

Important : Avant d'exercer votre choix, veuillez prendre connaissance des instructions situées au verso - *Important : Before selecting please refer to instructions on reverse side*
 Quelle que soit l'option choisie, noircir comme ceci ■ la ou les cases correspondantes, dater et signer au bas du formulaire - *Whichever option is used, shade box(es) like this ■, date and sign at the bottom of the form*

JE DÉSIRE ASSISTER À CETTE ASSEMBLÉE et demande une carte d'admission : dater et signer au bas du formulaire / *I WISH TO ATTEND THE SHAREHOLDER'S MEETING and request an admission card: date and sign at the bottom of the form*

NICOX SA
 DRAKKAR D - 2405 ROUTE DES DOLINES
 06560 VALBONNE SOPHIA ANTIPOLIS

Au Capital de 43 223 135 EUR
 403 942 642 R.C.S. GRASSE

ASSEMBLEE GENERALE EXTRAORDINAIRE
 Du Lundi 11 Juillet 2022 à 14H00

EXTRAORDINARY GENERAL MEETING
 On Monday the 11th of July 2022 at 2.00 p.m.

CADRE RÉSERVÉ À LA SOCIÉTÉ - FOR COMPANY'S USE ONLY

Identifiant - Account
 Nominatif Registered
 Porteur Bearer
 Vote simple Single vote
 Vote double Double vote
 Nombre d'actions Number of shares
 Nombre de voix - Number of voting rights

JE VOTE PAR CORRESPONDANCE / I VOTE BY POST
 Cf. au verso (2) - See reverse (2)

Je vote **OUI** à tous les projets de résolutions présentés ou agréés par le Conseil d'Administration ou le Directoire ou la Gérance, à l'EXCEPTION de ceux que je signale en noircissant comme ceci ■ l'une des cases "Non" ou "Abstention". / I vote **YES** all the draft resolutions approved by the Board of Directors, EXCEPT those indicated by a shaded box, like this ■, for which I vote No or I abstain.

Sur les projets de résolutions non agréés, je vote en noircissant la case correspondant à mon choix. *On the draft resolutions not approved, I cast my vote by shading the box of my choice.*

JE DONNE POUVOIR AU PRÉSIDENT DE L'ASSEMBLÉE GÉNÉRALE
 Cf. au verso (3)

I HEREBY GIVE MY PROXY TO THE CHAIRMAN OF THE GENERAL MEETING
 See reverse (3)

JE DONNE POUVOIR À : Cf. au verso (4) pour me représenter à l'Assemblée
I HEREBY APPOINT: See reverse (4)
 to represent me at the above mentioned Meeting
 M. Mme ou Mlle, Raison Sociale / Mr, Mrs or Miss, Corporate Name

Adresse / Address

ATTENTION : Pour les titres au porteur, les présentes instructions doivent être transmises à votre banque.

CAUTION: As for bearer shares, the present instructions will be valid only if they are directly returned to your bank.

Nom, prénom, adresse de l'actionnaire (les modifications de ces informations doivent être adressées à l'établissement concerné et ne peuvent être effectuées à l'aide de ce formulaire). Cf au verso (1)
 Surname, first name, address of the shareholder (Change regarding this information have to be notified to relevant institution, no changes can be made using this proxy form). See reverse (1)

	1	2	3	4	5	6	7	8	9	10	A	B
Non / No	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Abs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	11	12	13	14	15	16	17	18	19	20	C	D
Non / No	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Abs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	21	22	23	24	25	26	27	28	29	30	E	F
Non / No	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Abs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	31	32	33	34	35	36	37	38	39	40	G	H
Non / No	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Abs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	41	42	43	44	45	46	47	48	49	50	J	K
Non / No	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Abs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Si des amendements ou des résolutions nouvelles étaient présentés en assemblée, je vote **NON** sauf si je signale un autre choix en noircissant la case correspondante :

In case amendments or new resolutions are proposed during the meeting, I vote **NO** unless I indicate another choice by shading the corresponding box:

- Je donne pouvoir au Président de l'assemblée générale. / I appoint the Chairman of the general meeting.....

