595,655 subscription rights (warrants) are outstanding, giving the right to their holders to subscribe up to 1,595,655 Shares. The increase of the number of outstanding warrants compared to the one mentioned in the 2019 annual financial report is due to allocations of warrants that took place since 1<sup>st</sup> January 2020.

The Company has not issued convertible bonds.

For more information about history of the capital of the Company please see section 5.13 share capital of the 2019 annual financial report. For more information about warrants plans please see sections of the 2019 annual financial report, where they are described, e.g. sections 3.3 warrants plans and 5.14 share-based payment.

### **3.3. LEGAL PROCEEDINGS**

The Company is not, nor has been, involved in any governmental, legal or arbitration proceedings (including any such proceedings which are pending or threatened of which the Company is aware) during the 12 months preceding the date of this Registration Document which may have or has dad in the recent past significant effects on the financial position or profitability.

### 3.4. SIGNIFICANT CHANGE IN THE FINANCIAL POSITION OF CELYAD SINCE 31 DECEMBER 2019

On March 11, 2020 the World Health Organization declared the novel strain of coronavirus (COVID-19) a global pandemic and recommended containment and mitigation measures worldwide. As of the date of this Registration Document, Belgium, where Celyad operates, has been impacted by temporary closures. The length or severity of this pandemic cannot be predicted, but Celyad anticipates that there may be a potential impact from COVID-19 on its planned development activities.

With COVID-19 continuing to spread in the United States and Europe, Celyad's business operations could be delayed or interrupted, particularly if a large portion of its employees become ill. COVID-19 may also affect employees of third-party organizations located in affected geographies that Celyad relies upon to carry out its clinical trials. The spread of COVID-19, or another infectious disease, could also negatively affect the operations at Celyad's third-party suppliers, which could result in delays or disruptions in the supply of drug product used in its clinical trials. In addition, Celyad is taking temporary precautionary measures intended to help minimize the risk of the virus to its employees, including temporarily requiring all employees to work remotely, suspending all non-essential travel worldwide for its employees and discouraging employee attendance at industry events and in-person work-related meetings, which could negatively affect Celyad's business.

Further, timely enrolment in clinical trials is reliant on clinical trial sites which may be adversely affected by global health matters, including, among other things, pandemics such as COVID-19. For example, many of Celyad's clinical trial sites are located in regions currently being afflicted by COVID-19. Some factors from the COVID-19 outbreak that Celyad believes may adversely affect enrolment in its trials include:

- the diversion of healthcare resources away from the conduct of clinical trial matters to focus on pandemic concerns, including the attention of physicians serving as Celyad's clinical trial investigators, hospitals serving as its clinical trial sites and hospital staff supporting the conduct of its clinical trials;
- limitations on travel that interrupt key trial activities, such as clinical trial site initiations and monitoring;
- interruption in global shipping affecting the transport of clinical trial materials, such as investigational drug product used in its trials; and
- employee absences that delay necessary interactions with local regulators, ethics committees and other important agencies and contractors.

In the beginning of the crisis the clinical trial sites we had selected temporarily suspended enrollment of patients in our CYAD-01 clinical program for r/r AML and MDS, however as the pandemic has evolved, a few of these clinical sites have re-engaged and begun to recruit patients for the studies. Recruitment in both CYAD-01 trials, THINK and DEPLETHINK has stabilized during Q2. The delay is consistent to our update in on March 24 with regard to clinical data being available for the broader r/r AML and MDS programs during the second half of 2020.

Recruitment delays in the CYAD-02 program has been less affected due to the Covid-19 pandemic as the trial is a dose-escalation trial and enrollment is staggered based on safety at the various dose levels.

For CYAD-101, we are currently operating the tech transfer of the asset into our manufacturing facility and we haven't experienced any major delays to date with the program due to Covid-19. We continue to move towards initiating the expansion segment of the Phase 1 alloSHRINK trial for CYAD-101 during fourth quarter 2020.

Lastly, regarding our lead preclinical program, CYAD-211, we have progressed towards the filing of the IND application guided for mid-2020 and recently submitted the application to Health Authorities both in Belgium and the United States. To date, we have not been notified by the Health Authorities with regards to any potential delays in the review of the CYAD-211 application.

To date, the impact of COVID-19 on the business of Celyad remains uncertain at this time and will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity of the coronavirus and the actions to contain the coronavirus or treat its impact, among other things, but prolonged closures or other business disruptions may negatively affect its operations and the operations of its agents, contractors, consultants or collaborators, which could have a material adverse impact Celyad's business, results of operations and financial condition.

#### 3.5. DIVIDENDS AND DIVIDEND POLICY

The Company has never declared or paid any cash dividends on its ordinary shares. The Company does not anticipate paying cash dividends on its equity securities in the foreseeable future and intend to retain all available funds and any future earnings for use in the operation and expansion of its business. In general, distributions of dividends proposed by the board of directors require the approval of the shareholders at a meeting of shareholders with a simple majority vote, although the board of directors may declare interim dividends without shareholder approval, subject to the terms and conditions of the Belgian Companies and Associations Code ("BCCA").

Pursuant to Belgian law, the calculation of amounts available for distribution to shareholders, as dividends or otherwise, must be determined on the basis of its non-consolidated statutory financial accounts prepared under Belgian GAAP, and not on the basis of IFRS consolidated accounts. In addition, under the BCCA, the Company may declare or pay dividends only if, following the declaration and issuance of the dividends, the amount of its net assets on the date of the closing of the last financial year according to its statutory annual accounts (i.e., the amount of the assets as shown in the balance sheet, decreased with provisions and liabilities, all as prepared in accordance with Belgian accounting rules), decreased with the non-amortized costs of incorporation and expansion and the non-amortized costs for research and development, does not fall below the amount of the paid-up capital (or, if higher, the called capital), increased with the amount of non-distributable reserves. Finally, prior to distributing dividends, the Company must allocate at least 5% of its annual net profits (under its non-consolidated statutory accounts prepared in accordance with Belgian accounting rules) to a legal reserve, until the reserve amounts to 10% of its share capital.

### 3.6. FINANCIAL COMMITMENTS

#### Financial commitments resulting from material agreements

Based on material agreements with Celdara, Dartmouth and Horizon, referring to the acquisition of the Company's immuno-oncology platform, the Company will be subject to payment obligations in the form of development and regulatory milestones, sales milestones and royalties based on the net sales generated by the Company from its products candidates.

For additional information on these commitments, please refer to Notes 5.19.2 – Financial instruments reported at fair value on balance sheet and Note 5.33 – Commitments of the consolidated financial statements appended to the 2019 annual report of the Company.

#### Recoverable cash advances towards Walloon Region

As described in the consolidated financial statements appended to the 2019 annual report of the Company (see Notes 5.2.5 – Government Grants (Other income) and Note 5.16 – Advances repayable), the Company has to reimburse certain government grants received to partially finance its research and development programs, in the form of recoverable cash advances under certain conditions. The reimbursement of the funding starts after that the research and development programs partially financed by the Company enter in the "exploitation phase" and has the following characteristics:

- sales-independent reimbursements represent in the aggregate 30% of the principal amount;
- sales-independent reimbursements and sales-dependent reimbursements are, in the aggregate (including the accrued interests), capped at 200% of the principal amount paid out by the Region; and
- interests (at Euribor 1 year as applicable on the first day of the month in which the decision to grant the relevant RCA was made + 100 basis points) accrue as of the 1st day of the exploitation phase.

#### **3.7. OVERVIEW FUNDING**

Up to date of this Registration Document, the Company has been able to fund its operations with a long-term perspective through the following funding transactions:

- proceeds of €42.0 million from private financing rounds;
- proceeds of €26.5 million from an initial public offering of the Company's ordinary shares on Euronext Brussels and Euronext Paris in July 2013, or the Euronext IPO;
- proceeds of €25.0 million from a private financing by Medisun International Limited, or Medisun, in June 2014;
- proceeds of €31.7 million from a private placement in March 2015;
- proceeds of €88.0 million from a global offering of 1,460,000 ordinary shares, consisting of an underwritten public offering of 1,168,000 ADSs and a concurrent European private placement of 292,000 ordinary shares, in June 2015.

- proceeds of €46.1 million from a global offering of 2,070,000 ordinary shares, consisting of an underwritten public offering of 568,500 ordinary shares in the form of ADSs and 1,501,500 ordinary shares, in May 2018.
- proceeds of €18.2 million from a global offering of 2,000,000 ordinary shares, consisting of an underwritten public offering of 1,675,000 ordinary shares in the form of ADSs and 325,000 ordinary shares, in September 2019.
- proceeds of €28.3 million from recoverable cash advances, or RCAs, granted by Walloon Region government, a non-dilutive financing source;
- proceeds of €1.1 million from bank loans provided by BNP Paribas Fortis and ING Belgique SA/NV to partially finance the leasehold improvements brought on a regular basis to our manufacturing facility and corporate office;
- proceeds of €2.5 million from three-year maturity finance leases to finance most of laboratory and office equipment.

### 3.8. CURRENT CASH POSITION

The Company ended first quarter 2020 with a treasury position of  $\notin$  33.8 million (\$37.3 million). Net cash burn over the first quarter of 2020 amounted to  $\notin$  5.5 million, which is in line with expectations.

The Company confirms its previous guidance that its treasury position should be sufficient to fund operating expenses and capital expenditure requirements, based on the current scope of activities, until end of first half 2021.

### 4. INDUSTRY AND BUSINESS OVERVIEW

# 4.1. INDUSTRY AND BUSINESS OVERVIEW

## 4.1.1. Principal activities

# 4.1.1.1. Overview

We are a clinical-stage biotechnology company focused on the discovery and development of chimeric antigen receptor T (CAR T) cell therapies for cancer. The Company is developing a pipeline of allogeneic and autologous CAR T cell therapy candidates for the treatment of both hematological malignancies and solid tumors.

Our clinical drug product candidates include the autologous cell therapies CYAD-01 and CYAD-02 for the treatment of relapsed / refractory acute myeloid leukemia (r/r AML) and the allogeneic, or off-the-shelf, cell therapy CYAD-101 for the treatment of metastatic colorectal cancer (mCRC). All three candidates incorporate the receptor NKG2D, an activating receptor from Natural Killer, or NK, cells as the chimeric antigen receptor, or CAR, transduced on T-lymphocytes, or T cells. NK cells are lymphocytes of the immune system that kill diseased cells. The receptors of the NK cells used in our product candidates target the binding molecules, called ligands, that are expressed in cancer cells, but are absent or expressed at very low levels in normal cells. We believe the NKG2D-based CAR-T approach has the potential to treat a broad range of both solid and hematologic tumors.

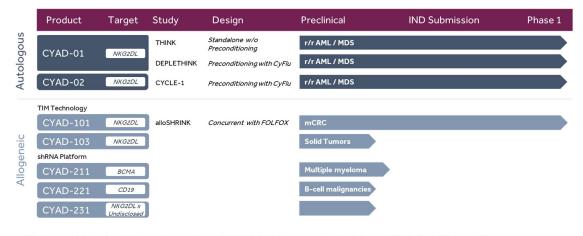
In December 2016, following the successful completion of a proof-of-concept clinical trial conducted at the Dana-Farber Cancer Institute, in which no treatment related safety concerns and initial signs of clinical activity were observed, we initiated the Phase 1 clinical trial, called THINK, to assess the safety and clinical activity of multiple administrations of CYAD-01 in seven refractory cancers, including both solid tumors and hematologic malignancies. Based on encouraging results from the THINK trial, we initiated additional trials in 2018 to further evaluate CYAD-01 both in r/r AML and patients with metastatic colorectal cancer (mCRC). These trials included the Phase 1 DEPLETHINK and SHRINK trials, respectively. The DEPLETHINK trial is assessing CYAD-01 after lymphodepletion with cyclophosphamide and fludarabine, or CyFlu, for the treatment of r/r AML. The SHRINK trial was an open-label Phase 1 study evaluating the safety and clinical activity of multiple doses of CYAD-01, administered concurrently with the FOLFOX treatment in patients with advanced mCRC. As of December 31, 2019, the THINK and DEPLETHINK trials are ongoing, while the SHRINK trial has completed enrolment and ended.

In November 2018, we also initiated the Phase 1 alloSHRINK trial, evaluating our second clinical candidate CYAD-101. CYAD-101 is a first-in-class, non-gene edited allogeneic (donor derived) CAR-T product candidate that co-expresses the chimeric antigen receptor NKG2D and the novel inhibitory peptide TIM (T cell receptor, or TCR, Inhibiting Molecule). The expression of TIM reduces signaling of the TCR complex and we believe could therefore reduce or eliminate Graft versus Host Disease (GvHD) in patients treated with CYAD-101. The alloSHRINK trial is ongoing and is evaluating CYAD-

101 administered concurrently with FOLFOX chemotherapy in the treatment of patients with unresectable metastatic colorectal cancer (mCRC).

Beyond CYAD-01 and CYAD-101, we are also investigating several novels, next-generation NKG2Dbased CAR-T product candidates including CYAD-02 and CYAD-103. Like CYAD-01, CYAD-02 is an autologous, CAR-T product candidate for the treatment of r/r AML. CYAD-02 builds upon the construct of CYAD-01 with the addition of a short hairpin RNA (shRNA) which targets the NKG2D ligands MICA and MICB. In January 2020, we initiated the Phase 1 CYCLE-1 trial evaluating CYAD-02 after lymphodepletion with CyFlu for the treatment of r/r AML. Similar to CYAD-101, CYAD-103 is an allogeneic CAR-T product candidate that co-expresses the NKG2D receptor and TIM peptide. CYAD-103 is in preclinical development for the treatment of solid tumors.

Additionally, we are currently investigating a series of shRNA-based allogeneic CAR-T candidates referred to as the CYAD-200 series. These preclinical candidates include CYAD-211, a CAR-T candidate targeting B-cell maturation antigen, or BCMA, for the treatment of multiple myeloma, CYAD-221, a CAR-T candidate targeting CD19 for the treatment of B-cell malignancies and CYAD-231, dual specific CAR-T candidate targeting NKG2D and an undisclosed membrane protein.



# 4.1.1.2. <u>Pipeline and Approach</u>

AML: Acute myeloid leukemia; mCRC: Metastatic colorectal cancer; MDS: Myelodysplastic syndrome; r/r: relapse/refractory; NKG2DL: Natural killer group 2D ligands. CyFlu: cyclophosphamide and fludarabine; FOLFOX: leucovorin, fluorouracil, and oxaliplatin.

Our clinical candidates, including CYAD-01 and CYAD-02 (autologous CAR-T cell therapies) and CYAD-101 (an allogeneic CAR-T therapy), use the native sequence of the NKG2D receptor in the CAR construct. Importantly, CYAD-101 also expresses the peptide TIM which is used to dampen the signaling of the TCR complex and classify the product as allogeneic. In all three, CYAD-01, CYAD-02 and CYAD-101, the human natural sequence of NKG2D is expressed outside the T cell and bound to an intracellular domain called CD3 Zeta. This intracellular domain is used in most other CARs and is responsible for the activation of the T cell once NKG2D recognizes and binds to its target. In addition,

the complex NKG2D CD3 Zeta binds to endogenous DAP 10, which is a co-stimulatory molecule present on T cells, which means that the activation triggered by the primary stimulatory chain CD3 Zeta is further strengthened by DAP 10, a secondary or co-stimulatory domain.

NKG2D receptor ligands are expressed in numerous solid tumors and blood cancers, including ovarian, bladder, breast, lung and liver cancers, as well as leukemia, lymphoma and myeloma. In preclinical studies, we have observed bioactivity of CYAD-01 when as few as 7% of the cancer cells within a given cell population expressed a NKG2D receptor ligand.

Cells under stress induced by factors such as viral infection, cancer or inflammation express the ligands recognized by the NKG2D receptor, which is naturally present on NK cells. Eight NKG2D ligands have been characterized (namely ULBP families 1 to 6, MICA and MICB). Those ligands are a signal for NK cells that the stressed cells are malfunctioning and should be destroyed. NKG2D ligands are present in most cells, but their expression at the cell surface is tightly regulated, meaning that expression at the cell surface is absent or limited in healthy cells but overexpressed in infected or stressed cells. Preclinical studies have demonstrated that multiple solid and hematological cancer tumors express one or more NKG2D ligands. However, in preclinical studies we have not observed the cell surface expression of NKG2D ligands in healthy tissue.

In addition, preclinical mouse studies conducted by Charles Sentman, Ph.D., of our academic collaborator Dartmouth College, have demonstrated that CAR-T NKG2D may have bioactivity beyond a direct cytotoxic effect of the CAR on the targeted tumor cell. Three additional potential modes of such activity are:

- i. Both regulatory T cells that modulate the immune system and bone marrow immune cells, called myeloid-derived suppressor cells, or MDSCs, were shown to express NKG2D ligands when they are present in tumors. Hence, those immune suppressive cells are also a target of our NKG2D-based CAR-T product candidates, thereby potentially suppressing immune inhibition in the tumor cell.
- Cells from rapidly dividing micro vessels in the tumor mass were shown to express NKG2D ligands. Hence, the blood supply to the tumor is a potential target of our NKG2D-based CAR-T product candidates.
- iii. In animals in which the tumors were eliminated following the administration of CAR-T NKG2D, a re-challenge by the same tumor cell line was ineffective, rendering the animal potentially "immunized" against this tumor cell line. Surviving animals challenged with other tumor cell lines showed evidence of tumor growth.

# **Clinical Development Program for CYAD-01**

The CM-CS1 Phase 1 Clinical Trial

In December 2016, results from the first clinical trial of CYAD-01, called the CM-CS-1 trial, were presented at the American Society of Hematology, or ASH, Annual Meeting. The CM-CS-1 trial was a Phase 1 dose escalation clinical trial conducted at the Dana-Farber Cancer Institute in patients with AML and multiple myeloma, or MM. Patients received doses from  $1 \times 10^6$  up to  $3 \times 10^7$  CAR-T NKR-2 in a single intravenous injection. One AML patient treated with the highest dose level was observed to have normalized hematologic parameters for six months following treatment. No serious treatment-related adverse events were reported at the four doses tested in this trial, and signs of clinical activity were observed.

#### THINK Phase 1 Clinical Trial

# Overview

In December 2016, we initiated the THINK (Therapeutic Immunotherapy with NKR-2) trial, a multinational (E.U./U.S.), open-label Phase 1 clinical trial to assess the safety and clinical activity of multiple administrations of CYAD-01 in seven metastatic tumor types, including five solid tumors (colorectal, ovarian, bladder, triple-negative breast and pancreatic cancers) and two hematological malignancies (AML and MM) in patients who did not respond to or relapsed after first and second line therapies. In the THINK trial, CYAD-01 is administered as a monotherapy in patients without chemotherapy preconditioning.