- Je m'abstiens. / I abstain from voting

- Je donne procuration [cf. au verso renvoi (4)] à M., Mme ou Mlle, Raison Sociale pour voter en mon nom

I appoint [see reverse (4)] Mr, Mrs or Miss, Corporate Name to vote on my behalf.....

Pour être pris en considération, tout formulaire doit parvenir au plus tard :
 To be considered, this completed form must be returned no later than:

à la banque / to the bank 08/07/2022

Date & Signature

« Si le formulaire est renvoyé daté et signé mais qu'aucun choix n'est coché (carte d'admission / vote par correspondance / pouvoir au président / pouvoir à mandataire), cela vaut automatiquement pouvoir au Président de l'assemblée générale »
 "If the form is returned dated and signed but no choice is checked (admission card / postal vote / power of attorney to the President / power of attorney to a representative), this automatically applies as a proxy to the Chairman of the General Meeting"

CONDITIONS D'UTILISATION DU FORMULAIRE

<p>(1) GENERALITES : Il s'agit d'un formulaire unique prévu par l'article R. 225-76 du Code de Commerce. QUELLE QUE SOIT L'OPTION CHOISIE : Le signataire est prié d'inscrire très exactement, dans la zone réservée à cet effet, ses nom (en majuscules), prénom usuel et adresse (les modifications de ces informations doivent être adressées à l'établissement concerné et ne peuvent être effectuées à l'aide de ce formulaire). Pour les personnes morales, le signataire doit renseigner ses nom, prénom et qualité. Si le signataire n'est pas l'actionnaire (exemple : Administrateur légal, Tuteur, etc.) il doit mentionner ses nom, prénom et la qualité en laquelle il signe le formulaire de vote. Le formulaire adressé pour une assemblée vaut pour les assemblées successives convoquées avec le même ordre du jour (article R. 225-77 alinéa 3 du Code de Commerce). Le texte des résolutions figure dans le dossier de convocation joint au présent formulaire (article R. 225-81 du Code de Commerce). Ne pas utiliser à la fois « Je vote par correspondance » et « Je donne pouvoir » (article R. 225-81 paragraphe 8 du Code de Commerce). Un guide méthodologique de traitement des assemblées générales, incluant une grille de lecture de ce formulaire de vote par correspondance est disponible sur le site de l'AFTI : www.afti.asso.fr La version française de ce document fait foi.</p>	<p>(3) POUVOIR AU PRÉSIDENT DE L'ASSEMBLÉE GÉNÉRALE <u>Article L. 225-106 du Code de Commerce (extrait) :</u> "Pour toute prorogation d'un actionnaire sans indication de mandataire, le président de l'assemblée générale émet un vote favorable à l'adoption de projets de résolutions présentés ou agréés par le conseil d'administration ou le directoire, selon le cas, et un vote défavorable à l'adoption de tous les autres projets de résolution. Pour émettre tout autre vote, l'actionnaire doit faire choix d'un mandataire qui accepte de voter dans le sens indiqué par le mandant".</p>	<p>Cette information porte notamment sur le fait que le mandataire ou, le cas échéant, la personne pour le compte de laquelle il agit : 1° Contrôle, au sens de l'article L. 233-3, la société dont l'assemblée est appelée à se réunir ; 2° Est membre de l'organe de gestion, d'administration ou de surveillance de cette société ou d'une personne qui la contrôle au sens de l'article L. 233-3 ; 3° Est employé par cette société ou par une personne qui la contrôle au sens de l'article L. 233-3 ; 4° Est contrôlé ou exerce l'une des fonctions mentionnées au 2° ou au 3° dans une personne ou une entité contrôlée par une personne qui contrôle la société, au sens de l'article L. 233-3.</p>
<p>(2) VOTE PAR CORRESPONDANCE <u>Article L. 225-107 du Code de Commerce (extrait) :</u> "Tout actionnaire peut voter par correspondance, au moyen d'un formulaire dont les mentions sont fixées par décret en Conseil d'Etat. Les dispositions contraires des statuts sont réputées non écrites. Pour le calcul du quorum, il n'est tenu compte que des formulaires qui ont été reçus par la société avant la réunion de l'assemblée, dans les conditions de délais fixées par décret en Conseil d'Etat. Les formulaires ne donnant aucun sens de vote ou exprimant une abstention ne sont pas considérés comme des votes exprimés". La majorité requise pour l'adoption des décisions est déterminée en fonction des voix exprimées par les actionnaires présents ou représentés. Les voix exprimées ne comprennent pas celles attachées aux actions pour lesquelles l'actionnaire n'a pas pris part au vote, s'est abstenu ou a voté blanc ou nul. (articles L. 225-96 et L. 225-98 du Code de Commerce et, s'agissant des sociétés ayant adopté le statut de la société européenne, et articles 57 et 58 du Règlement du Conseil (CE) N°2157/2001 relatif au statut de la société européenne). Si vous votez par correspondance : vous devez obligatoirement noircir la case "Je vote par correspondance" au recto. 1 - il vous est demandé pour chaque résolution en noircissant individuellement les cases correspondantes : - soit de voter "Oui" (vote exprimé par défaut pour les projets de résolutions présentés ou agréés, en l'absence d'un autre choix); - soit de voter "Non"; - soit de voter "Abstenu" en noircissant individuellement les cases correspondantes. 2 - Pour le cas où des amendements aux résolutions présentées ou des résolutions nouvelles seraient déposées lors de l'assemblée, il vous est demandé d'opter entre vote contre (vote exprimé par défaut en l'absence d'un autre choix), pouvoir au président de l'assemblée générale, abstention ou pouvoir à personne dénommée en noircissant la case correspondant à votre choix.</p>	<p>(4) POUVOIR À UNE PERSONNE DÉNOMMÉE <u>Article L. 225-106 du Code de Commerce (extrait) :</u> "I - Un actionnaire peut se faire représenter par un autre actionnaire, par son conjoint ou par le partenaire avec lequel il a conclu un pacte civil de solidarité. II - Le mandat ainsi que, le cas échéant, sa révocation sont écrits et communiqués à la société. Les conditions d'application du présent alinéa sont précisées par décret en Conseil d'Etat. III - Avant chaque réunion de l'assemblée générale des actionnaires, le président du conseil d'administration ou le directoire, selon le cas, peut organiser la consultation des actionnaires mentionnés à l'article L. 225-102 afin de leur permettre de désigner un ou plusieurs mandataires pour les représenter à l'assemblée générale conformément aux dispositions du présent article. Cette consultation est obligatoire lorsque, les statuts ayant été modifiés en application de l'article L. 225-23 ou de l'article L. 225-71, l'assemblée générale ordinaire doit nommer au conseil d'administration ou au conseil de surveillance, selon le cas, un ou des salariés actionnaires ou membres des conseils de surveillance des fonds communs de placement d'entreprise détenant des actions de la société. Cette consultation est également obligatoire lorsque l'assemblée générale extraordinaire doit se prononcer sur une modification des statuts en application de l'article L. 225-23 ou de l'article L. 225-71. Les clauses contraires aux dispositions des alinéas précédents sont réputées non écrites."</p>	<p>Cette information est également délivrée lorsqu'il existe un lien familial entre le mandataire ou, le cas échéant, la personne pour le compte de laquelle il agit, et une personne physique placée dans l'une des situations énumérées aux 1° à 4°. Lorsqu'en cours de mandat, survient l'un des faits mentionnés aux alinéas précédents, le mandataire en informe sans délai son mandant. A défaut par ce dernier de confirmation expresse du mandat, celui-ci est caduc. La caducité du mandat est notifiée sans délai par le mandataire à la société. Les conditions d'application du présent article sont précisées par décret en Conseil d'Etat."</p>
<p>Les informations à caractère personnel recueillies dans le cadre du présent document sont nécessaires à l'exécution de vos instructions de vote. Vous disposez d'un certain nombre de droits concernant vos données (accès, rectification, etc.). Ces droits peuvent être exercés auprès de votre teneur de compte aux coordonnées indiquées par ce dernier.</p>		