The trial contains two consecutive segments: a dose escalation segment with two arms (one in solid tumor types and one in hematological tumor types) at three dose levels adjusted to body weight (up to  $3x10^8$ ,  $1x10^9$  and  $3x10^9$  CYAD-01 cells) and a dose-expansion segment. At each dose, the patients are intended to receive three successive administrations of the specified dose, two weeks apart. In 2018, we made several amendments to the trial including: 1) as of dose level 2, patients were eligible for a second cycle of three injections in absence of progressive disease; 2) in the hematological malignancy portion of the trial, a more frequent dosing schedule of CYAD-01, referred to as schedule optimization, assessed six injections without preconditioning over two months of administration; and 3) in the solid tumor segment of the trial, treatment of CYAD-01 after non-myeloablative preconditioning chemotherapy regimen of CyFlu was assessed.

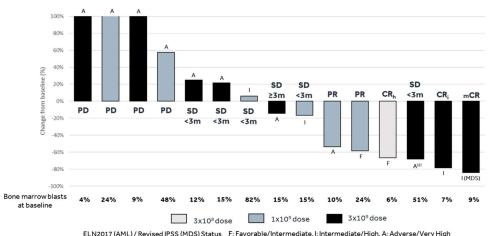
As of December 31, 2019, the dose-escalation segment of the Phase 1 study had concluded, as well as the aforementioned amended cohorts. No further development of CYAD-01 in solid tumors is expected. The primary endpoint of the dose escalation segment of the trial is a safety endpoint—the occurrence of dose limiting toxicities in patients during the treatment until 14 days after the last treatment.

In first quarter 2020 we initiated the dose-expansion segment of the trial. We plan to enroll up to 10 r/r AML and MDS patients evaluating  $3x10^8$  CYAD-01 cells without preconditioning infused three times every two weeks. The primary endpoint in the expansion segment is objective response rate. Enrolment in the study is ongoing and preliminary data from the expansion segment of the trial are expected in the second half of 2020.

## Hematological Malignancy Segment of the THINK Phase 1 Trial

In December 2019, at the 61<sup>st</sup> ASH Annual Meeting we reported interim results from the hematological portion of the THINK Phase 1 trial. Data from 22 patients treated across all three dose levels showed that treatment with monotherapy CYAD-01 without preconditioning was well tolerated. Out of 15 r/r AML patients evaluable per protocol (at least one cycle of treatment) in the dose escalation segment of the trial, eight patients showed anti-leukemic activity with five out of eight patients exhibiting objective response, with three patients exhibiting a complete response, defined as either a complete response with partial hematological recovery, or CRh, complete response with incomplete marrow recovery, or Cri, or marrow complete response, or mCR. The r/r AML patient who achieved a CRh was bridged to allotransplant and remains in minimal residual disease negative complete response, or CR<sub>MRD</sub>, defined as no detection of tumor cells by high sensitivity methods) for over 24 months.

# Evidence of Anti-Leukemic Activity in relapsed/refractory AML and MDS Patients with CYAD-01 Without Preconditioning Chemotherapy



\_\_\_\_\_\_

CRh: Complete response with partial hematological recovery

CRi: Complete response with incomplete hematological recovery

mCR: Marrow complete response

CR (MRD-): Complete response without minimal residual disease

- PR: Partial response
- SD: Stable disease
- ELN: European LeukemiaNet.

**IPSS:** International Prognostic Scoring System

# Solid Tumor Segment of the THINK Phase 1 Trial

In November 2018, at the Society for Immunotherapy of Cancer, or SITC, 33<sup>rd</sup> Annual Meeting we reported results from the solid tumor portion of the THINK trial. Data from 14 patients treated across all three dose levels showed that treatment with monotherapy CYAD-01 without preconditioning was well tolerated. Out of eleven patients with mCRC evaluable per protocol (at least one cycle of treatment) in the dose escalation segment of the trial, the best clinical response observed was stable disease in three patients (27%) based on RECIST 1.1 criteria. In addition, one patient with ovarian cancer treated at dose level 2 also experienced a stable disease.

In February 2018, the THINK trial was amended to include a cohort known as THINK CyFlu. The cohort evaluated a single injection of CYAD-01 following treatment with the standard preconditioning regimen of CyFlu.

In July 2019, we reported that treatment with CYAD-01 following the standard preconditioning regimen of CyFlu was well tolerated with no occurrence of DLT nor an increase of treatment-related adverse events rate. Translational data from the cohort also suggest an improvement in cell engraftment of CYAD-01 induced by the CyFlu preconditioning as compared to the same dose of CYAD-01 without preconditioning chemotherapy. Of the three patients enrolled, one patient achieved stable disease, while two patients experienced disease progression.

# **Nature of Interim Data**

It should be noted that the interim data summarized above are current as of June 1, 2020, and are preliminary in nature. As of the date of the approval of this registration document, our THINK trial is not yet complete in the hematological malignancy segment of the trial.

#### Additional Clinical Development for CYAD-01

## **AML Clinical Development Program**

AML is one of the deadliest cancers in hematological malignancies, with a five-year survival rate of 27.4%. Currently the only available potentially curative therapy for AML is allogenic Hematopoietic stem cell transplantation, or HSCT. However, this approach has significant limitations, including difficulties in finding appropriate genetically-matched donors and the risk of transplant-related rejection, graft-versus-host disease, or GvHD, and mortality, and is therefore typically only available on a limited basis. First line therapies can result in a complete response, but the risk of relapse is high. Until 2017, there were no therapies approved by the U.S. Food and Drug Administration, or FDA, for relapsed refractory patients. Based on data from the National Cancer Institute (NCI), the incidence of AML in the United States was approximately 19,520 new cases in 2018.

As an initial matter, we seek to complete the hematological malignancy arm of the THINK trial. Based on the encouraging interim results of the THINK trial, we are currently exploring and intend to further explore the administration of CYAD-01 in AML and MDS patients in the dose-expansion segment of the trial. Enrolment in the dose-expansion segment of the THINK trial, evaluating monotherapy CYAD- 01 produced with our proprietary OptimAb manufacturing process, began in first quarter 2020. Preliminary data from the expansion segment of the trial are expected in the second half of 2020. See "—Manufacturing" below.

### DEPLETHINK Phase 1 Clinical Trial

In October 2018, we initiated a new Phase 1 clinical trial in AML and MDS patients to evaluate the administration of CYAD-01 after patients have undergone a conventional chemotherapy preconditioning program, which is intended to provide an environment for the engineered T cells to thrive, and could result in a higher rate of objective response. However, because chemotherapy preconditioning can lead to undesirable side effects, we expect that a proper risk-benefit ratio will be considered and contrasted with a monotherapy approach as we progress this program into later stages of clinical development.

The trial, referred to as DEPLETHINK (LymphoDEPLEtion and THerapeutic Immunotherapy with NKR-2), was initiated in October 2018. The open-label, dose-escalation trial will evaluate a single injection of CYAD-01 following treatment with the standard low-intensity preconditioning regimen of cyclophosphamide (300 mg/m<sup>2</sup>) and fludarabine (30 mg/m<sup>2</sup>), or CyFlu. The trial includes two different intervals between lymphodepletion and administration of CYAD-01. In addition, the trial will evaluate three dose levels of CYAD-01 including 100 million, 300 million and 1 billion cells per injection, respectively. Following disease assessment, patients presenting no signs of progression are eligible to receive a cycle of three CYAD-01 injections without preconditioning with two-week intervals at their initial dose levels. The study will enroll up to 18 patients. The primary endpoint of the trial is safety and secondary endpoints include clinical activity and pharmacokinetics. Like the THINK trial expansion segment, the ongoing dose cohorts from the DEPLETHINK trial will evaluate CYAD-01 produced with the OptimAb manufacturing process. See "—Manufacturing" below.

In December 2019, we reported initial data from the nine patients enrolled in the first two dose levels of the trial, in which the administration of CYAD-01 following the preconditioning regimen of CyFlu was well-tolerated. At the first CYAD-01 infusion of the consolidation cycle (3 billion cells per infusion), one patient experienced both grade 4 cytokine release syndrome (CRS) and grade 3 CAR-T cell-related encephalopathy and another patient experienced grade 3 CRS. Both patients recovered following the appropriate treatment. In addition, preconditioning chemotherapy led to improved, dose-dependent engraftment of CYAD-01 cells as compared to cells infused with no preconditioning. Tumor assessment of the first nine patients treated with CYAD-01 produced with the mAb manufacturing process showed no objective response at the first two dose levels of the trial. As of June 2020, enrolment in the study is ongoing at the 1 billion cell dose-level. Results from all dose cohorts from the Phase 1 DEPLETHINK trial are expected by year-end 2020.

## **CRC Clinical Development Program**

CRC is the third most diagnosed cancer and the second in terms of deaths. The median progression free survival rate of patients treated with the current standards of care (regorafinib or trifluridine/tipiracil) is between 1.9 and 3.2 months. We estimate the incidence of CRC in the United States is approximately 134,000 new cases per year.

Based on the encouraging interim results of the THINK trial, we also evaluated the administration of CYAD-01 in CRC patients.

# SHRINK Phase 1 Clinical Trial

In May 2018, we enrolled our first patient into the dose-escalation Phase 1 SHRINK (Standard cHemotherapy Regimen and Immunotherapy with NKR-2) trial. SHRINK was designed to assess the safety and clinical activity of multiple administrations of CYAD-01 concurrently with a conventional chemotherapy for CRC called FOLFOX (a combination of 5-fluorouracil, leucovorin and oxaliplatin), with the goal of reducing liver metastasis and allowing for surgical resection. Patients will receive six cycles of FOLFOX chemotherapy every two weeks and three administrations of CYAD-01 every two weeks 48 hours after the end of chemotherapy at cycles two, three and four. Based upon initial assessment of clinical activity, patients could be eligible to receive three additional administrations of CYAD-01 at the same dose level.

In November 2019, we reported results from the trial with nine total patients (four first-line, neoadjuvant and five refractory mCRC patients, respectively) were enrolled. CYAD-01 concurrent with FOLFOX was well-tolerated with only one patient experiencing a Grade 3 related adverse event (AE) and no patient experiencing Grade  $\geq$  4 related AEs. There was no report of dose-limiting toxicity. In the neoadjuvant first-line mCRC patients, one partial response and two patients with stable disease (greater than three months) were observed. In the refractory mCRC setting four patients presented stable disease (greater than 3 months) with three out of four stable disease patients showing some evidence of tumor burden decrease.

As of December 31, 2019, the trial has completed. Given the encouraging results from the alloSHRINK Phase 1 trial, future evaluation of an NKG2D receptor CAR-T will be focused on the allogeneic candidate CYAD-101. See "—Clinical Development Program for CYAD-101" below.

#### Clinical Development Program for Next-Generation, Autologous CYAD-02

Over the past year we have continued to explore opportunities to enhance the characteristics of CYAD-01, including increasing the persistence of the product candidate as well as the product candidate's ability to infiltrate the tumor and combat the hostile tumor microenvironment. At the Company's R&D Day held in March 2019, management unveiled the next-generation, autologous NKG2D-based CAR-T candidate, CYAD-02. CYAD-02 incorporates shRNA technology to target the NKG2D ligands MICA and MICB. The single shRNA modulates the expression of both ligands which translates to encouraging increases in *in vitro* proliferation, *in vivo* engraftment and anti-tumor activity. CYAD-02 also incorporates the OptimAb manufacturing process. In late June 2019, our IND application for CYAD-02 went into effect with the FDA.

# **CYCLE-1** Phase 1 Clinical Trial

In November 2019, we initiated the Phase 1 CYCLE-1 trial. The open-label, dose-escalation trial will evaluate the safety and clinical activity of a single infusion of CYAD-02 produced with the OptimAb manufacturing process following preconditioning chemotherapy CyFlu in patients with r/r AML and MDS. In addition, patients are also eligible to receive bridging therapy, based on physician's choice, in advance of treatment with CYAD-02. The trial will evaluate three dose levels of CYAD-02, at 100 million, 300 million and one billion cells per infusion.

As of June 2020, enrolment in the study is ongoing at the 300 million cell dose-level. Preliminary results from all dose cohorts from the dose-escalation Phase 1 CYCLE-1 trial are expected by year-end 2020.

# Allogenic Platform – TCR Inhibiting Molecule (TIM)

While autologous CAR-T cells have yielded impressive results in B cell malignancies, addressing larger indications such as mCRC using the current centralized manufacturing paradigm may be more challenging, at least from a cost and logistical perspective. However, we believe that an allogeneic approach must address two key challenges: (1) graft versus host disease (GvHD) which is the rejection of the patient tissues by the grafted cells, and (2) rejection of the graft by the host immune system, or transplant rejection. GvHD is mediated by the T Cell Receptor (TCR) complex on T lymphocytes. We have developed a method to interfere with the TCR signaling through the expression of a TCR Inhibiting Molecule (TIM). In preclinical mouse models, we observed that mice treated with TIM transduced T cells did not demonstrate GvHD, while 80% of the animals treated with control T cells died from GvHD within a 50-day window. In addition, we demonstrated in a similar mouse model bearing a colorectal cancer that the antitumor activity of CYAD-101 (the allogeneic version of our CYAD-01 drug product candidate) is maintained.

## Clinical Development Program for CYAD-101

#### Background on CYAD-101

CYAD-101 is an investigational, non-gene edited, allogeneic (donor derived) CAR-T therapy that coexpresses the chimeric antigen receptor NKG2D found in our CYAD-01 clinical candidate with the novel inhibitory peptide TIM (T cell receptor [TCR] Inhibiting Molecule). TCR signaling is responsible for Graft versus Host Disease (GvHD) and the expression of TIM reduces signaling of the TCR complex and could therefore reduce or eliminate GvHD in patients treated with CYAD-101.

# alloSHRINK Phase 1 Clinical Trial

In November 2018, we initiated the open-label, dose-escalation, Phase 1 alloSHRINK trial evaluating our non-gene edited allogeneic CAR-T product candidate, CYAD-101, administered concurrently with

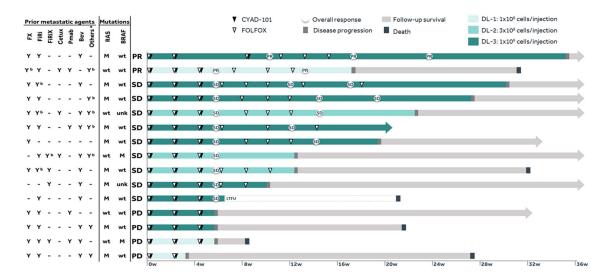
FOLFOX chemotherapy in the treatment of patients with unresectable metastatic CRC. Patients will receive six cycles of FOLFOX chemotherapy every two weeks and three administrations of CYAD-101 every two weeks 48 hours after the initiation of chemotherapy cycles one, two and three. The three dose levels to be evaluated are 100 million, 300 million and 1 billion cells per injection, respectively.

As of June 2020, enrolment in the Phase I dose-escalation segment of the study had completed with 15 patients, including 9 patients at the 1 bilion cells dose level.

Results from dose-escalation alloSHRINK Phase 1 trial were reported at the 2020 American Society of Clinical Oncology (ASCO) Virtual Scientific Program. As of June 2020, a total of 15 patients with relapsed/refractory mCRC who progressed after previous treatment with oxaliplatin or irinotecan were enrolled in the trial. The number of prior therapies received by patients enrolled in the trial ranged from one to six with a mean of three. Initial results showed no clinical evidence of GvHD, was observed following 44 injections of CYAD-101. These data support the ability of the Company's TIM technology to reduce signaling of the TCR complex through a non-gene edited approach. Overall, treatment with CYAD-101 in association with FOLFOX chemotherapy was well-tolerated, with no report of dose-limiting toxicity. Seven of 15 patients enrolled in the trial reported at least one treatment-related adverse event, or AE, however all AEs reported were grade 1 or 2 including one patient who experienced cytokine-release syndrome (grade 1). No patient discontinued treatment due to AEs.

Anti-tumor activity was observed in the trial with two patients who achieved a confirmed partial response, or PR, according to RECIST 1.1 criteria, including one patient with a KRAS-mutation, the most common oncogenic alteration found in all human cancers. In addition, nine patients achieved stable disease, or SD, with seven patients demonstrating disease stabilization lasting more than or equal to three months of duration No correlation was observed between clinical responses and the degree of human leukocyte antigen (HLA) matching between patients and CYAD-101 donor cells, indicating that CYAD-101 can be used in a broad patient population regardless of the HLA haplotype.

# Best Overall Response Following Treatment with CYAD-101 in Heavily Pre-Treated mCRC Patients Who Received Prior Oxaliplatin-Based Chemotherapy



FX: FOLFOX FiRi: FOLFIRI FiRiX: FOLFIRINOX Cetux: Cetuximab Pmab: Panitumumab Bev: Bevacizumab LTFU: Lost to follow-up PR: Partial response SD: Stable disease PD: Progressive disease

Based on the encouraging data observed to date for the Phase 1 alloSHRINK trial, we plan to expand the trial to further evaluate CYAD-101 with prior FOLFIRI (combination of 5-fluorouracil, leucovorin and irinotecan) preconditioning chemotherapy in refractory mCRC patients, at the recommended dose of one billion cells per infusion. Enrollment in the expansion segment of the trial is expected to begin by year-end 2020 following the tech transfer of the manufacturing process of CYAD-101 into our Mont-Saint-Guibert manufacturing facility, approval of necessary CMC amendments and production of additional CYAD-101 cells which is currently planned during the mid- 2020. Overall, the expansion segment will enroll a maximum of 34 patients in two-stages.

To date, the tech transfer process from our previous contract manufacturer based in the UK, associated with the cell production of CYAD-101 into our Mont-Saint-Guibert facility, is progressing according to plans. To date, we have completed and passed three engineering runs of CYAD-101 production in our facility associated with the process and we are now in the middle of performing the production of three consistency lots of CYAD-101 which will be incorporated into our CMC amendment for CYAD-101. The CMC amendment is expected to be filed by the end of August. At this date, we consider there is any material risk associated with approval of the CMC amendment, as we have had multiple CMC amendments associated with our CYAD-01 program approved over the past few years. The CMC

amendments (both in Belgium and U.S) are needed as the original batch of CYAD-101 cells was manufactured by third-party contract manufacturing in the U.K.

# Short hairpin RNA (shRNA) Allogenic Platform and CYAD-200 Series

In October 2018, we announced we had entered into an exclusive agreement with Horizon Discovery Group for the use of its shRNA technology to generate a novel, next-generation, non-gene-edited allogeneic platform for CAR-T therapies, by targeting the CD3 $\zeta$  component of the TCR complex on the surface of the T-cell. Horizon Discovery's SMARTvector technology to express shRNA optimized by us provides an alternate method to knockdown the TCR complex in allogeneic CAR-T therapies compared to gene editing techniques as well as the specificity to target a broad range of proteins.