FORM TERMS AND CONDITIONS

<p>(1) GENERAL INFORMATION: This is the sole form pursuant to article R. 225-76 du Code de Commerce WHICHEVER OPTION IS USED: The signatory should write his/her exact name and address in capital letters in the space provided e.g. a legal guardian: (Change regarding this information have to be notified to relevant institution, no change can be made using this proxy form). If the signatory is a legal entity, the signatory should indicate his/her full name and the capacity in which he is entitled to sign on the legal entity's behalf. If the signatory is not the shareholder (e.g. a legal guardian), please specify your full name and the capacity in which you are signing the proxy. The form sent for one meeting will be valid for all meetings subsequently convened with the same agenda (art. R. 225-77 alinéa 3 du Code de Commerce). The text of the resolutions is in the notification of the meeting which is sent with this proxy (article R. 225-81 du Code de Commerce). Please do not use both "I vote by post" and "I hereby appoint" (article R. 225-81 du Code de Commerce). A guide relating to the general meetings processing, including an interpretation grid of this proxy form, is available on the AFTI website at: www.afti.asso.fr The French version of this document governs; The English translation is for convenience only.</p>	<p>(3) PROXY TO THE CHAIRMAN OF THE GENERAL MEETING <u>Article L. 225-106 du Code de Commerce (extract):</u> "In case of any power of representation given by a shareholder without naming a proxy, the chairman of the general meeting shall issue a vote in favor of adopting a draft resolutions submitted or approved by the Board of Directors or the Management Board, as the case may be, and a vote against adopting any other draft resolutions. If issued any other vote, the shareholder must appoint a proxy who agrees to vote in the manner indicated by his principal."</p>	<p>This information relates in particular to the event that the proxy or, as the case may be, the person on behalf of whom it acts: 1° Controls, within the meaning of article L. 233-3, the company whose general meeting has to meet; 2° Is member of the management board, administration or supervisory board of the company or a person which controls it within the meaning of the article L. 233-3; 3° Is employed by the company or a person which controls it within the meaning of article L. 233-3; 4° Is controlled or carries out one of the functions mentioned with the 2° or the 3° in a person or an entity controlled by a person who controls the company, within the meaning of the article L. 233-3.</p>
<p>(2) POSTAL VOTING FORM <u>Article L. 225-107 du Code de Commerce (extract):</u> "Any shareholder may vote by post, using a form the wording of which shall be fixed by a decree approved by the Conseil d'Etat. Any provisions to the contrary contained in the memorandum and articles of association shall be deemed non-existent. When calculating the quorum, only forms received by the company before the meeting shall be taken into account, on conditions to be laid down by a decree approved by the Conseil d'Etat. The forms giving no voting direction or indicating abstention shall not be considered as votes cast." The majority required for the adoption of the general meeting's decisions shall be determined on the basis of the votes cast by the shareholders present or represented. The votes cast shall not include votes attaching to shares in respect of which the shareholder has not taken part in the vote or has abstained or has returned a blank or spoilt ballot paper (articles L. 225-96 and L. 225-98 du Code de Commerce and, for the companies which have adopted the statute of European company, articles 57 and 58 of the Council Regulation (EC) n°2157/2001 on the statute for a European company). If you wish to use the postal voting form, you have to shade the box on the front of the document: "I vote by post". 1 - In such event, please comply for each resolution the following instructions by shading boxes of your choice: - either vote "Yes" (in absence of choice, vote expressed by default for the approved draft resolutions), - or vote "No", - or vote "Abstention" by shading boxes of your choice. 2 - In case of amendments or new resolutions during the general meeting, you are requested to choose between vote "No" (vote expressed by default in absence of choice), proxy to the chairman of the general meeting, "Abstention" or proxy to a mentioned person individual or legal entity by shading the appropriate box.</p>	<p>(4) PROXY TO A MENTIONED PERSON (INDIVIDUAL OR LEGAL ENTITY) <u>Article L. 225-106 du Code de Commerce (extract):</u> "I - A shareholder may be represented by another shareholder, by his or her spouse, or by his or her partner who he or she has entered into a civil union with. II - The proxy as well as its dismissal, as the case may be, must be written and made known to the company. A Conseil d'Etat decree specifies the implementation of the present paragraph. III - Before every general meeting, the chairman of the board of directors or the management board, as the case may be, may organise a consultation with the shareholders mentioned in article L. 225-102 to enable them to appoint one or more proxies to represent them at the meeting in accordance with the provisions of this Article. Such a consultation shall be obligatory where, following the amendment of the memorandum and articles of association pursuant to article L. 225-23 or article L. 225-71, the ordinary general meeting is required to appoint to the board of directors or the supervisory board, as the case may be, one or more shareholder employees or members of the supervisory board of the company investment funds that holds company's shares. Such a consultation shall also be obligatory where a special shareholders' meeting is required to take a decision on an amendment to the memorandum and articles of association pursuant to article L. 225-23 or article L. 225-71. Any clauses that conflict with the provisions of the preceding sub-paragraphs shall be deemed non-existent."</p>	<p>This information is also delivered when a family tie exists between the proxy or, as the case may be, the person on behalf of whom it acts, and a natural person placed in one of the situations enumerated from 1° to 4° above. When during the proxy, one of the events mentioned in the preceding subparagraphs occurs, the proxy informs without delay his constituent. Failing by the latter to confirm explicitly the proxy, this one is null and void. The termination of the proxy is notified without delay by the proxy to the company. The conditions of application of this article are determined by a Conseil d'Etat decree."</p>
<p>Personal data included in this form are necessary for the execution of your voting instructions. You have certain minimum rights regarding your data (access, correction...). These rights may be exercised using the contact details provided by your custodian.</p>		