*In vivo* data demonstrate that shRNA targeting of CD3 $\zeta$  effectively protects against Graft-versus-Host Disease (GvHD) to a level equivalent to CRISPR-Cas9 gene-editing-based knock-out. Furthermore, results from preclinical tests show significant increase in persistence of allogeneic T cells using shRNA targeting when compared to gene editing technologies, such as CRISPR-Cas9.

At the 2020 ASCO Virtual Scientific Program, preclinical data from the shRNA platform demonstrated the proof-of-principle that the concurrent knockdown of four genes using an optimized framework is feasible. In addition, the shRNA platform coupled with company's all-in-one vector approach provides the opportunity to design novel, allogeneic CAR-T candidates through a single step engineering process.

We continue to pursue the development of the proprietary non-gene edited allogeneic shRNA SMARTvector platform and progress towards the IND applications for the CYAD-200 series of shRNAbased allogeneic CAR-T candidates, including CYAD-211, our CAR-T therapy targeting B-cell maturation antigen (BCMA) for the treatment of patients with multiple myeloma. Submission of an IND application for CYAD-211 is anticipated by the end of second quarter 2020, and has not been impacted by the COVID-19 pandemic. We expect to initiate the Phase 1 dose-escalation trial evaluating CYAD-211 in patients with relapsed/refractory multiple myeloma by year-end 2020.

# Seasonality

Our business is currently not materially affected by seasonality.

# Manufacturing

We recently modified the manufacturing process we use to produce our CYAD-01 drug product candidate, in order to significantly increase the potency of the drug product candidate while enriching for T cells with a memory-like phenotype.

From late 2017 until mid-2019, our CYAD-01 drug product candidate was manufactured using a process, which we refer to as the monoclonal (mAb) process. This second manufacturing process replaced the previous manufacturing process, referred to as the LY manufacturing process in response to manufacturing challenges that were faced with the LY manufacturing process. In June 2019, we

announced a strategic update to our autologous r/r AML and MDS program, including that the FDA accepted our proposal to utilize the OptimAb manufacturing process with CYAD-01 under the current IND application.

The OptimAb manufacturing process utilizes a shortened eight-day cell culture and incorporates a selective PI3K inhibitor. This results in a product that is more potent and enriched for T cells with a memory-like phenotype while maintaining the high level of manufacturing reliability required to support clinical development. Preclinical data demonstrate that CYAD-01 produced using the OptimAb manufacturing process drives improved anti-tumor activity in an aggressive AML model compared to CYAD-01 produced with the previous mAb manufacturing process.

The first patient in our THINK trial to be administered drug product candidate manufactured using the OptimAb process was treated in September 2019. Throughout the remainder of 2019, all patients treated with CYAD-01 were administered drug product candidate manufactured using the OptimAb process. There can be no assurance that drug product candidate manufactured using the OptimAb process will result in similar or improved safety data and clinical activity compared to drug product candidate manufactured using either the LY or mAb manufacturing processes.

In addition to CYAD-01, the OptimAb manufacturing process will also be used in the autologous CYAD-02 development program.

#### **Termination of C-Cure and Heart-XS Programs**

Until mid-2016, we were focused on the development of a cardiovascular drug product candidate called C-Cure, an autologous cell therapy for the treatment of patients with ischemic heart failure. This program was funded in part through various research programs from the Walloon Region of Belgium. In June 2016, we reported topline results from a Phase 3 clinical trial for this drug product candidate. Following the announcement of these results, we explored strategic options to further develop and commercialize C-Cure, while we focused on our CAR-T oncology drug product candidates. In December 2017, we elected to shelve this program, as a result of which the research data and intellectual property rights associated with this development program were transferred to the Walloon Region, which partially financed the C-Cure program.

Also, in December 2017, our board of Directors decided to pause the development of the Heart-XS platform.

Pursuant to our decision to shift our focus away from cardiovascular drug candidates, on November 22, 2019, our affiliate, CorQuest Medical Inc., sold its portfolio of Heart-XS patents and related rights to CorQuest MedTech SRL, for consideration of  $\notin 1$  in addition of the reimbursement of certain maintenance costs of these patents. CorQuest Medical Inc. also has the right to receive royalties on the future sales and a percentage on the capital gains in the case of a re-sale or a change of control of Corquest MedTech SRL.

# 4.1.2. Principal markets on which the Company competes

The market sizes the Company is targeting are determined by the patient population enrolled in its clinical trials. Currently, the Company is targeting relapsed or refractory (r/r) AML patients in the THINK and DEPLETHINK trials with CYAD-01 and the CYCLE-1 trial with CYAD-02. Overall, in aggregate (between USA and top five European Union countries) there are approximately 17,500 new cases per year of r/r AML addressable by CYAD-01 or CYAD-02 based on these three clinical trials. In the context of metastatic CRC, the Company is targeting refractory or advanced metastatic CRC patient with CYAD-101 in the alloSHRINK trial. Overall, in aggregate (between United States and top five European Union countries), there are approximately 50,000 new patients every year in the refractory or advanced metastatic CRC patient populations.

# 4.1.3. Strategy

Celyad's strategy is to continue the advancement of CAR-T therapies. Key components of our strategy include:

- Rapidly progress the clinical development program of our autologous CYAD-01 and CYAD-02 NKG2D candidates for the treatment of relapsed / refractory AML and MDS
- Further investigate our TIM-based, non-gene edited allogeneic candidate CYAD-101 for the treatment of advanced mCRC patients
- Progress our led shRNA-based, non-gene edited allogeneic candidate CYAD-211 targeting BCMA for the treatment of r/r MM
- Develop our innovative allogeneic approaches including our TIM technology within our CYAD-100 series and novel shRNA platform for our CYAD-200 series while further leveraging our broad allogeneic intellectual property to become a leading player in the off-the-shelf CAR-T landscape

# **Background on Cancer and CAR T-Cell Therapy**

Cancer is the second leading cause of death in the United States after cardiovascular diseases, according to the U.S. Centers for Disease Control and Prevention. According to the American Cancer Society, in 2014, there were an estimated 1.6 million new cancer cases diagnosed and over 550,000 cancer deaths in the United States alone. In the past decades, the cornerstones of cancer therapies have been surgery, chemotherapy and radiation therapy. Since 2001, molecules that specifically target cancer cells have emerged as standard treatments for a number of cancers. For example, Gleevec is marketed by Novartis AG for the treatment of leukemia, and Herceptin is marketed by Genentech, Inc. for the treatment of breast and gastric cancer. Although targeted therapies have significantly improved the outcomes for certain patients with these cancers, there is still a high unmet need for the treatment of these and many other cancers.

Below are the statistics regarding certain forms of solid and hematological cancers and their estimated death rates in the United States for 2018:

	2018 estimates for the United States	
	New cases	Deaths
Acute myeloid leukemia	19,520	10,670
Multiple myeloma	30,770	12,770
Colorectal cancer	140,250	50,630
Non-Hodgkin lymphoma	74,680	19,910

Source: SEER, American Cancer Society

# CAR T-Cell Therapy

The immune system has a natural response to cancer, as cancer cells express antigens that can be recognized by cells of the immune system. Upon recognition of a cancer antigen, activated T-cells release substances that kill cancer cells and attract other immune cells to assist in the killing process. However, cancer cells can develop the ability to release inhibitory factors that allow them to evade immune response, resulting in the formation of cancers.

CAR T-cell therapy is a new technology that broadly involves engineering patients' own T-cells to express CARs so that these re-engineered cells recognize and kill cancer cells, overcoming cancer cells' ability to evade the immune response. CARs are comprised of the following elements:

- binding domains that encode proteins, such as variable fragments of antibodies that are expressed on the surface of a T-cell and allow the T-cell to recognize specific antigens on cancer cells;
- intracellular signaling domains derived from T-cell receptors that activate the signaling pathways responsible for the immune response following binding to cancer cells. This allows the T cell to trigger the killing activity of the target cancer cell once it is recognized; and
- costimulatory and adaptor domains, which enhance the effectiveness of the T-cells in their immune response.

Once activated, CAR T-cells proliferate and kill cancer cells directly through the secretion of cytotoxins that destroy cancer cells, and these cytokines attract other immune cells to the tumor site to assist in the killing process.

The CAR T-cell manufacturing process starts with collecting cells from a patient's blood. T-cells are then selected, following which the CAR is introduced into the T-cells using vectors. The CAR T-cells are then expanded prior to injection back into the patient.

# Current Investigational Treatments of Cancer Using CAR T-Cells

CAR-T cell therapy is an emerging approach for the treatment of some cancers, such as B-cell malignancies.

CAR CD19 is the most studied CAR. CAR CD19 has an antigen binding domain that recognizes the CD19 antigen that is present on all B lymphocytes. This means that if a cancer originates from B lymphocytes, such as acute lymphoblastic leukemia (ALL), then a CAR bearing the CD19 antibody could potentially recognize it and destroy it. Indeed, results of a clinical trial reported in the New England Journal of Medicine in October 2014 demonstrated that CAR CD19 CAR therapy was effective in treating patients with relapsed and refractory ALL. Treatment was associated with a complete remission rate of 90% and sustained remissions of up to two year after treatment. Despite its promise, CAR CD19 therapy is inherently limited to the treatment of B-cell malignancies. CAR CD19 also targets normal B lymphocytes leading to the need to treat those patients with gamma globulins.

# 4.1.4. Licensing and Collaboration Agreements and Intellectual Property

# 4.1.4.1. Licensing and Collaboration Agreements

For more information about the financial commitments of Celyad regarding material agreement, please see section 5.33 Commitments of the 2019 annual financial report.

### **Dartmouth College and Celdara**

#### Background

In January 2015, we entered into a stock purchase agreement with Celdara Medical, LLC, or Celdara, pursuant to which we purchased all of the outstanding membership interests of OnCyte, LLC, or OnCyte. In connection with this transaction, we, Celdara and OnCyte entered into an asset purchase agreement pursuant to which Celdara sold to OnCyte certain data, protocols, regulatory documents and intellectual property, including the rights and obligations under two license agreements between OnCyte and Dartmouth College, or Dartmouth, related to our CAR-T development programs. In connection with the asset purchase agreement, OnCyte and Celdara entered into a services agreement under which Celdara provided certain development activities related to the development of CAR-T products.

## Amended Asset Purchase Agreement

On August 3, 2017, we, Celdara and OnCyte, our wholly-owned subsidiary, entered into an amendment to the asset purchase agreement described above. In connection with the amendment, the following payments were made to Celdara: (i) an amount in cash equal to \$10.5 million, (ii) newly issued shares of Celyad valued at \$12.5 million, (iii) an amount in cash equal to \$6.0 million in full satisfaction of any payments owed to Celdara in connection with a clinical milestone related to our CAR-T NKR-2 product candidate, (iv) an amount in cash equal to \$0.6 million in full satisfaction of any payments owed to Celdara in connection with Novartis International Pharmaceutical Ltd., and

(v) an amount in cash equal to \$0.9 million in full satisfaction of any payments owed to Celdara in connection with our license agreement with Ono Pharmaceutical Co., Ltd<sup>1</sup>.

Under the amended asset purchase agreement, OnCyte is obligated to make certain development-based milestone payments to Celdara up to \$40.0 million for our clinical-stage product candidate (using autologous NKR-2 T-cells), the first product candidate in the first of four defined product groups. We are also obligated to make certain development-based milestone payments up to \$36.5 million for the first product candidate in one of three additional defined preclinical-stage product groups. Under the prior agreement these payments were payable once per licensed product whereas under the amended asset purchase agreement these payments are now payable for the first CAR-T product in each of these four defined CAR-T product groups. We are also obligated to make sales-based milestone payments up to \$76.0 million for the first CAR-T product in the first of the four defined CAR-T product groups and up to \$80.0 million for the first CAR-T product in the next three defined CAR-T product groups. Under the amended asset purchase agreement, OnCyte is required to make tiered single-digit royalty payments to Celdara in connection with the sales of CAR-T products within each of the four defined CAR-T product groups, subject to reduction in countries in which there is no patent coverage for the applicable product or in the event OnCyte is required to secure licenses from third parties to commercialize the applicable product. Such royalties are payable on a product-by-product and country-by-country basis until the later of (i) the last day that at least one valid patent claim covering the applicable product exists, or (ii) the tenth anniversary of the day of the first commercial sale of the applicable product in such country.

Under the amended asset purchase agreement, in lieu of royalties previously payable on sales by sublicensees, OnCyte is now required to pay Celdara a percentage of sublicense income, including royalty payments, for each sublicense ranging from the mid-single digits to the mid-twenties, depending on which of a specified list of clinical and regulatory milestones the applicable product has achieved at the time the sublicense is executed. These percentages will be applied on a product-by-product basis to each payment included within sublicense income that is attributable to the grant of rights in, or the achievement of a milestone with respect to a specific product that is subject to, such sublicense. Under the amended asset purchase agreement, OnCyte is required to pay Celdara a single-digit percentage of any research and development funding received by OnCyte for each of the four defined CAR-T product groups, not to exceed \$7.5 million for each product group. We can opt out of the development of any product if the data does not meet the scientific criteria of success. We may also opt out of development of any product for any other reason upon payment of a termination fee of \$2.0 million to Celdara.

In connection with the amended asset purchase agreement, OnCyte and Celdara terminated the services agreement related to certain development activities related to the development of CAR-T products in consideration of a cash payment to Celdara in the amount of \$0.9 million out of the \$1.8 million remaining contractual amount.

<sup>&</sup>lt;sup>1</sup> This license agreement has been terminated by Ono Pharmaceutical.

#### Amended Dartmouth License

As described above, as a result of our acquisition of all of the outstanding membership interests of OnCyte and the asset purchase agreement among us, Celdara and OnCyte, OnCyte became our whollyowned subsidiary and acquired certain data, protocols, regulatory documents and intellectual property, including the rights and obligations under two license agreements between OnCyte and Dartmouth. The first of these two license agreements concerned patent rights related, in part, to methods for treating cancer involving chimeric NK and NKP30 receptor targeted therapeutics and T cell receptor-deficient T cell compositions in treating tumor, infection, GVHD, transplant and radiation sickness, or the CAR-T License, and the second of these two license agreements concerned patent rights related, in part, to anti-B7-H6 antibody, fusion proteins and methods of using the same, or the B7H6 License. On August 2, 2017, OnCyte and Dartmouth entered into an amendment agreement in order to combine OnCyte's rights under B7H6 Agreement with OnCyte's rights under the CAR-T License, resulting in the termination of the B7H6 License, and in order to make certain other changes to the agreement. In connection with the amendment, OnCyte paid Dartmouth a non-refundable, non-creditable amendment fee in the amount of \$2.0 million, charged to the income statement of 2017 as part of the costs of the amendments of the Celdara Medical and Dartmouth College agreements.

Under the amended license agreement, Dartmouth granted OnCyte an exclusive, worldwide, royaltybearing license to certain know-how and patent rights to make, have made, use, offer for sale, sell, import and commercialize any product or process for human therapeutics, the manufacture, use or sale of which, is covered by such patent rights or any platform product. Dartmouth reserves the right to use the licensed patent rights and licensed know-how, in the same field, for education and research purposes only. The patent rights included in the amended license agreement also include the patents previously covered by the B7H6 License.

In consideration for the rights granted to us under the amended license agreement, OnCyte is required to pay to Dartmouth an annual license fee as well as a low single-digit royalty based on annual net sales of the licensed products by OnCyte, with certain minimum net sales obligations beginning April 30, 2024 and continuing for each year of sales thereafter. Under the amended license agreement, in lieu of royalties previously payable on sales by sublicensees, OnCyte is now required to pay Dartmouth a percentage of sublicense income, including royalty payments, (i) for each product sublicense ranging from the mid-single digits to low-single digits, depending on which of a specified list of clinical and regulatory milestones the applicable product has achieved at the time the sublicense is executed and (ii) for each platform sublicense in the mid-single digits. These percentages will be applied on a product-by-product basis to each payment included within sublicense income that is attributable to the grant of rights in, or the achievement of a milestone with respect to a specific product that is subject to, such sublicense. Additionally, the agreement requires that OnCyte exploit the licensed products, and OnCyte has agreed to meet certain developmental and regulatory milestones. Upon successful completion of such milestones, OnCyte is obligated to pay to Dartmouth certain clinical and regulatory milestone payments up to an aggregate amount of \$1.5 million and a commercial milestone payment in the amount

of \$4.0 million. We are responsible for all expenses in connection with the preparation, filing, prosecution and maintenance of the patents covered under the agreement.

After April 30, 2024, Dartmouth may terminate the amended license if Celyad (as mentioned above and described below, Oncyte is actually Celyad) fails to meet the specified minimum net sales obligations for any year (USD 10 million during first year of sales, USD 40 million during the second year of sales and USD 100 million during the third year of sales and every year of sales thereafter), unless Celyad pays to Dartmouth the royalty which Celyad would otherwise have been obligated to pay had Celyad met such minimum net sales obligation. Dartmouth may also terminate the license if Celyad fails to meet a milestone within the specified time period, unless Celyad pays the corresponding milestone payment. Either party may terminate the agreement in the event the other party defaults or breaches any of the provisions of the agreement, subject to 30 days' prior notice and opportunity to cure. In addition, the agreement automatically terminates in the event Celyad becomes insolvent, make an assignment for the benefit of creditors or file, or have filed against us, a petition in bankruptcy. Absent early termination, the agreement will continue until the expiration date of the last to expire patent right included under the agreement will expire in 2033, absent extensions or adjustments.

## **Dissolution of OnCyte**

In March 2018, we dissolved and wound up the affairs of our wholly owned subsidiary OnCyte, LLC, or OnCyte, pursuant to the Delaware Limited Liability Company Act. As a result of the dissolution of OnCyte, all the assets and liabilities of OnCyte, including the contingent consideration payable and our license agreement with Dartmouth College, were fully distributed to and assumed by Celyad SA. Celyad SA will continue to carry out the business and obligations of OnCyte, including under our license agreement with Dartmouth College.

# Novartis

In May 2017, we announced that we had entered into a non-exclusive license agreement with Novartis International AG, or Novartis, regarding U.S. patents related to allogeneic CAR-T cells. The agreement includes our intellectual property rights under U.S. Patent No. 9,181,527. This agreement is related to two undisclosed targets currently under development by Novartis. Under the terms of the agreement, we received an upfront payment of \$4<sup>.0</sup> million and we are eligible to receive additional milestone payments in aggregate amounts of up to \$92.0 million. In addition, we are eligible to receive royalties based on net sales of the licensed target associated products at percentages in the single digits. We retain all rights to grant further licenses to third parties for the use of allogeneic CAR-T cells.

# **Horizon Discovery Group**

In 2018, we signed exclusive agreements with Horizon Discovery Group plc for the use of its shRNA technology to generate our second non-gene-edited allogeneic platform. Data from preclinical studies have demonstrated the versatility of the shRNA platform in the allogeneic setting and may pave the way

for the next steps in the development of our differentiated non-gene-edited allogeneic approach to CAR-T cell therapy.

In October 2019, we capitalized the milestone payments for a total amount of \$0.2 million related to both the exercise of the option on the exclusive agreement and to the first effective IND application, filed by Celyad, relating to the first product (CYAD-02).

# 4.1.4.2. Intellectual Property

# **Patents and Patent Applications**

Patents, patent applications and other intellectual property rights are important in the sector in which we operate. We consider on a case-by-case basis filing patent applications with a view to protecting certain innovative products, processes, and methods of treatment. We may also license or acquire rights to patents, patent applications or other intellectual property rights owned by third parties, academic partners or commercial companies which are of interest to us.

Our patent portfolio includes pending patent applications and issued patents in the United States and in foreign countries.

The term of a U.S. patent may be eligible for patent term extension under the Hatch-Waxman Act to account for at least some of the time the drug or device is under development and regulatory review after the patent is granted. With regard to a drug or device for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one U.S. patent. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug or device. Some foreign jurisdictions have analogous patent term extension provisions that allow for extension of the term of a patent that covers a device approved by the applicable foreign regulatory agency.

# NKR-T Cell Platform Patents

As of February 29, 2020, our CAR T-cell portfolio includes four patent families exclusively licensed to us by Dartmouth. This portfolio includes twelve issued U.S. patents; nine pending U.S. patent applications; and 25 foreign granted patents and applications pending in jurisdictions including Australia, Brazil, Canada, China, Europe, Hong Kong, India, Japan, Mexico and Russia. These patents and patent applications relate to specific chimeric antigen receptors and to T-cell receptor deficient T-cells, and are further detailed below.

• A first patent family relates to chimeric NK receptors and methods for treating cancer. There are three granted U.S. patents in this family (US 7,994,298; US 8,252,914 and US 10,336,804) and two further pending US applications. The scope of this patent family includes chimeric natural killer cell

receptors (NKR CARs), T-cells with such receptors (NKR CAR-T cells) and methods of treating cancer with these NKR CAR-T cells.

• A second patent family is entitled "NKp30 receptor targeted therapeutics" and describes a specific NKR CAR based on the NKp30 receptor. One U.S. patent is granted (US 9,833,476) and there is a further U.S. application pending.

• A third family relates to an anti-B7H6 antibody, CARs and BiTE molecules containing the antibody; to CAR-T cells; and methods of treating cancer with the CAR-T cells. One U.S. patent is granted (US9,790,278), and applications are pending in China, Europe, Japan and the United States.

• A fourth patent family relates to T-cell receptor-deficient compositions. T-cell receptor, or TCR, deficient human T-cells could be particularly useful to generate allogeneic CAR-T cells. The family includes members that relate to the concept (irrespective of the way the T-cell is made TCR deficient), as well as members describing specific ways of making the cells TCR deficient. There are seven granted U.S. patents in this family (US 9,181,527;US 9,273,283; US9,663,763; US9,822,340; US9,821,011; US 9,938,497; and US 9,957,480), as well as five further pending US applications and ten applications in other jurisdictions.

## Trade Secrets

In addition to our patents and patent applications, we keep certain of our proprietary information as trade secrets, which we seek to protect by confidentiality agreements with our employees and third parties, and by fragmenting know-how between different individuals, in accordance with standard industry practices.

## 4.1.5. Competition

The industry in which we operate is subject to rapid technological change. We face competition from pharmaceutical, biopharmaceutical and medical devices companies, as well as from academic and research institutions. Some of these competitors are pursuing the development of medicinal products and other therapies that target the same diseases and conditions that we are targeting.

Some of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our programs are likely to be their efficacy, safety and convenience.

Many of our competitors have substantially greater financial, technical and other resources.

For a breakdown of our total revenues by activity and geographic market, please see "Note 6—Operating segment information" in our consolidated financial statements appended to this Annual Report.

# CAR T-Cell Therapy

Early results from clinical trials have fueled continued interest in CAR T-cell therapies and our competitors as of the date of this Registration Document include Adaptimmune Therapeutics plc, Adicet Bio, Inc., Allogene Therapeutics Inc., Arcellx. Inc., Astellas Pharma Inc., Atara Biotherapeutics, Inc., Autolus Therapeutics plc, Bellicum Pharmaceuticals, Inc., BioNTech SE, bluebird bio, Inc., Bristol-Myers Squibb Company, CARsgen Therapeutics Co. Ltd., Cellectis S.A., Cellular Biomedicine Group, Celularity, Inc., Editas Medicine, Inc., Fate Therapeutics, Inc., CRISPR Therapeutics, Inc., Gilead Sciences Inc, Immatics Biotechnologies GmbH, Intellia Therapeutics, Inc., Iovance Biotherapeutics, Inc., NantKwest, Inc., Nkarta Therapeutics, Inc., Novartis AG, Poseida Therapeutics, Inc., Precigen, Inc. Precision Biosciences, Inc., Servier Laboratories Limited, Sorrento Therapeutics, Inc., Vor BioPharm and Ziopharm Oncology, Inc.

# 4.1.6. Investments

Celyad's actual capital expenditures excluding impact of recognition of right-of-use assets for the years ended 31 December 2017, 2018 and 2019 amounted to  $\notin 0.9$  million,  $\notin 0.8$  million and  $\notin 0.4$  million, respectively. These capital expenditures primarily consisted of the acquisition of laboratory equipment and industrial tools, the refurbishment of research and development laboratories and leasehold improvements of corporate offices located in Belgium and the United States. Celyad expects its capital expenditures to increase in absolute terms in the near term as Celyad continues to advance its research and development programs and grow its operations.

## 4.1.7. Government Regulation

## U.S. Regulation

Government authorities in the United States at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and biological products, or biologics, such as our drug product candidates. Generally, before a new drug or biologic can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and an application for marketing authorization must be approved by the regulatory authority.

#### U.S. Biological Product Development

In the United States, the FDA regulates biologics under the Federal Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Service Act, or PHSA, and their implementing regulations. Biologics are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval or license revocation, a clinical hold, untitled or warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Our drug product candidates must be approved by the FDA through the Biologics License Application, or BLA, process before they may be legally marketed in the United States. The process required by the FDA before a biologic may be marketed in the United States generally involves the following:

- completion of extensive nonclinical, sometimes referred to as preclinical, laboratory tests, animal studies and formulation studies in accordance with applicable regulations, including the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practices, or GCPs, and other clinical trial-related regulations to establish the safety and efficacy of the proposed drug product candidate for its proposed indication;
- submission to the FDA of a BLA;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the product is produced to assess compliance with the FDA's current good

manufacturing practice, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality, purity and potency;

- potential FDA audit of the preclinical study sites and/or clinical trial sites that generated the data in support of the BLA; and
- FDA review and approval of the BLA prior to any commercial marketing or sale of the product in the United States.

The data required to support a BLA is generated in two distinct development stages: preclinical and clinical.

• The preclinical development stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The conduct of the preclinical studies must comply with federal regulations, including GLPs. The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, as well as other information, to the FDA as part of the IND.

An IND is a request for authorization from the FDA to administer an investigational drug product to humans for the clinical development stage. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug product candidate at any time before or during clinical trials due to safety concerns, non-compliance, or other issues affecting the integrity of the trial. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

Where a trial is conducted at, or sponsored by, institutions receiving NIH funding for recombinant DNA research, the investigator must comply with the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. Many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. Pursuant to the NIH Guidelines, clinical trials must be evaluated and assessed by an Institutional Biosafety Committee, or IBC, a local committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial.

• The clinical stage of development involves the administration of the drug product candidate to healthy volunteers and patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their

participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products, including biologics, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. However, there are evolving rules and increasing requirements for publication of trial-related information, and it is possible that data and other information from trials involving biologics that never garner approval could in the future require disclosure. In addition, publication policies of major medical journals mandate certain registration and disclosures as a pre-condition for potential publication, even if not currently mandated as a matter of law. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Clinical trials are generally conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the drug product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug product candidate and, if possible, to gain early evidence on effectiveness. For the Oncology indications that Celyad is currently developing, patients with cancer are enrolled in the Phase 1 clinical trials.
- Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks and preliminary evaluation of efficacy.

- Phase 3 clinical trials generally involve large numbers of patients at multiple sites, in multiple countries, and are designed to provide the data necessary to demonstrate the efficacy of the product for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. Phase 3 clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of a BLA.
- Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may condition approval of a BLA on the sponsor's agreement to conduct additional clinical trials to further assess the biologic's safety and effectiveness after BLA approval.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and the investigators within 15 calendar days of receipt by the sponsor or its agents after determining that the information qualifies for such expedited reporting. IND safety reports are required for serious and unexpected suspected adverse events, findings from other studies or animal or in vitro testing that suggest a significant risk for human subjects, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Additionally, a sponsor must notify FDA within 7 calendar days after receiving information concerning any unexpected fatal or life-threatening suspected adverse reaction. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated intervals based on access to certain data from the trial. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug product candidate does not undergo unacceptable deterioration over its shelf life.

A manufacturer of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug. This requirement applies on the earlier of the first initiation of a Phase 2 or Phase 3 trial of the investigational drug.

# BLA and FDA Review Process

Following trial completion, trial data are analyzed to assess safety and efficacy. The results of preclinical studies and clinical trials are then submitted to the FDA as part of a BLA, along with proposed labeling for the product and information about the manufacturing process and facilities that will be used to ensure product quality, results of analytical testing conducted on the chemistry of the drug product candidate, and other relevant information. The BLA is a request for approval to market the biologic for one or more specified indications and must contain proof of safety, purity, and potency, or efficacy, which is demonstrated by extensive preclinical and clinical testing. The application may include both negative or ambiguous results of preclinical and clinical trials as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety, purity and potency of the investigational product to the satisfaction of the FDA. FDA approval of a BLA must be obtained before a biologic may be marketed in the United States.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a significant user fee, which is adjusted on an annual basis. PDUFA also imposes an annual prescription drug product program fee. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business.

Once a BLA has been accepted for filing, which occurs, if at all, sixty days after the BLA's submission, the FDA's goal is to review BLAs within 10 months of the filing date for standard review or six months of the filing date for priority review, if the application is for a product intended for a serious or life-threatening condition and the product, if approved, would provide a significant improvement in safety or effectiveness. The review process is often significantly extended by FDA requests for additional information or clarification.

After the BLA submission is accepted for filing, the FDA reviews the BLA to determine, among other things, whether the proposed drug product candidate is safe, pure and potent for its intended use, and whether the drug product candidate is being manufactured in accordance with cGMP to assure and preserve the drug product candidate's identity, strength, quality, purity and potency. The FDA may refer applications for novel drug product candidates or drug product candidates which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the applications of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA

and us during the review process. The review and evaluation of a BLA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

Before approving a BLA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving a BLA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process and manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the BLA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, withdraw the application or request a hearing. Even if such data and information is submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than we interpret the same data.

There is no assurance that the FDA will ultimately approve a product for marketing in the United States, and we may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific populations, and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or may condition the approval of the BLA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase 4 testing which involves clinical trials designed to further assess the product's safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a Risk Evaluation and Mitigation Strategy, or REMS, to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS. The FDA will not approve the BLA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product licenses may be revoked or suspended for non-compliance with regulatory standards or if problems occur following initial marketing.

#### **European Union Drug Development**

In the European Union, our future drug product candidates will also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization, or MA, from the competent regulatory agencies has been obtained.

# Clinical Trials

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the European Union clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the European Union Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the Member State regimes. To improve the current system, a new Regulation No. 536/2014, or the Regulation, on clinical trials on medicinal drug product candidates for human use, which repealed Directive 2001/20/EC, was adopted on April 16, 2014, and published in the European Official Journal on May 27, 2014. The new Regulation aims at harmonizing and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials, and increasing their transparency. The new Regulation entered into force on June 16, 2014, but the timing of its application depends on the development of a fully functional EU clinical trials portal and database. The Regulation becomes applicable six months after the European Commission publishes a notice of this confirmation. So far, however, such confirmation has not been published. Until then the Clinical Trials Directive 2001/20/EC will still apply. In addition, the transitory provisions of the new Regulation offer the sponsors the possibility to choose between the requirements of the Directive and the Regulation if the request for authorization of a clinical trial is submitted in the 12 months after the new Regulation becomes applicable. In that case, the clinical trial continues to be governed by the Directive until 36 months after the new Regulation becomes applicable.

Under the current regime, before a clinical trial can be initiated it must be approved in each of the European Union countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. More specifically, a clinical trial may not be started until the relevant EC has issued a favorable opinion, and the NCA has not informed the Sponsor of the trial of any grounds for non-acceptance or confirmed that no such grounds exist. Approval will only be granted if satisfactory information demonstrating the quality of the investigational agent and its non-clinical safety has been provided, together with a study plan that details the manner in which the trial will be carried out.

ECs determine whether the proposed clinical trial will expose participants to unacceptable conditions of hazards, while considering, among other things, the trial design, protocol, facilities, investigator and supporting staff, recruitment of clinical trial subjects, the Investigator's Brochure, or IB, indemnity and insurance, etc. The EC also determines whether clinical trial participants have given informed consent to participate in the trial. Following receipt of a complete application (which must be submitted in the national language), ECs must deliver their opinion within 60 days (or sooner if the Member State has

implemented a shorter time period). For clinical trials of gene therapy, somatic cell therapy, and all medicinal products containing genetically modified organisms, the normal statutory time limit is extended to 90 days, and this may be extended (by an additional 90 days).

Similarly, a valid request for authorization (in the national language) must be submitted to the NCA of each Member State where the trial will be conducted. Sponsors must be notified of the decision within 60 days of receipt of the application (unless shorter time periods have been fixed), in the absence of which, the trial is considered approved. However, for clinical trials of gene therapy, somatic cell therapy, and all medicinal products containing genetically modified organisms, a written authorization by the competent NCA is required. Similar timeline extensions as for ECs exist.

Studies must comply with ethical guidelines and Good Clinical Practice, or GCP, guidelines. Monitoring of adverse reactions that occur during clinical trials, including, where applicable, notification of the same to the competent NCA and ECs, is also required. Trials can be terminated early if a danger to human health is established or continuing the trial would be considered unethical. Consequently, the rate of completion of clinical trials may be delayed by many factors, including slower than anticipated patient enrollment or adverse events occurring during clinical trials.

#### Drug Review and Approval

In the United Kingdom and the European Economic Area, or EEA (which is comprised of the 27 Member States of the European Union plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA.

There are two types of marketing authorizations:

- The Centralized MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines, and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions, and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which is in the interest of public health in the European Union.
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in other Member State(s) through the Mutual Recognition Procedure, or MRP. If the product has not

received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure, or DCP. Under the DCP an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of product characteristics, or SmPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Concerned Member States, or CMSs) for their approval. If the CMSs raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the relevant Member States (i.e. in the RMS and the CMSs).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Celyad intends to follow the mandatory Centralized procedure for Marketing Authorization review and approval at the time of future registration for a CART product.

## Marketing Authorization Application

Following positive completion of clinical trials, pharmaceutical companies can submit a MA application. The MA application shall include all information that is relevant to the evaluation of the medicinal products, whether favorable or unfavorable. The application dossier must include, among other things, the results of pharmaceutical (physicochemical, biological, or microbiological) tests, preclinical (toxicological and pharmacological) tests, and clinical trials, including the therapeutic indications, contra-indications, and adverse reactions, and the recommended dosing regimen or posology.

In addition to demonstrating the safety and efficacy of the medicinal product, pharmaceutical companies are required to guarantee the consistent quality of the product. Therefore, the conditions for obtaining a MA include requirements that the manufacturer of the product complies with applicable legislation including Good Manufacturing Practice, or GMP, related implementing measures and applicable guidelines that involve, amongst others, ongoing inspections of manufacturing and storage facilities.

#### Supplementary Protection Certificates and Data/market Exclusivity

In Europe, the extension of effective patent term to compensate originator pharmaceutical companies for the period between the filing of an application for a patent for a new medicinal product and the first MA for such product, has been achieved by means of a Supplementary Protection Certificate, or SPC, which can be applied for by the originator pharmaceutical company within six months from the granting of the first MA and comes into effect on expiry of the basic patent. Such SPC attaches only to the active ingredient of the medicinal product for which the MA has been granted. The SPC for an active ingredient

has a single last potential expiry date throughout the EEA, and cannot last for more than five years from the date on which it takes effect (*i.e.*, patent expiry). Furthermore, the overall duration of protection afforded by a patent and a SPC cannot exceed 15 years from the first MA. The duration of a medicinal product SPC can be extended by a single six-month period, or pediatric extension, when all studies in accordance with a pediatric investigation plan, or PIP, have been carried out.

Innovative medicines benefit from specific data and marketing exclusivity regimes. These regimes are intended to provide general regulatory protection to further stimulate innovation. The current rules provide for (i) an 8-year data protection (from the MA of an innovative medicine) against the filing of an abridged application for a follow-on product, referring to the data supporting the MA of the innovative medicine (data exclusivity); and (ii) an additional 2-year period of protection against the marketing of a follow-on product (marketing exclusivity), with a possible extension by 1 year if, during the first 8 years, a new therapeutic indication (which is considered to bring a significant clinical benefit in comparison with existing therapies) is approved. This protection is often referred to as the "eight, plus two, plus one" rule. Additional reward mechanisms exist, most notably a 10-year orphan medicines' marketing exclusivity, and a 1-year data exclusivity for developing a new indication for an old substance and for switch data supporting a change in prescription status.

#### Pricing and Reimbursement

## United States

Sales of our products will depend, in part, on the extent to which our products, once approved, will be covered and reimbursed by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly reducing reimbursements for medical products and services. The process for determining whether a third-party payor will provide coverage for a drug product, including a biologic, typically is separate from the process for setting the price of a drug product or for establishing the reimbursement rate that a payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the approved drugs for a particular indication.

In order to secure coverage and reimbursement for any drug product candidate that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the drug product candidate, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Whether or not we conduct such studies, our drug product candidates may not be considered medically necessary or cost-effective. A third-party payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage, and adequate reimbursement, for the product. Third party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development. The containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs, including biologics, have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our drug product candidate or a decision by a third-party payor to not cover our drug product candidate could reduce physician usage of the drug product candidate and have a material adverse effect on our sales, results of operations and financial condition.