BALO

BULLETIN DES ANNONCES LEGALES OBLIGATOIRES



**PREMIER
MINISTRE**

*Liberté
Égalité
Fraternité*

Direction de l'information
légale et administrative

DIRECTION DE L'INFORMATION LÉGALE ET ADMINISTRATIVE

26, rue Desaix, 75727 PARIS CEDEX 15

www.dila.premier-ministre.gouv.fr

www.journal-officiel.gouv.fr

Avis de convocation / avis de réunion

NICOX SA

Société anonyme au capital social de € 43.223.135

Siège social : Drakkar D - 2405 route des Dolines

06560 Valbonne, Sophia Antipolis

403 942 642 R.C.S. Grasse

N° d'immatriculation Insee : 403 942 642 00055

AVIS DE REUNION VALANT AVIS DE CONVOCATION

Mesdames et Messieurs les actionnaires de Nicox (la « **Société** ») sont informés qu'ils sont convoqués en Assemblée générale extraordinaire le **lundi 11 juillet 2022 à 14 heures**, dans les bureaux de **BuroClub – Drakkar 2 Bâtiment D – 2405 route des Dolines – 06560 Valbonne Sophia Antipolis**, à l'effet de délibérer sur l'ordre du jour et les résolutions ci-après reproduits.

Pour le cas où le quorum requis pour la délibération de l'Assemblée générale extraordinaire ne serait pas atteint sur première convocation, une seconde réunion avec le même ordre du jour serait convoquée dans les bureaux de BuroClub – Drakkar 2 Bâtiment D – 2405 route des Dolines – 06560 Valbonne Sophia Antipolis pour le jeudi 28 juillet 2022 à 14 heures.