For example, the ACA, enacted in March 2010, has had a significant impact on the health care industry. The ACA has expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, the ACA expanded and increased industry rebates for drugs covered under Medicaid programs and made changes to the coverage requirements under the Medicare Part D program.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, started in April 2013 and will stay in effect through 2027 unless additional Congressional action is taken. On January 2, 2013, then-President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Some of the provisions of ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. On January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of ACA that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the

ACA for plans sold through such marketplaces. Congress may consider other legislation to replace elements of the ACA.

The Tax Cuts and Jobs Act of 2017, or TCJA, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plan, the annual fee imposed on certain high cost employer-sponsored insurance plan, the annual fee imposed on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain high cost employer sponsored insurance plans, the annual fee imposed on certain high cost employer sponsored insurance plans, the annual fee imposed on certain high cost employer sponsored insurance plans, the annual fee imposed on certain high cost employer sponsored insurance plans, the annual fee imposed on certain high cost employer sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device exercise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to reduce the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress also could consider subsequent legislation to replace elements of ACA that are repealed. Thus, the full impact of ACA, any law replacing elements of it, or the political uncertainty related to any repeal or replacement legislation on our business remains unclear.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country.

#### European Union

In Europe, pricing and reimbursement for pharmaceutical products are not harmonized and fall within the exclusive competence of the national authorities, provided that basic transparency requirements (such as maximum timelines) defined at the European level are met as set forth in the EU Transparency Directive 89/105/EEC. A Member State may approve a specific price for a medicinal product, or it may instead adopt a system of direct or indirect controls on the profitability of the Company placing the medicinal product on the market. For example, in France, effective access to the market assumes that our future products will be reimbursed by social security. The price of medications is negotiated with the Economic Committee for Health Products, or CEPS.

As a consequence, reimbursement mechanisms by public national healthcare systems, or private health insurers also vary from country to country. In public healthcare systems, reimbursement is determined by guidelines established by the legislator or a competent national authority. In general, inclusion of a product in reimbursement schemes is dependent upon proof of the product efficacy, medical need, and economic benefits of the product to patients and the healthcare system in general. Acceptance for reimbursement comes with cost, use and often volume restrictions, which again vary from country to country.

The pricing and reimbursement level for medicinal products will depend on the strength of the clinical data set and, as for most novel therapies, restrictions may apply. In most countries, national competent authorities ensure that the prices of registered medicinal products sold in their territory are not excessive.

In making this judgment, they usually compare the proposed national price either to prices of existing treatments and/or to prices of the product at issue in other countries – so-called "international reference pricing" – also taking into account the type of treatment (preventive, curative or symptomatic), the degree of innovation, the therapeutic breakthrough, volume of sales, sales forecast, size of the target population and/or the improvement (including cost savings) over comparable treatments. Given the growing burden of medical treatments on national healthcare budgets, reimbursement and insurance coverage is an important determinant of the accessibility of medicines.

The various public and private plans, formulary restrictions, reimbursement policies, patient advocacy groups, and cost-sharing requirements may play a role in determining effective access to the market of our product candidates. The national competent authorities may also use a range of policies and other initiatives intended to influence pharmaceutical consumption. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our drug product candidates. Historically, products launched in the European Union do not follow price structures of the United States and generally tend to be priced at a significantly lower level.

# **Other Healthcare Laws and Compliance Requirements**

Our business operations in the United States and our arrangements with clinical investigators, healthcare providers, consultants, third-party payors and patients may expose us to broadly applicable federal and state fraud and abuse and other healthcare laws. These laws may impact, among other things, our research, proposed sales, marketing and education programs of our drug product candidates that obtain marketing approval. The laws that may affect our ability to operate include, among others:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order, or recommendation of, an item, good, facility or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which impose penalties and provide for civil whistleblower or qui tam actions against individuals and entities for, among other things, knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent, or making a false statement or record material to payment of a false claim or avoiding, decreasing, or concealing an obligation to pay money to the federal government, including for example, providing inaccurate billing or coding information to customers or promoting a product offlabel;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created federal criminal statutes that prohibit, among other things, executing a scheme to

defraud any healthcare benefit program, obtaining money or property of the health care benefit program through false representations, or knowingly and willingly falsifying, concealing or covering up a material fact, making false statements or using or making any false or fraudulent document in connection with the delivery of or payment for healthcare benefits or services.

- the federal Physician Payments Sunshine Act, enacted as part of the ACA, which requires applicable manufacturers of covered drugs, devices, biologics and medical supplies to track and annually report to CMS payments and other transfers of value provided to physicians and teaching hospitals and certain ownership and investment interest held by physicians or their immediate family members in applicable manufacturers and group purchasing organizations;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements on covered entities and their business associates relating to the privacy, security and transmission of individually identifiable health information; and
- state law equivalents of each of the above federal laws, such as state anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements, state laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect as HIPAA, thus complicating compliance efforts.

The ACA broadened the reach of the federal fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and certain applicable federal criminal healthcare fraud statutes. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant administrative, civil, and/or criminal penalties, damages, fines, disgorgement, individual imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with

applicable laws, they also may be subject to administrative, civil, and/or criminal sanctions, including exclusions from government funded healthcare programs.

### 5. MANAGEMENT AND CORPORATE GOVERNANCE

#### 5.1. GENERAL

This section summarizes the rules and principles on the basis of which the corporate governance of the Company has been organized pursuant to BCCA, and the Company's corporate governance charter (the "**Charter**") adopted in accordance with the Belgian Corporate Governance Code 2020 (the "**CGC**") and updated regularly by the Board of Directors.

The Charter is available on the Company's website (<u>www.celyad.com</u>) under Investors/Corporate Governance tab.

The text of the CGC is available on the website of the Commission of Corporate Governance at https://www.corporategovernancecommittee.be/fr/over-de-code-2020/code-belge-de-gouvernance-dentreprise-2020.

The Board of Directors intends to comply with the provisions of the CGC but believes that the size and the current state of development of the Company justifies certain deviations. These deviations are further detailed in the Section 5.5 hereinafter.

The Charter includes the following main chapters:

- Structure and organization;
- Shareholder structure;
- The Board: terms of reference;
- Chairman of the Board;
- Company Secretary;
- Board committees;
- Executive Committee;
- Rules preventing market abuse;
- Miscellaneous and annexes.

#### 5.2. BOARD OF DIRECTORS

#### 5.2.1. Composition of the Board of Directors

As provided by articles 7:85 et sq. of the BCCA, the Company is managed by a Board of Directors acting as a collegiate body. The Board of Directors' role is to pursue the long-term success of the Company by providing entrepreneurial leadership and enabling risks to be assessed and managed. The Board of Directors determines the Company's values and strategy, its risk preference and key policies. The Board of Directors ensures that the necessary leadership, financial and human resources are in place for the Company to meet its objectives.

The Company has opted for a one-tier governance structure. As provided by Article 7:93 of the BCCA, the Board of Directors is the ultimate decision-making body in the Company, except with respect to those areas that are reserved by law or by the Company's articles of association to the Shareholders Meeting.

The Company's articles of association state that the number of directors of the Company, who may be natural persons or legal entities and who need not be shareholders, must be at least 3. At least half of the members of the Board of Directors must be non-executive directors and at least three of them must be independent directors.

A meeting of the Board of Directors is validly constituted if at least half of its members are present in person or represented at the meeting. If this quorum is not met, a new board meeting may be convened by any director to deliberate and decide on the matters on the agenda of the board meeting for which a quorum was not met, provided that at least two members are present. Meetings of the Board of Directors are convened by the Chairman of the Board or the CFO or Chief Legal Officer, or by at least two directors, whenever the interest of the Company so requires. In principle, the Board of Directors will meet at least four times per year.

The Chairman of the Board of Directors shall have a casting vote on matters submitted to the Board of Directors in the event of a tied vote.

At the date of this Registration Document, the Board of Directors consists of 9 members, one of which is an executive director (with daily management authority) and 8 of which are non-executive directors, including six independent directors. The Board of Directors is composed of 6 men and 3 women.

Name	Position	Term	Board Committee Membership
Michel Lussier	Chairman	2024	Chairman of the Nomination and
Michel Lussier	Non-Executive	2024	Remuneration Committee
Filippo Petti <sup>(1)</sup>	Executive	2024	
Serge Goblet	Non-executive director	2024	
			Member of the Nomination and
Chris Buyse	Independent director	2024	Remuneration Committee
			Chairman of the Audit Committee
R.A.D Lifesciences	T 1 1 4 1° 4	2024	Member of the Nomination and
BV (2)	Independent director	2024	Remuneration Committee
Hilde Windels	Independent director	2022	Member of the Audit Committee
Margo Roberts	Independent director	2022	
Maria Koehler (3)	Independent director	2024	
Dominic Piscitelli (4)	Independent director	2024	Member of the Audit Committee

[1] Filippo Petti has replaced LSS Consulting SRL, represented by Christian Homsy, as CEO of the Company as of April 1st, 2019. Filippo Petti has then been coopted as Board member as of November 28, 2019 in replacement of LSS Consulting SRL, who resigned. The Board mandate of Filippo Petti

has been confirmed until 2024 by resolution of the extraordinary shareholders meeting of March 23, 2020.

(2) R.A.D. Lifesciences BV, represented by Rudy Dekeyser, has been appointed as Director of the Company by resolution of the shareholders meeting of May 5, 2020.

(3) Maria Koehler has been appointed as Director of the Company by resolution of the extraordinary shareholders meeting of March 23, 2020.

(4) Dominic Piscitelli has been appointed as Director of the Company by resolution of the shareholders meeting of May 5, 2020.

The following paragraphs contain brief biographies of each of the directors, or in case of legal entities being director, their permanent representatives, with an indication of other relevant mandates as member of administrative, management or supervisory bodies in other companies during the previous five years.

**Michel Lussier** serves as Chairman of the Board of Directors. Mr. Lussier founded MedPole Ltd, the North American satellite of MedPole SA, a European incubator for medical technology start-up companies located in Belgium and serves as the Chief Executive Officer for the group. In this capacity, he is an advisor to Fjord Ventures, a Laguna Hills, California based medical technology accelerator / incubator. Since May 2014, Mr. Lussier has also served as the Chief Executive Officer of Metronom Health Inc, an early stage medical device company founded by Fjord Ventures, developing a continuous glucose monitoring system. Prior to that, from 2002 to 2013, he worked for Volcano Corporation, where he served several positions, most recently as President, Clinical and Scientific Affairs from 2012 to 2013, and prior to that from 2007 to 2012, Group President, Advanced Imaging Systems, Global Clinical & Scientific Affairs and General Management of Europe, Africa and the Middle East. Mr. Lussier obtained a Bachelor of Sciences degree in Electrical Engineering and Master's Degree in Biomedical Engineering at the University of Montreal. He also holds an MBA from INSEAD (European Institute of Business Administration), France. In addition to serving on the Company's Board of Directors, he also serves on the boards of several early stage medical devices companies.

**Filippo Petti** joined the Company in September 2018 as the Chief Financial Officer and was then appointed as Chief Executive Officer on April 1st, 2019. He was appointed as a Director on November 28, 2019, and his appointment was confirmed at the shareholders meeting of March 23, 2020. Prior to joining the Company, Mr. Petti worked in healthcare investment banking both at Wells Fargo Securities and William Blair & Company. Prior to his roles in investment banking, Mr. Petti spent several years in equity research covering U.S. biotechnology companies both at William Blair & Company and Wedbush Securities. He began his career as a research scientist at OSI Pharmaceuticals, Inc. focused on drug discovery and translational research, and later transitioning into corporate development with the company. Mr. Petti holds a Master of Business Administration from Cornell University, a Master of Science from St. John's University and a Bachelor of Science from Syracuse University.

Serge Goblet has served as a member of the Board of Directors of the Company since 2008. He holds a Master Degree in Business and Consular Sciences from ICHEC, Belgium and has many years of

international experience as director in Belgian and foreign companies. He is the managing director of TOLEFI SA, a Belgian holding company and holds director mandates in subsidiaries of TOLEFI. Mr. Goblet also holds director mandates in the following companies: SG Holding SA, Essege SA, Le Haras des Isas SA, Green Holding SA, Carbobois SA, Green Real Estate SA, BSM Immo SA, Bioway Holding SA, Tolefi France SA, Ligne Plus SA, Ligne Plus Combustible SA, Bioway SA, Tecnoair System SA and Uton Ltd.

Chris Buyse has served as a member of the Board of Directors of the Company since 2008. He brings more than 30 years of international financial expertise and experience in introducing best financial management practices. He is currently Managing Director of FUND+, a fund that invests in innovative Belgian Life Sciences companies, Between August 2006 and June 2014, Mr. Buyse served as the Chief Financial Officer and board member of ThromboGenics NV, a leading biotech company that is listed on NYSE Euronext Brussels. Before joining ThromboGenics, he was the Chief Financial Officer of the Belgian biotech company CropDesign, where he coordinated the acquisition by BASF in July 2006. Prior to joining CropDesign NV he was financial manager of WorldCom/MCI Belux, a European subsidiary of one of the world's largest telecommunication companies and he was also the Chief Financial Officer and interim Chief Executive Officer of Keyware Technologies. Mr. Buyse holds a Master's Degree in applied economic sciences from the University of Antwerp and a Master of Business Association from Vlerick School of Management in Gent. He currently serves, in his own name or as permanent representative of a management company, as member of the board of directors of the following publicly and privately held companies: Iteos SA, Bioxodes SA, Bio Incubator NV, Immo David NV, Pinnacle Investments SA, CreaBuild NV, Sofia BVBA, Pienter-Jan BVBA, Life Sciences Research Partners VZW, Inventiva SA, The Francqui Foundation and EyeDPharma SA.

**Rudy Dekeyser** has served as a member of the Company's Board of Directors since 2008. Since 2012 Rudy has been partner at LSP Health Economics Fund, or LSP, one of Europe's leading venture capital firms in healthcare. Prior to joining LSP, Rudy has been co-managing director of VIB (Flanders Institute for Biotechnology), where he was also responsible for all activities related to the intellectual property portfolio, business development and the establishment of new companies. He holds non-executive director positions in Curetis AG, Sequana Medical AG, Lumeon Inc and Remynd NV, and held nonexecutive director positions in Devgen NV, CropDesign NV, Ablynx NV, Actogenix NV, Pronota NV, Bioincubator Leuven NV, Flandersbio VZW and Multiplicom NV. He is a co-founder of ASTP (the European associations of technology transfer managers) and Chairman of EMBLEM (EMBL's business arm). Rudy is member of the advisory boards of several foundations investing in life sciences research and innovation. He obtained a Ph.D. in molecular biology at the University Ghent.

**Hilde Windels** has served as a member of the Company's Board of Directors since August 2018. She is currently the Chief Executive Officer of the privately held diagnostics companies Mycartis NV and Antelope Dx BV and she is also member of their respective boards of directors. Ms. Windels brings 20

years of experience in biotech with a track record of business and corporate strategy, building and structuring organizations, private fundraising, mergers and acquisitions and public capital markets. Ms. Windels has worked as Chief Financial Officer for several biotech companies, amongst those Belgium based molecular Dx company Biocartis where she started as Chief Financial Officer CFO in 2011. She transitioned to the co-Chief Executive Officer role in 2015 and became Chief Executive Officer in 2017. Later that year, she also joined MyCartis NV as Chief Executive Officer. Ms. Windels is member of the boards of Erytech, MdxHealth and VIB. She holds a Master's Degrees in Economics (Commercial Engineer) from the University of Leuven (Belgium).

Dr. Margo Roberts, Ph.D., has more than three decades of biomedical research experience in both biotechnology and academia. Dr Roberts is currently Chief Scientist Officer at Lyell Immunotherapy. She serves also on the board of directors of Unity Biotechnology, a United States public company focused on developing medicines that slow or reverse age-associated diseases, and on the board of directors of InsTIL Bio, a United States start-up company focused on developing Timor infiltrating lymphocyte (TIL) - based therapies for the treatment of cancer. Until July 2018, Dr. Roberts served as Senior Vice President of Discovery Research at Kite Pharma focusing on the development of next generation therapeutic approaches, including heading up Kite's universal allogeneic T-cell programs. Prior that, in 2013, she was Chief Scientific Officer at Kite Pharma Inc., where she built a talented research organization that played an instrumental role in the successful development of Yescarta®, and the clinical advancement of additional CAR/TCR-engineered T-cell therapies. Prior to her tenure at Kite Pharma, Dr. Roberts was Principal Scientist and Director of Immune and Cell Therapy at Cell Genesys, Inc., where she led the development and application of CAR technology to T-cells and stem cells, culminating in the very first CAR T-cell trial initiated in 1994. Dr. Roberts was also an associate professor at the University of Virginia, has authored over 30 scientific publications, and is the inventor on 13 issued US patents and three published US patent applications related to CAR technology and tumor vaccine therapies. Dr. Roberts received both her Bachelor of Science degree with honors and her Ph.D. degree from the University of Leeds in England.

**Dr Maria Koehler, Ph.D.,** has served as a member of the Company's Board of Directors since March 2020. From September 2017 until April 2019, Dr. Koehler served as the Chief Medical Officer of a Bicycle Therapeutics plc, a biotechnology company. From March 2009 until September 2017, she was the Vice President of Strategy and Innovation for the Oncology Unit at Pfizer Inc, a pharmaceutical company. Prior to that, Dr. Koehler was a Senior Medical Director for oncology research and development at AstraZeneca plc. Dr. Koehler has also served as the Clinical Director of Bone Marrow Transplantation at University Hospital in Pittsburgh and the Director of the Bone Marrow Transplant Program and Associate Professor at St. Christopher's Hospital in Philadelphia. Dr. Koehler is a board-certified hematology/oncology physician. Dr. Koehler received her M.D. and Ph.D. from Silesian School of Medicine in Katowice, Poland.

**Dominic Piscitelli** brings more than 20 years of industry experience, including debt and equity financings, in-licensing transactions, acquisitions, marketing partnerships and commercial product launches (XTANDI® and Tarceva®). Since September 2019 Dominic has served as the Chief Financial Officer of ORIC Pharmaceuticals, a private biotech company. Prior to joining ORIC, Mr. Piscitelli was CFO of AnaptysBio, a Nasdaq-listed biotechnology company, where he helped raise over \$500 million in an IPO and follow-on financings. From 2012 until 2017, Mr. Piscitelli was Vice President of Finance, Strategy and Investor Relations at Medivation and played a key role in its acquisition by Pfizer. Previously, he served as Senior Director of Collaborations and Operations Finance at Astellas Pharma. Prior to that, Mr. Piscitelli served in various roles of increasing responsibility culminating as the Vice President, Treasury & Management Finance at OSI Pharmaceuticals, and played a significant role in their acquisition by Astellas. Mr. Piscitelli began his career with KPMG and is a certified public accountant. He earned a bachelor's degree in accounting and an MBA from Hofstra University (New York).

As of the date of this registration document, the directors have been holding the following companies mandates over the past five years:

Name of the company	Starting year of mandate	Current	Expired	Bankrupt or liquidated (Y/N)
Board Members				
MICHEL LUSSIER				
Biological Manufacturing Services SA	2018	Yes	No	No
iSTAR Medical	2014	Yes	No	No
Metronom Health Inc	2014	Yes	No	No
Metronom Health Europe SPRL	2017	Yes	No	No
Medpole SA	2002	Yes	No	No
MEL Management	2017	Yes	No	No
RUDY DEKEYSER				
Curetis AG	2014	Yes	No	No
Sequana Medical AG	2014	Yes	No	No
Remynd NV	2010	Yes	No	No
EMBLEM GmbH	2008	Yes	No	No
Lumeon Inc.	2018	Yes	No	No
R.A.D. Lifes sciences BVBA	2013	Yes	No	No
CHRIS BUYSE				
Fund+ NV	2015	Yes	No	No
Iteos therapeutics SA	2008	Yes	No	No
Bone Therapeutics SA	2008		Expired in 2018	No

#### 5.2.2. Board mandates

Inventiva SA (Fr)	2016	Yes	No	No
CoBioRes NV	2014	Yes	No	No
Bioxodes SA	2011	Yes	No	No
Immo David NV	2005	Yes	No	No
CreaBuild NV	2006	Yes	No	No
Pinnacle Investments NV	2007	Yes	No	No
Keyware Technologies NV	2005		Expired in 2019	No
Bio Incubator NV	2008	Yes	No	No
Ogeda SA	2016		Expired in 2017	No
Sofia BVBA	1999	Yes	No	No
Pienter Jan BVBA	2010	Yes	No	No
EyeDPharma SA	2019	Yes	No	No
Life Sciences Research Partners VZW		Yes	No	No
The Francqui Foundation	2018	Yes	No	No
HILDE WINDELS				
MDx Health NV	2017	Yes	No	No
Mycartis NV	2017	Yes	No	No
Biocartis Group	2018	Yes	No	No
Erytech SA	2014	Yes	No	No
VIB	2013	Yes	No	No
BVBA Hilde Windels	2001	Yes	No	No
Ablynx NV	2017		Expired in 2018	No
MARGO ROBERTS				
Unity Biotechnology	2018	Yes	No	No
InsTIL Bio	2018	Yes	No	No
SERGE GOBLET			No	
Tolefi SA	2014	Yes	No	No
Essege SA	2014	Yes	No	No
SG Holding SA	2014	Yes	No	No
CarBoBois SA	2014	Yes	No	No
Green Holding SA	2014	Yes	No	No
Ligne Plus	2018	Yes	No	No
Tecno Air System	2015	Yes	No	No
Linea Plus SA	2012	Yes	No	No
Tolefi Wellington	2014	Yes	No	No
BioWay Holding	2014	Yes	No	No
Green Real Estate	2014	Yes	No	No
Le Haras des Isas	2014	Yes	No	No
BSM Immo	2016	Yes	No	No
Immobilière Levasseur	2017	Yes	No	No
Ligne Plus Combustible SA		Yes	No	No
Tolefi France SA		Yes	No	No

Bioway SA	Yes	No	No
Uton Ltd	Yes	No	No
MARIA KOEHLER			
Not applicable			
DOMINIC PISCITELLI			
Not applicable			
FILIPPO PETTI			
Not applicable			

#### 5.2.3. Director Independence

In application of the article 7:87 of the BCCA, a director of a listed company is considered as independent if he does not entertain with the Company or an important shareholder of the Company any relation the nature of which could put his independence at risk. If the director is a legal entity, the independence must be assessed both in the case of the legal entity and its permanent representative. In order to verify if a candidate director fulfils those conditions, the independence criteria of the article 3.5 of the BCG are applied and can be summarized as follows:

- the director has not been an executive member of the Board of Directors, or daily manager of the Company (or an affiliate of the Company, if any), during a term of three years prior to his or her election and does not possess any stock option of the Company related to that function;
- the director has not been a non-executive director for a cumulative period of more than 12 years;
- the director has not been a member of the managerial staff of the Company (or an affiliate of the Company, if any) during a term of three years prior to his or her election and does not possess any stock option of the Company related to that function;
- the director does not receive and has not received any remuneration or other significant financial advantage from the Company (or an affiliate of the Company, if any), other than the profit share ("tantièmes") and remuneration received in his or her capacity as a non-executive director or as a member of the supervisory body;
- the director does not own any corporate rights that represent 10% or more of the share capital or voting rights of the Company, Further, the director cannot be appointed by a shareholder who falls under the conditions set forth in this criterion;
- the director does not and, during the year preceding his appointment, did not, have a significant business relationship with the Company (or an affiliate of the Company, if any), either directly or as a partner, shareholder, member of the Board of Directors or member of the managerial staff of a company or of a person that maintains such a relationship;
- the director is not and has not been at any time during the past three years, a partner or an employee of its current or former statutory auditor or of a company or person affiliated therewith;

- the director is not an executive director of another company in which an executive director of the Company is a non-executive director or a member of the supervisory body, and has no other significant ties with executive directors of the Company through his or her involvement in other companies or bodies;
- the director's spouse, unmarried legal partner and relatives (via birth or marriage) up to the second degree do not act as a member of the Board of Directors, member of the management board ("directiecomité / comité de direction") (should such corporate body be created) or daily manager or member of the managerial staff in the Company (or an affiliate of the Company, if any), and do not meet one of the criteria set out above.

Chris Buyse and Rudy Dekeyser will lose their status as independent directors as of December 2020 and will be considered as non-executive directors as of that date. The Company will adjust the composition of the committees accordingly to comply with laws and regulations.

#### 5.2.4. Role of the Board in Risk Oversight

The Board of Directors is primarily responsible for the oversight of its risk management activities and has delegated to the Audit Committee the responsibility to assist its Board of Directors in this task. While its board oversees its risk management, its management is responsible for day-to-day risk management processes. Its Board of Directors expects its management to consider risk and risk management in each business decision, to proactively develop and monitor risk management strategies and processes for day-to-day activities and to effectively implement risk management strategies adopted by the Board of Directors. The Company believes this division of responsibilities is the most effective approach for addressing the risks the Company face.

#### 5.2.5. Committees within the Board of Directors

#### 5.2.5.1. <u>General</u>

Without prejudice to the role, responsibilities and functioning of the Executive Committee as set out below under section "Executive Committee", the Board of Directors may set up specialized committees to analyze specific issues and advise the Board of Directors on those issues. Such committees are advisory bodies only and the decision-making remains the collegiate responsibility of the Board of Directors. The Board of Directors determines the terms of reference of each committee with respect to the organization, procedures, policies and activities of the committee.

#### 5.2.5.2. Audit Committee

At the date of this Registration Document, the Audit Committee consists of 3 members: Chris Buyse (Chairman), Dominic Piscitelli and Hilde Windels.

The role of the Audit Committee is to ensure the effectiveness of the internal control and risk management systems, the internal audit (if any) and its effectiveness and the statutory audit of the annual

and consolidated accounts, and to review and monitor the independence of the external auditor, in particular regarding the provision of additional services to the Company. The Audit Committee reports regularly to the Board of Directors on the exercise of its functions. The Audit Committee informs the Board of Directors about all areas in which action or improvement is necessary in its opinion and produces recommendations concerning the necessary steps that need to be taken. The audit review and the reporting on that review cover the Company and its subsidiaries as a whole. The members of the Audit Committee are entitled to receive all information which they need to perform their function from the Board of Directors, Executive Committee and employees. Each member of the Audit Committee shall exercise this right in consultation with the Chairman of the Audit Committee.

The Audit Committee's duties and responsibilities include, among other things: the financial reporting, review of internal controls and risk management, and managing the internal and external audit process. These tasks are further described in the Audit Committee charter as set out in the Charter and in Article 7:99§4 of the BCCA.

Chris Buyse and Hilde Windels have been identified by the Company's Board of Directors as having the necessary expertise in accounting and audit matters to serve as experts on the Audit Committee.

The Audit Committee holds a minimum of four meetings per year.

#### 5.2.5.3. Nomination and Remuneration Committee

As of the date of this Registration Document, the Nomination and Remuneration Committee is composed of three members: Michel Lussier (Chairman), Chris Buyse and R.A.D. Lifesciences BV represented by Rudy Dekeyser.

The Nomination and Remuneration Committee consists of not less than three directors, or such greater number as determined by the Board of Directors at any time. All members must be non-executive directors and at least a majority of its members must be independent in accordance with Article 7:87 of the BCCA. The Company's Board of Directors has determined that a majority of the members of the Nomination and Remuneration Committee are independent in accordance with Article 7:87 of the BCCA. Chris Buyse and Rudy Dekeyser will lose their status as independent directors as of December 2020 and will be considered as non-executive directors as of that date. The Company will adjust the composition of the committees accordingly to comply with laws and regulations.

The Nomination and Remuneration Committee must have the necessary expertise as regards the remuneration policy, and this condition is fulfilled if at least one member has had a higher education and has had at least three years of experience in personnel management or in the field of remunerating directors and managers. As of the date of this Registration Document, Michel Lussier (Chairman), Chris Buyse and Rudy Dekeyser satisfy this requirement.

The CEO has the right to attend the meetings of the Nomination and Remuneration Committee in an advisory and non-voting capacity on matters other than those concerning himself. The Nomination and

Remuneration Committee will elect a chairman from amongst its members. The Chairman of the Nomination and Remuneration Committee is actually Michel Lussier.

The role of the Nomination and Remuneration Committee is to assist the Board of Directors in all matters:

- relating to the selection and recommendation of qualified candidates for membership of the Board of Directors;
- relating to the nomination of the CEO;
- relating to the nomination of the members of the Executive Committee, other than the CEO, upon proposal by the CEO;
- relating to the remuneration of independent directors;
- relating to the remuneration of the CEO;
- relating to the remuneration of the members of the Executive Committee, other than the CEO, upon proposal by the CEO;
- on which the Board of Directors or the Chairman of the Board of Directors requests the Nomination and Remuneration Committee's advice.

Additionally, with regard to matters relating to remuneration, except for those areas that are reserved by law to the Board of Directors, the Nomination and Remuneration Committee will at least have the following tasks:

- preparing the remuneration report (which is to be included in the Board of Director's corporate governance statement); and
- explaining its remuneration report at the Annual General Shareholders Meeting.

It will report to the Board of Directors on the performance of these tasks on a regular basis. These tasks are further described in the terms of reference of the Nomination and Remuneration Committee as set out in the Charter. The Nomination and Remuneration Committee will meet at least twice per year, and whenever it deems it necessary to carry out its duties.

#### 5.2.5.4. <u>Strategy Committee</u>

The Strategy Committee was created by the Board of Directors on April 1<sup>st</sup>, 2019 with the objective to help the Executive Committee along the strategic cycle and to facilitate the discussion on the strategy of the Company with the Board of Directors.

The Committee was composed of LSS Consulting SRL, represented by Christian Homsy (Chairman), Rudy Dekeyser and Margo Roberts.

The Committee held several informal meetings but was dissolved by a decision of the Board of Directors on November 28, 2019. Further to the departure of Christian Homsy the Board of Directors decided that the Strategy Committee was no longer needed and the strategy could be discussed at the level of the Board of Directors.

#### 5.2.5.5. Meetings of the Board and the committees

In 2019, the Board held 4 in-person meetings and 5 meetings by telephone conference.

	2019								
Board Members	17Ja n	28 Marc h	15 May	26 June	9 July	22 Aug	10 Oct	28 Nov	17 Dec
M. Lussier	Prese nt	Prese nt	Present	Present	Prese nt	Prese nt	Prese nt	Prese nt	Prese nt
LSS Consulting SRL <sup>(1)</sup>	Prese nt	Prese nt	Present	Present	Prese nt	Prese nt	Prese nt	N/A	N/A
S. Goblet	Abse nt	Prese nt	Represent ed	Represent ed	Prese nt	Prese nt	Prese nt	Prese nt	Prese nt
D. Roychowdh ury <sup>(2)</sup>	Abse nt	Prese nt	N/A	N/A	N/A	N/A	N/A	N/A	N/A
R. Dekeyser	Prese nt	Prese nt	Present	Represent ed	Prese nt	Prese nt	Prese nt	Prese nt	Prese nt
H. Windels	Abse nt	Prese nt	Present	Present	Prese nt	Prese nt	Prese nt	Prese nt	Prese nt
C. Buyse	Prese nt	Prese nt	Present	Present	Abse nt	Prese nt	Prese nt	Prese nt	Prese nt
M. Roberts	Abse nt	Prese nt	Present	Represent ed	Abse nt	Prese nt	Prese nt	Prese nt	Abse nt
Filippo Petti (3)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Prese nt	Prese nt

**Board and committees – Dates and Attendance** 

(1) LSS Consulting SRL resigned from the Board of Directors on November 25, 2019.

(2) The mandate of D. Roychowdhury has expired on May 6, 2019 and was not renewed.

(3) Filippo Petti has been coopted as member of the Board of Directors on November 28, 2019.

In addition, three notarized meetings of the Board of Directors took place on July 16, September 11 and October 24, 2019, in relation to a capital increase or the issuance of warrants:

Describert		2019	
<b>Board members</b>	16 July	11 September	24 October
M. Lussier	Represented	Present	Represented

LSS Consulting SRL	Present	Represented	Represented
S. Goblet	Represented	Represented	Represented
R . Dekeyser	Represented	Represented	Present
H. Windels	Represented	Present	Represented
C. Buyse	Present	Represented	Present
M. Roberts	Represented	Represented	Represented

						2019					
Remuneration Committee	15- 16 Jan	30 Jan	6 Mar	14 Mar	22 Mar	26 Mar	11 Apr	14 May	13 Jun	4 Nov	25 Nov
M. Lussier	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres
WI. LUSSIE	ent	ent	ent	ent	ent	ent	ent	ent	ent	ent	ent
C During	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres
C. Buyse	ent	ent	ent	ent	ent	ent	ent	ent	ent	ent	ent
	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres
R. Dekeyser	ent	ent	ent	ent	ent	ent	ent	ent	ent	ent	ent
LSS Consulting	Invit	Invit	Invit	Invit	Invit	Invit	Pres	Pres	Pres	Pres	NT/A
SRL	ed	ed	ed	ed	ed	ed	ent	ent	ent	ent	N/A

		2	019	
Audit Committee	28 March	21 August	29 November	17 December
C. Buyse	Present	Present	Present	Present
R. Dekeyser	Present	Present	Present	Present
H. Windels	Present	Present	Absent	Present
F. Petti	Invited	Invited	Invited	Invited

#### **5.3. EXECUTIVE COMMITTEE**

The Board of Directors has established an Executive Committee. The terms of service of the Executive Committee have been determined by the Board of Directors and are set out in the Company's Corporate Governance Charter, or the Company's Charter. A copy of this Charter is available on the Company's website at https://www.celyad.com/en/investors/corporate-governance. The Company does not incorporate the information contained on, or accessible through, its corporate website into this Report, and you should not consider it a part of this Report.

The Executive Committee consists of the "Chief Executive Officer", or CEO (who is the chairman of the Executive Committee), the "Chief Financial Officer", or CFO, currently Filippo Petti ad interim, the

"Chief Legal Officer" and the "Vice President Clinical Development and Medical Affairs", the "Chief Scientific Officer", the Vice President Human Resources and the "Chief Business Development Officer".

The Executive Committee discusses and consults with the Board of Directors and advises the Board of Directors on the day-to-day management of the Company in accordance with the Company's values, strategy, general policy and budget, as determined by the Board of Directors.

Each member of the Executive Committee has been made individually responsible for certain aspects of the day-to-day management of the Company and its business (in the case of the CEO, by way of delegation by the Board of Directors; in the case of the other member of the Executive Committee, by way of delegation by the CEO). The further tasks for which the Executive Committee is responsible are described in greater detail in the sections referencing the Executive Committee, as set out in the Company's Charter.

The members of the Executive Committee are appointed and may be dismissed by the Board of Directors at any time. The Board of Directors appoints them following the recommendation of the Nomination and Remuneration Committee, which shall also assist the Board of Directors on the remuneration policy of the members of the Executive Committee, and their individual remunerations.

The remuneration, duration and conditions of dismissal of Executive Committee members is governed by the contract entered into between the Company and each member of the Executive Committee with respect to their function within the Company.

The remuneration policy of the executive managers describes the various elements of their remuneration and establishes an appropriate balance between the fixed portion and the variable portion and between cash and differed remuneration.

The variable portion of the remuneration is structured in order to be linked to the individual and company performances.

The stock options (warrants) are not granted in an indefinite manner and cannot be exercised fewer than three years after the grant.

In principle, the Executive Committee meets every month. Additional meetings may be convened at any time by the Chairman of the Executive Committee or at the request of two of its members. The Executive Committee will constitute a quorum when all members have been invited and the majority of the members are present or represented at the meeting. Absent members may grant a power of attorney to another member of the Executive Committee. Members may attend the meeting physically or by telephone or video conference. The absent members must be notified of the discussions in their absence by the Chairman (or the Company Secretary, if the Executive Committee has appointed a Company Secretary from among its members).

The members of the Executive Committee must provide the Board of Directors with information in a timely manner, if possible in writing, on all facts and developments concerning the Company that the Board of Directors may need in order to function as required and to properly carry out its duties. The CEO (or, in the event that the CEO is not able to attend the Board of Directors' meeting, the CFO or, in the event that the CFO is not able to attend the Board of Directors' meeting, another representative of the Executive Committee) must report at every ordinary meeting of the Board of Directors on the material deliberations of the previous meeting(s) of the Executive Committee.

Year Name Function of birth Chief Executive Officer and Chief 1976 Filippo Petti **Financial Officer** NandaDevi SRL, represented by Philippe Chief Legal Officer 1970 Dechamps MC Consult, represented by Philippe Vice President of Human Resources 1966 Nobels ImXense SRL, represented by Frederic Vice President Clinical Development & 1964 Lehmann Medical Affairs Chief Business Development Officer 1958 Stephen Rubino David Gilham Chief Scientific Officer 1965

The following table sets forth the members of the Executive Committee as of the date of this Registration Document.

The following paragraphs contain brief biographies of each of the current members of the Executive Committee or in case of legal entities being a member of the Executive Committee or key manager, their permanent representatives.

Filippo Petti, CEO and CFO ad interim- reference is made to section "Composition of the Board of Directors".

**Philippe Dechamps (representative of NandaDevi SRL),** has served as Chief Legal Officer since September 2016. Philippe started his legal career as an associate in Brussels with the law firm Linklaters De Bandt from 1994 to 1998. He left private practice in 1998 and until 2003, he served as an in-house counsel at Solvay Group to assist the company in its turnaround through several M&A operations in Europe, India and Far-East Asia. In 2003, he took over the position of Legal Director at Guidant, the United States company formerly active in the medical devices business before its acquisition by Boston

Scientific and Abbott Laboratories in 2005. Within Abbott, Philippe took over responsibility for the legal affairs of Abbott Vascular International outside of the United States. In 2008, Philippe joined Delhaize Group taking responsibility for the legal and government affairs in Europe and Asia, before becoming Group General Counsel and Secretary to the Board of Directors in 2015. In this position, he piloted the legal strategy to merge Delhaize Group with Royal Ahold in July 2016. Since December 2018, Philippe is also member of the Board of Directors of Petserco SA, the holding company of the Tom&Co group. Philippe earned law degrees from the Université Catholique de Louvain (UCL) and Vrije Universiteit Brussel (VUB), and a Master of Law (LL.M) from Harvard University.

**Philippe Nobels (representative of MC Consult SRL)** has served as Vice President of Human Resources since October 2016. He started his career at Price Waterhouse (now PricewaterhouseCoopers) as auditor in 1989. He also went in rotational assignment in Congo during 2 years on consulting missions for the World Bank. In 1995, he joined Fourcroy as plant controller. Then, he joined Dow Corning in 1997 where he held different positions in Finance and Human Resources. He led the HR operations in Europe, became the HR manager for Dow Corning in Belgium, and HR Business Partner for the sales and marketing functions globally. As a member of the sales and marketing Leadership teams, he contributed to Dow Corning's major transformation initiatives to increase organizational effectiveness, employees' engagement & performance as well as Business results. Mr. Nobels holds a Master's Degree in Economics from the University of Namur.

**Frédéric Lehmann (representative of ImXense SRL),** has served as the Vice President Clinical Development & Medical Affairs since July 2016 and prior to that he has served as the Vice President Immuno-Oncology since September 2015. Dr. Lehmann is a physician by training, specialized in hematology and oncology. Dr. Lehmann has extensive experience in oncology drug development spanning early to late phase, including clinical trial design, translational research, regulatory interactions, and clinical risk management. He started his academic career at the Ludwig Institute for Cancer Research in Brussels, followed by a position at the Institute Jules Bordet. He then moved to the European Organization for Research and Treatment of Cancer (EORTC) as Medical Advisor. Dr. Lehmann began his corporate career at GlaxoSmithKline, where he led the early worldwide clinical development program for the Company's cancer vaccines and went on to lead the research and development incubator for cancer immunotherapeutics.

**David Gilham**, has served as Vice President Research and Development since September 2016 and as Chief Scientific Officer since May 18, 2020. Prior to joining the Company, Mr. Gillham was a Reader and Group Leader within the Manchester Cancer Research Centre at the University of Manchester, United Kingdom leading a research group of 15 scientists in the area of cellular immunotherapy. Mr. Gilham obtained his Ph.D from the University of Dundee in 1998 in Molecular Pharmacology under the supervision of Professor Roland Wolf, OBE. After a short post-doctoral position at the University of Bristol, Mr. Gilham moved to the University of Manchester with Professor Robert Hawkins to establish translational research activity in the field of engineered cellular therapy. The group has carried out several clinical trials of CAR-T cells of which Mr. Gilham has been Lead scientific advisor and led

several European framework programs bringing together researchers from all over Europe (for example, the ATTACK and ATTRACT programs). In 2010, along with Professor Hawkins and other colleagues, Mr. Gilham co-founded Cellular Therapeutics, a cell production company based in Manchester, England. He has published more than 60 peer reviewed articles and further book chapters and reviews. He sits on many review boards and charity grant committees and consulted for several biotech's and pharma concerning immune cell therapies.

**Dr. Stephen Rubino, Ph.D.,** has served as the Company's Chief Business Officer since February 1<sup>st</sup>, 2020. Dr. Rubino brings over 30 years of pharmaceutical leadership experience to the role of Chief Business Officer, with emphasis in the areas of business development and licensing, new product development, commercial operations, pharmaceutical strategy and investor relations. Dr. Rubino currently serves as an independent board member of both ILKOS Therapeutics and Sermonix Pharmaceuticals. Dr. Rubino has also served Novartis Pharmaceuticals in a wide range of roles and therapeutic areas, the last of which was as Global Head of Business Development and New Product Marketing, responsible for developing and building the product pipeline for Novartis' Cell & Gene Therapies Unit. Prior to Novartis, Dr. Rubino worked for Schering–Plough (Merck) where his last role was head of the Global Solid Tumor Oncology & Autoimmune Business Unit responsible for the licensing and launch of Remicade, as well as the launch and commercialization of several global oncology brands. Dr. Rubino received his Ph.D. from Weill Cornell University (New York) and his Master of Business Association from Baruch University (New York).

	Starting year	Ongoing	Expired	Bankrupt or liquidated (Y/N)
FILIPPO PETTI Not applicable DAVID GILHAM Not applicable FREDERIC LEHMANN ImXsense SRL	2015	Yes	No	No
PHILIPPE NOBELS MC Consult SRL PHILIPPE DECHAMPS NandaDevi SRL Petserco SA STEPHEN RUBINO ILKOS Therapeutics Sermonix Pharmaceuticals	2016 2016 2018 2017 2019	Yes Yes Yes No Yes	No No No	No No No Yes No

The mandates of the members of the executive Committee are the followings:

# 5.4. CONFLICT OF INTEREST OF DIRECTORS AND MEMBERS OF THE EXECUTIVE TEAM AND TRANSACTIONS WITH AFFILIATED COMPANIES

#### 5.4.1. General

Each director and member of the Executive Committee is encouraged to arrange his or her personal and business affairs so as to avoid direct and indirect conflicts of interest with the Company. The Company's Charter contains specific procedures to deal with potential conflicts. To the best knowledge of the Company, no member of the Board of Directors or the executive Committee has been convicted in relation to fraudulent offences for at least the last five years. Furthermore, the Company is not aware of any official public incrimination and/or sanctions involving such persons by statutory or regulatory authorities (including designated professional bodies) nor any disqualification by a court from acting as members of the administrative, management or supervisory bodies of the Company nor from acting in the management or conduct of the affairs of any issuer for at least the previous five years.

#### 5.4.2. Conflicts of interest of directors

Article 7:96 of the BCCA provides for a special procedure within the Board of Directors in the event of a possible personal financial conflict of interest of one or more directors with one or more decisions or transactions to be adopted by the Board of Directors. In the event of a conflict of interest, the director concerned must inform his or her fellow directors of his or her conflict of interest before the Board of Directors deliberates and takes a decision in the matter concerned. Furthermore, the conflicted director may not participate in the deliberation and voting by the Board of Directors on the matter that gives rise to the potential conflict of interest. The minutes of the meeting of the Board of Directors must contain the relevant statements made by the conflicted director, as well as a description by the Board of Directors of the conflicting interests and the nature of the relevant decision or transaction to be adopted. The minutes must also contain a justification by the Board of Directors for the decision or transaction adopted, and a description of the financial consequences thereof for the Company. The relevant minutes must be included in the (statutory) annual report of the Board of Directors.

The Company must notify the Statutory Auditor of the conflict. The Statutory Auditor must describe in its statutory annual audit report the financial consequences of the decision or transaction that gave rise to the potential conflict.

This procedure does not apply to decisions or transactions in the ordinary course of business at customary market conditions.

#### 5.4.3. Existing conflicts of interest of members of the Board of Directors

Except as reported hereinafter, as far as the Company is aware, none of the directors have a conflict of interest within the meaning of Article 7:96 of the BCCA which has not been disclosed to the Board of

Directors. Other than potential conflicts arising in respect of compensation-related matters, the Company does not foresee any other potential conflicts of interest in the near future.

In 2019, certain members of the Board declared a conflict of interest. The following declaration were made in that respect:

"Excerpt from the minutes of the Board meeting of January 17, 2019":

The Article 523, paragraph 1, of the Belgian Company Code provides that "If a director has, directly or indirectly, a conflicting financial interest in a decision or operation to be decided by the Board of Directors, he has to inform the other directors before the deliberation of the Board of Directors. His declaration, including the reasons for his conflicting financial interest, must be recorded in the minutes of the board meeting that will take [...] the decision. The auditor must also be informed. (...) In listed companies, the concerned directors cannot deliberate nor vote on the concerned decisions".

The directors present in the meeting informed the other directors that they have a conflict of interest as they have a conflicting financial interest in the decision proposed at the present point of the agenda of this meeting of the Board of Directors relating to the allocation of warrants. As mentioned in the supporting documents, it is contemplated to allocate warrants to:

- Michel Lussier (10,000 warrants);
- Rudy Dekeyser (10,000 warrants);
- Debasish Roychowdhury (10,000 warrants);
- Chris Buyse (10,000 warrants);
- Hilde Windels (10,000 warrants);
- Margo Roberts (10,000 warrants);
- Serge Goblet (10,000 warrants);
- Christian Homsy (40,000 warrants).

Each warrant will give the right to its holder to acquire one new share of the Company. The exercise price will be equal to the average closing price of the share during a period of 30 days before the offer date or the price of the share on the last day before the offer date.

The Chairman thanks the directors for their declarations. These declarations will be communicated to the statutory auditor of the Company and inserted in the annual report 2019 in accordance with Article 523 of the Company Code. (...)

The Board then validly deliberated on this item of the agenda.

After deliberation, the Board unanimously decided to allocate an aggregate of 465,800 warrants, out of which 240,000 will be allocated to Board members and the Senior Leadership Team as follows (the Directors concerned by a conflict of interest abstained from voting on themselves):

- Michel Lussier (10,000 warrants);

- Rudy Dekeyser (10,000 warrants);
- Debasish Roychowdhury (10,000 warrants);
- Chris Buyse (10,000 warrants);
- Hilde Windels (10,000 warrants);
- Margo Roberts (10,000 warrants);
- Serge Goblet (10,000 warrants);
- Christian Homsy (40,000 warrants).

Finally, in so far as appropriate, the Board of Directors unanimously confirmed that the abovementioned allocations of warrants will take place under the terms and conditions of the template Warrants Plan 2018. (...).

#### "Excerpt from the minutes of the Board meeting of March 28, 2019":

Article 523, paragraph 1, of the Company Code provides that "If a director has, directly or indirectly, a conflicting financial interest in a decision or operation to be decided by the Board of Directors, he has to inform the other directors before the deliberation of the Board of Directors. His declaration, including the reasons for his conflicting financial interest, must be recorded in the minutes of the board meeting that will take [...] the decision. The auditor must also be informed. (...) In listed companies, the concerned directors cannot deliberate nor vote on the concerned decisions".

*Mr.* Roychowdhury informed the other directors that he is in a position of conflict of interest with respect to the decision proposed under point 2.2 of the agenda. It is proposed by the Nomination and Remuneration Committee to grant a forward vesting of his warrants to Mr. Roychowdhury further to the termination of his mandate as director. This forward vesting would not have direct financial impact on the Company.

The Chairman thanks Mr. Roychowdhury for his declaration, it will be mentioned in the management report and communicated to the Statutory Auditor of the Company in accordance with Article 523 of the Company Code.

LSS Consulting SRL, represented by Mr. Christian Homsy, informed the other directors that he is in a position of conflict of interests with respect to the decision proposed under point 2.2 of the agenda, relating to the terms and conditions of the termination of LSS Consulting SRL as CEO of the Company. It is proposed by the Nomination and Remuneration Committee to pay to LSS Consulting SRL a termination fee of EUR 300,000 (excluding VAT) and to conclude a 3-month consulting agreement against compensation of EUR 70,000 (excluding VAT).

The Chairman thanks LSS Consulting for his declaration, it will be mentioned in the management report and communicated to the Statutory Auditor of the Company in accordance with Article 523 of the Company Code.

(...)

*Mr.* Roychowdhury leaves the room. The Board expressly approves the waiver to the condition of presence imposed by the warrants plans of the Company in favor of Mr. Roychowdhury, meaning that Mr. Roychowdhury will be allowed to exercise all his warrants during the Exercise Periods provided by the plans, even if he stopped his professional activities in favor of the Company in May 2019 and even if all his warrants have not been vested. Mr. Roychowdhury comes back to the meeting.

(...)

*Mr.* Homsy leaves the room. (...) After discussion, the Committee recommended to approve the following terms and conditions to LSS Consulting's retirement as CEO of the Company:

- a) The Management Services Agreement between the Company and LSS Consulting SRL ("LSS") will terminate as of April 1st, 2019 and the Company will pay to LSS a termination compensation of 300.000 EUR (excluding VAT);
- b) The Company will sign with LSS a consultancy agreement as of April 1st, 2019 and for a period of 3 months, whereby LSS will provide services to assist the Company in its next fund raising and assist Mr. Petti in his transition as new CEO. The Company will pay 70.000 EUR (excluding VAT) to LSS in remuneration for those services;
- c) The Company will pay to LSS its annual group insurance of 26,000 EUR, its fees for services delivered until March 31, 2019; however, the Company will not pay to LSS any bonus for the year 2019;
- d) As of April 1st, LSS will be remunerated for his Board membership and will be appointed and remunerated as member of the Committee, and Chairman of the new Strategy Committee, all in accordance with the Company's remuneration policy;
- e) In recognition of the accomplishments of Mr. Homsy for the Company over the past 12 years, the Board will agree that the warrants accepted by Mr. Homsy in 2017 and 2019, but not yet vested, will not be forfeited and will vest and in accordance with the terms and conditions of the 2017 and 2019 plan;
- f) The Company on one hand, Mr. Homsy and LSS on the other hand, will waive any claim against one another; the Company will not impose any non-compete clause on LSS or Mr. Homsy.

The Board of Directors had a thorough discussion about those terms and conditions and deemed in the best interest of the Company to approve the recommendations of the Committee.

The Board decided also to appoint LSS as member of the Nomination & Remuneration Committee and to create a new Strategy Committee chaired by LSS. (...)

"Excerpt from the minutes of the Board meeting of October 10, 2019":

"The Board discussed the allocation of warrants to Board members:

- Michel Lussier (10,000 warrants);

- Hilde Windels (10,000 warrants);
- Margo Roberts (10,000 warrants);
- Serge Goblet (10,000 warrants);
- Christian Homsy (10,000 warrants);
- Chris Buyse (10,000 warrants);
- Rudy Dekeyser (10,000 warrants).

The warrants would be allocated under the Warrants Plan 2019. Each warrant will give the right to its owner to acquire one new share of the Company. The exercise price will be equal to the fair market value of the Company's shares at the time of the offer, this value corresponding to the closing price of the share on the day before the date of the offer.

The article 7:96 of the BCAC provides that "if a director has, directly or indirectly, a conflicting financial interest in a decision or operation to be decided by the Board of Directors, he has to inform the other directors before the deliberation of the Board of Directors. His declaration, including the reasons for his conflicting financial interest, must be recorded in the minutes of the board meeting that will take [...] the decision. The auditor must also be informed. The concerned directors cannot deliberate nor vote on the concerned decisions".

Michel Lussier informed the other directors that he has a conflicting financial interest in the decision proposed. This declaration will be communicated to the statutory auditor of the Company and inserted in the annual report 2019 in accordance with the article 7:96 of the BCAC. Michel Lussier left the meeting room and the Board unanimously approved the allocation of 10,000 warrants to Michel Lussier. Michel Lussier then came back in the meeting room.

Serge Goblet informed the other directors that he has a conflicting financial interest in the decision proposed. The Chairman thanked Serge Goblet for his declaration. This declaration will be communicated to the statutory auditor of the Company and inserted in the annual report 2019 in accordance with the article 7:96 of the BCAC. Serge Goblet left the meeting room and the Board unanimously approved the allocation of 10,000 warrants to Serge Goblet. Serge Goblet then came back in the meeting room.

Chris Buyse informed the other directors that he has a conflicting financial interest in the decision proposed. The Chairman thanked Chris Buyse for his declaration. This declaration will be communicated to the statutory auditor of the Company and inserted in the annual report 2019 in accordance with the article 7:96 of the BCAC. Chris Buyse left the meeting room and the Board unanimously approved the allocation of 10,000 warrants to Chris Buyse. Chris Buyse then came back in the meeting room.

Rudy Dekeyser informed the other directors that he has a conflicting financial interest in the decision proposed. The Chairman thanked Rudy Dekeyser for his declaration. This declaration will be communicated to the statutory auditor of the Company and inserted in the annual report 2019 in accordance with the article 7:96 of the BCAC. Rudy Dekeyser left the meeting room and the Board

unanimously approved the allocation of 10,000 warrants to Rudy Dekeyser. Rudy Dekeyser then came back in the meeting room.

Christian Homsy informed the other directors that he has a conflicting financial interest in the decision proposed. The Chairman thanked Christian Homsy for his declaration. This declaration will be communicated to the statutory auditor of the Company and inserted in the annual report 2019 in accordance with the article 7:96 of the BCAC. Christian Homsy left the meeting room and the Board unanimously approved the allocation of 10,000 warrants to Christian Homsy. Christian Homsy then came back in the meeting room.

Hilde Windels informed the other directors that she has a conflicting financial interest in the decision proposed. The Chairman thanked Hilde Windels for her declaration. This declaration will be communicated to the statutory auditor of the Company and inserted in the annual report 2019 in accordance with the article 7:96 of the BCAC. Hilde Windels left the meeting room and the Board unanimously approved the allocation of 10,000 warrants to Hilde Windels. Hilde Windels then came back in the meeting room.

Margo Roberts informed the other directors that she has a conflicting financial interest in the decision proposed. The Chairman thanked Margo Roberts for her declaration. This declaration will be communicated to the statutory auditor of the Company and inserted in the annual report 2019 in accordance with the article 7:96 of the BCAC. Margo Roberts left the meeting room and the Board unanimously approved the allocation of 10,000 warrants to Margo Roberts. Margo Roberts then came back in the meeting room."

#### 5.4.4. Related Party Transactions

Currently, no related party transaction involving the Company's Directors, or the members of the Executive Committee has been disclosed to the Company.

#### 5.4.5. Transactions with affiliates

Article 7:97 of the BCCA provides for a special procedure that applies to intra-group or related party transactions with affiliates. The procedure will apply to decisions or transactions between the Company and affiliates of the Company that are not a subsidiary of the Company. It will also apply to decisions or transactions between any of the Company's subsidiaries and such subsidiaries' affiliates that are not a subsidiary of the Company. This procedure was not applied by Celyad from January 1, 2019 until the date of this Registration Document.

Prior to any such decision or transaction, the Board of Directors of the Company must appoint a special committee consisting of three independent directors, assisted by one or more independent experts. This committee provides the Board of Directors with a written report giving the motives for the decision of the envisaged operation, addressing at least the following elements: the nature of the decision or the operation, a description and an estimation of the equity consequences, a description of the eventual other

consequences, the advantages and inconvenient resulting therefrom for the Company, as the case maybe. The committee puts the proposed decision or operation in the context of the strategy of the Company and determines if it causes any prejudice to the Company, if it is compensated by other elements of that strategy, or if it is manifestly abusive. The remarks of the expert are integrated in the opinion of the committee.

The Board of Directors must then take a decision, taking into account the opinion of the committee. Any deviation from the committee's advice must be explained. Directors who have a conflict of interest are not entitled to participate in the deliberation and vote. The committee's advice and the decision of the Board of Directors must be communicated to the Company's Statutory Auditor, who must render a separate opinion. The conclusion of the committee, an excerpt from the minutes of the Board of Directors and the opinion by the Statutory Auditor must be included in the (statutory) annual report of the Board of Directors.

The procedure does not apply to decisions or transactions in the ordinary course of business at customary market conditions, and transactions or decisions with a value of less than 1% of the consolidated net assets of the Company.

#### 5.4.6. Code of Business Conduct and Ethics

In 2015, the Company adopted a Code of Business Conduct and Ethics, or the Code of Conduct, that is applicable to all of its employees, members of its Executive Committee and directors. It has been updated on October 5, 2018. The Code of Conduct is on its website at <u>https://www.celyad.com/en/investors/corporate-governance</u>. The Audit Committee of its Board of Directors is responsible for overseeing the Code of Conduct and is required to approve any waivers of the Code of Conduct for employees, members of its Executive Committee and directors.

#### 5.4.7. Market abuse regulations

On June 17, 2013, the Board of the Company defined specific rules to prevent the illegal use of inside information by board members, shareholders, managers and employees or the appearance of such use ("the Market Abuse Policy"). The Market Abuse Policy has been amended by a resolution of the Board of Directors on December 7, 2017.

These provisions and their compliance are primarily intended to protect the market. To ensure that the law is respected and to uphold the reputation of the Company, it is therefore necessary to take a number of preventive measures in the form of a code of conduct.

The Policy applies to all Insiders. An Insider can be given access to inside information within the scope of the normal performance of his or her duties. The insider has the strict obligation to treat this information confidentially and is not allowed to trade financial instruments of the Company to which this inside information relates.

In accordance with art 25bis §1 of the law of August 2, 2002 and the EU Regulation 596/2014 of April 16, 2014 on market abuse (the "MAR"), the Company has established a list of persons in the Company who, based on an employment or service agreement, have contracted with the Company and have during the course of their duties access to inside information directly or indirectly. This list is updated regularly and remains at the disposal of the FSMA for a period of 5 years.

#### 5.5. CORPORATE GOVERNANCE CODE

The Company's Board of Directors complies with the principles of the CGC. However, the Company deviates from the following principles:

- Remuneration in company's shares (principle 7.6): given the legal constraints of Belgian laws, the non-executive directors do not receive a portion of their remuneration in company's shares;
- No grant of stock options (principle 7.6): given the technical impossibility to grant company's shares to non-executive directors, those directors can receive subscription rights (warrants). Those grants can attract profiles with high potential, incentivize the beneficiaries in the development of the Company, and play a role as retention tool of the teams;
- Absence of minimum detention of shares (principle 7.9): at the date of this Report, the Company has not fixed any minimum threshold for the detention of shares by the executive managers. However, the executive managers have subscription rights (warrants) on the Company's shares as described in the remuneration report 2019.

The Company has not adopted a diversity policy. The talents market is particularly tense and dynamics in the biopharmaceutical industry and developing a diversity policy adjusted to this fast-changing environment was not deemed to be the best tool to meet the Company's challenges in human resources. Over the past years, the Company has successfully achieved a broad degree of diversity from a gender, citizenship, expertise and educational background perspective at the Company's Board of Directors, Executive Committee, Management and staff levels. As such, the Company has attracted talents from various countries which reflects the Company's international footprint to support the Company's strategy in research and development, clinical and medical affairs, manufacturing, business and finance.

At the Board of Directors, the Company complies with Belgian law on gender with at least one third of the members who are from a different gender. One Board member is Canadian, three are Americans, and three are Belgians.

At the Executive Committee, two members are Americans, one is English, and 3 are from Belgium. At that level, an effort has been made to improve gender diversity. In the course of 2019, one female member was hired who left the Company on October 17, 2019. The Company will pursue its efforts to increase the female presence at the Executive Committee.

Regarding the Management team who is composed of 16 members, the Company counts 43.7% (7) of female and 56.3% (9) of male. Those managers or directors have different nationalities (from Belgium, Greece, Italy, Mexico, France and the US).

Regarding the employees not included above, the Company records 60% female employees and 40% male employees.

In accordance with the CGC, the Board of Directors of the Company will review its Charter from time to time and make such changes as it deems necessary and appropriate. The Charter, together with the Company's articles of association, is available on the Company's website (<u>www.celyad.com</u>) and can be obtained free of charge at the registered office of the Company. The Charter has been updated by resolution of the Board of Directors on November 28, 2019.

## **6. MAJOR SHAREHOLDERS**

The information in the table below is based on information known to the Company or ascertained by the Company from public filings made by the shareholders as of the date of this Registration Document, updated, as the case may be. Except as otherwise indicated in the table below, addresses of the directors, members of the executive management team and named beneficial owners are in care of Rue Edouard Belin 2, 1435 Mont-Saint-Guibert, Belgium.

Except as otherwise indicated, all of the shares reflected in the table are ordinary shares and all persons listed below have sole voting and investment power with respect to the shares beneficially owned by them, subject to applicable community property laws. The information is not necessarily indicative of beneficial ownership for any other purpose. On May 23, 2019 the Shareholders' Meeting decided to voluntarily "opt in" and submit the Company to the new Belgian Code of Companies and Associations. Furthermore, the Shareholders' Meeting decided to activate the possibility offered by Article 7:53 of the code of companies and associations and approved the grant of double voting right to the registered shares held by a shareholder in a registered form for more than two years. At the date of this registration document, the shares held by the persons listed below do not have double voting rights.

In computing the number of ordinary shares beneficially owned by a person and the percentage ownership of that person, the Company deemed outstanding ordinary shares subject to warrants held by that person that are immediately exercisable. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person. The information in the table below is based on information known to the Company or ascertained by the Company from public filings made by the shareholders. The denominator considered in computing the percentage of ownership of the persons within the table below has been taken into account as of the date of this Registration Document.

NAME OF BENEFICIAL OWNER	SHARES BENEFICIALLY OWNED		
	Number	Percentage	
TOLEFI SA, represented by Serge Goblet	2,295,701	16.47%	
Victory Capital Management Inc	992,858	7.12%	
Directors and Members of the Executive Management Team Michel Lussier <sup>[1]</sup>		1,12%	
	156,550	1.12/0	
Serge Goblet	56,180	0.40%	

SHARES BENEFICIALLY OWNED

Number

Percentage

[1] Of which 145,150 are ordinary shares and 11,400 are ADSs.

Each of its shareholders is entitled to one vote per ordinary share. None of the holders of its shares have different voting rights from other holders of shares.

The Company is not aware of any arrangement that may, at a subsequent date, result in a change of control of the Company.

At the date of this Registration Document the Company is not controlled under articles 1:14 and following of the Companies and associations Code.

### 7. SUMMARY OF INFORMATION DISCLOSED UNDER REGULATION (EU) NO 596-2014

The following information is a summary of the inside information that has been disclosed under the Market Abuse Regulation over the last 12 months and is relevant as at the date of the Registration Document:

#### Cash position;

On 16 September 2019, Celyad announced that is has successfully raised USD 20 million in a global offering on both US and European market remunerated by the issuance of 2 million new shares

**8. DEFINITION AND GLOSSARY** 

### Glossary

ADS	American Depositary Shares
Allogeneic cells	Cells of a type that is from the same specicies but genetically distinct – from a different donor as the recipient.
AML	Acute Myeloid Leukemia
Acute Myocardial Infarction (AMI)	Commonly known as a heart attack, is the interruption of blood supply to part of the heart, causing some heart cells to die. This is most commonly due to occlusion (blockage) of a coronary artery following the rupture of an atherosclerotic plaque, which is an unstable collection of lipids (like cholesterol) and white blood cells (especially macrophages) in the wall of an artery. The resulting ischemia (restriction in blood supply) and oxygen shortage, if left untreated for a sufficient period of time, can cause damage or death (infarction) of heart muscle tissue (myocardium).
Articles of Association	The articles of association of the Company
Autologous cells	Cells that are from the same donor as the recipient.
BCCA	New Belgian Code of Companies and Associations adopted by the Belgian Parliament on 28 February 2019
BLA	<i>Biologics Licence Application</i> . A BLA is a request for permission to introduce, or deliver for introduction, a biologic product into interstate commerce (21 CFR 601.2). The BLA is regulated under 21 CFR 600 – 680.
<b>Board of Directors</b>	The board of directors of the Company
CAR-T cell product	Chimeric antigen receptors are engineered receptors that combine a new specificity with an immune T-cell to target cancer cells.
CAR-T NKG2D	Chimeric antigen receptors using NKG2D as target
Cardiac Progenitor Cells (CPCs)	A cardioprogenitor cell is a cellular phenotype with the capacity to yield myocardial tissue and blood vessels upon differentiation.
Cardiac Resynchronisation Therapy (CRT)	A CRT is a type of pacemaker (a medical device which uses electrical impulses, delivered by electrodes contacting the heart muscles, to regulate the beating of the heart) that can pace both the septal and lateral walls of the left ventricle.
Cardiac Stem Cells (CSCs)	Cells that can give rise to all of the major cell types in the human heart.
Cardiogenic cocktail	A mixture of growth factors, cytokines and small molecules that have the capacity to drive Cardiopoiesis.

Cardiogenesis	Development of the heart in the embryo.
Cardiopoiesis	Process to drives stem cells towards the cardiac lineage
Cardiopoietic Cells (CPCs)	Cells that are precursors of fully differentiated cardiac muscle cells. In the lab, CPCs can be generated from stem cells by culture in the presence of a specific cocktail of cardiotrophic factors discovered at the Mayo Clinic.
Cardiovascular Disease (CVD)	A group of disorders of the heart and blood vessels which includes: <ul> <li>Coronary heart disease</li> <li>Cerebrovascular disease</li> <li>Peripheral arterial disease</li> <li>Rheumatic heart disease</li> <li>Congenital heart disease</li> <li>Deep vein thrombosis and pulmonary embolism</li> </ul>
Charter	The corporate governance charter of the Company
СМО	Contract Manufacturing Organization
C-Cure	Celyad' proprietary stem cell therapy for the treatment of heart failure
CM-CS1 Trial	A First-in-Human Phase I Trial of NKG2D Chimeric Antigen Receptor- T Cells in AML/MDS and Multiple Myeloma
Code on Corporate Governance	The Belgian Code on corporate
Company	Celyad Oncology SA
Consistency lots	Lots produced to document evidence that the process, operated within established parameters, can perform effectively and reproducibly to manufacture a product meeting its predetermined specifications and quality attributes.
Coronary Artery Disease (CAD) - also known as Coronary Heart Disease (CHD)	A condition in which atherosclerotic plaque builds up inside the coronary arteries. Plaque is made up of fat, cholesterol, calcium and other substances found in the blood. This can cause angina (chest pain or discomfort) or a heart attack (when the blood flow to an area of the heart muscle is completely blocked, preventing oxygen-rich blood from reaching that area and causing it to die).
CR	Complete response. See RECIST criteria
CRC	Colorectal Cancer
CRO	Contract Research Organization
CRS	Cytokine Release Syndrome

Cryopreservation	Cryopreservation is a process where cells or whole tissues are preserved by cooling to low sub-zero temperatures. At these low temperatures, any biological activity, including the biochemical reactions that would lead to cell death, is effectively stopped.
EMA	European Medicines Agency
Embryonic Stem Cells (ESCs)	Stem cells derived from the undifferentiated inner mass cells of a human embryo. Embryonic stem cells are pluripotent, meaning they are able to grow (i.e. differentiate) into all derivatives of the three primary germ layers: ectoderm, endoderm and mesoderm.
Ex vivo (experiments)	Experimentation done in or on tissue outside the organism with minimal alteration of natural conditions;
FDA	US Food and Drug Administration
Formulation	Formulation is the vehicle and the form in which an active compound is delivered in the body.
FSMA	The Belgian Financial Services and Markets Authority
Good Clinical Practices (GCP)	Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well- being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.
Good Manufacturing Practices (GMP)	GMP is part of a quality system covering the manufacture and testing of active pharmaceutical products. GMPs are guidelines that outline the aspects of production and testing that can impact the quality of a product.
Group	Celyad and its subsidiaries
Heart Failure (HF)	Heart Failure is a condition in which the heart has been damaged and cannot pump enough blood to meet the body's metabolic needs. HF can be of ischemic or non-ischemic origin: - Ischemic Origin (Coronary Artery Disease) - Non-ischemic Origin - Hypertension: high blood pressure; - Other conditions such as heart valve disease, congenital heart defect, endocarditis (infection of the heart valves) and/or myocarditis (infection of the heart muscle).
	The failing heart keeps working but not as efficiently as it should. HF patients cannot exercise because they become short of breath and tired.

	In the most severe forms, even slight exercises like walking a short distance are impossible.
Human MSCs	MSCs (see definition below) of human origin.
IFRS	International Financial Reporting Standards
Immunodeficient rodents	A lineage of rodents (like rats or mice) that are genetically modified to omit some components of the immune system (the system that defends against disease and foreign agents).
Implantable Cardioverter Defibrillator (ICD)	Small battery-powered electrical impulse generator which is implanted in patients who are at risk of sudden cardiac death due to ventricular fibrillation and ventricular tachycardia.
IND	Investigational New Drug
IND filing	First step in the application process to get a new drug approved
Induced Pluripotent Stems Cells (IPS)	IPSs are pluripotent cells derived from differentiated cells by forcing the expression of key pluripotency genes.
Ischemic HF	Ischemic Heart Failure
IRB	Institutional Review Board. An IRB/IEC reviews the appropriateness of the clinical trial protocol as well as the risks and benefits to study participants. It ensures that clinical trial participants are exposed to minimal risks in relation to any benefits that might result from the research.
Left Ventricular Assist Device (LVAD)	A LVAD is a mechanical circulatory device that is used to partially or completely replace the function of a failing heart.
Left Ventricular Ejection Fraction (LVEF)	The fraction of blood pumped out of the left ventricle with each heart beat.
In vivo (experiments)	Experiments done in animal living systems.
In vitro (experiment)	Experiments done outside animal living systems.
LY process	Manufacturing process in which the compound LY294002 is added to the cells
Mesenchymal Stem Cells (MSCs)	Cells located in many tissues serving to repair the organs and tissues. These cells are found in organs like bone marrow, adipose tissue, liver, and pancreas.
mCRC	Metastatic colorectal cancer
Multipotent Stem Cells	Cells that have the potential to give rise to cells from multiple, but a limited number of lineages; i.e. multipotent stem cells can differentiate into a number of cells, but only those of a closely related family of cells.

Neovasculogenesis	Development of new blood vessels.
New York Heart Association (NYHA) Class	The NYHA Functional Classification provides a simple way of classifying the extent of heart failure. Divides patients in one of four categories based on the extend of the disease during physical activity; the limitations/symptoms are related to normal breathing and varying degrees in shortness of breath and/or angina pain.
Paracrine	Paracrine signalling is a form of cell signalling in which the target cell is near ("para" = near) the signal-releasing cell.
PD	progressive disease. See RECIST criteria
PR	Partial response. See RECIST criteria
Proteomics analysis	Proteomics is the large-scale study of proteins, particularly their structures and functions
RECIST	Response Evaluation Criteria In Solid Tumors. A set of published rules that define when tumors in cancer patients improve ("respond"), stay the same ("stabilize"), or worsen ("progress") during treatment. The main categories are Complete response (CR): Disappearance of all target lesions; Partial response (PR): At least a 30% decrease of target lesions; Stable disease (SD): Neither sufficient shrinkage to qualify for partial response nor sufficient increase to qualify for progressive disease; Progressive disease (PD): At least a 20% increase in the sum of target lesions.
RNA	Ribonucleic acid, a molecule essential in various biological roles in coding, decoding, regulation and expression of genes
RVOT	Right ventricular outflow tract
SD	Stable disease. See RECIST criteria
Secretome	The set of proteins secreted by a cell, a tissue or an organism.
Shares	The shares of the Company
Shareholders	The shareholders of the Company
Shareholders' Meeting	The general shareholders' meeting of the Company
shRNA	Short hairpin RNA, artificial RNA molecule that can be used to silence target gene expression
Stem cells	Stem cells are primal cells. Stem cells retain the ability to renew themselves by division and can differentiate into a diverse range of specialised cell types. Stem cells can be found in adult tissues (adult stem cells), embryos (embryonic stem cells or ESCs) or umbilical cord blood.

Supra-Ventricular Tachycardia	A supra-ventricular tachycardia is a tachycardia, or fast heart rhythm, that originates above the ventricles of the heart (mostly in the atriums).
Systolic dysfunction	Impairment of the contractile function of the heart.
Takeover Law	The Belgian law of 1 April 2007 relating to public tender offers (Loi relative aux offres publiques d'acquisition)
Takeover Royal Decree	The Belgian Royal Decree of 27 April 2007 on public takeover bids (Arrêté royal sur les offres publiques d'acquisition)
TCR	T cell receptor
THINK trial	Therapeutic Immunotherapy with CAR-T NKG2D clinical trial
TIM	Cell receptor inhibitory molecule
Transparency Law	the Belgian Law of 2 May 2007 on the disclosure of significant shareholdings in issuers whose securities are admitted to trading on a regulated market and containing various provisions (Loi relative à la publicité des participations importantes dans des émetteurs dont les actions sont admises à la negotiation sur un marché règlementé et portant dispositions diverses)
Ventricular Tachycardia (VT)	A ventricular tachycardia is a tachycardia, or fast heart rhythm, that originates in one of the ventricles of the heart.
Ventricular fibrillation (VF)	Ventricular fibrillation is a condition in which there is uncoordinated contraction of the cardiac muscle of the ventricles in the heart.