AVERTISSEMENT – COVID 19 : En fonction d'éventuelles mesures de restrictions, les modalités de participation physique à l'assemblée générale pourraient évoluer. Les actionnaires sont invités à consulter régulièrement la rubrique dédiée à l'assemblée générale extraordinaire 2022 sur le site de la société www.nicox.com.

Les actionnaires ont la possibilité de voter aux assemblées générales sans y être physiquement présents, en votant par correspondance à l'aide du formulaire de vote ou en votant par Internet sur la plateforme de vote sécurisée VOTACCESS – voir ci-après la section relative aux modalités de participation à l'assemblée générale.

Ordre du jour de l'Assemblée générale extraordinaire

- Délégation de compétence consentie au Conseil d'administration pour émettre des actions, des titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que des valeurs mobilières donnant accès à des titres de capital à émettre de la Société, avec maintien du droit préférentiel de souscription des actionnaires (résolution n° 1).
- Délégation de compétence consentie au Conseil d'administration pour émettre des actions, des titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que des valeurs mobilières donnant accès à des titres de capital à émettre, avec suppression du droit préférentiel de souscription des actionnaires et par offre au public autre que celles visées à l'article L. 411-2 1° du Code monétaire et financier (résolution n° 2).
- Délégation de compétence consentie au Conseil d'administration pour émettre des actions, des titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que des valeurs mobilières donnant accès à des titres de capital à émettre, avec suppression du droit préférentiel de souscription des actionnaires et dans le cadre d'une offre au public visée à l'article L.411-2 1° du Code monétaire et financier (résolution n° 3).

- Autorisation consentie au Conseil d'administration pour fixer le prix d'émission des titres à émettre dans le cadre des émissions réalisées en application des deuxième et troisième résolutions dans la limite de 10% du capital social par an (résolution n° 4).
- Autorisation consentie au Conseil d'administration pour augmenter le nombre de titres à émettre dans le cadre des émissions, avec ou sans droit préférentiel de souscription, réalisées en application des première, deuxième, troisième, quatrième et huitième résolutions (résolution n° 5).
- Délégation de compétence consentie au Conseil d'administration pour augmenter le capital par incorporation de réserves, bénéfices, primes ou autres sommes dont la capitalisation serait admise (résolution n° 6).
- Délégation de pouvoirs consentie au Conseil d'administration pour augmenter le capital dans la limite de 10 % du capital social en vue de rémunérer des apports en nature consentis à la Société en dehors d'une offre publique d'échange (résolution n° 7).
- Délégation de compétence consentie au Conseil d'administration pour augmenter le capital au bénéfice d'une catégorie de bénéficiaires, avec suppression du droit préférentiel de souscription des actionnaires à leur profit (résolution n° 8).
- Délégation de compétence consentie au Conseil d'administration pour augmenter le capital au profit des adhérents à un plan d'épargne d'entreprise avec suppression du droit préférentiel de souscription des actionnaires à leur profit (résolution n° 9).
- Autorisation donnée au Conseil d'administration pour procéder à des attributions gratuites d'actions existantes ou à émettre, emportant de plein droit renonciation des actionnaires à leur droit préférentiel de souscription (résolution n° 10).
- Autorisation donnée au Conseil d'administration pour consentir des options donnant droit à la souscription d'actions nouvelles de la Société ou à l'achat d'actions existantes, emportant de plein droit renonciation des actionnaires à leur droit préférentiel de souscription (résolution n° 11).
- Autorisation à conférer au Conseil d'administration à l'effet de réduire le capital social par annulation d'actions précédemment rachetées dans le cadre d'un programme de rachat d'actions (résolution n° 12).
- Modification des statuts pour étendre à 75 ans la limite d'âge du Président du Conseil d'administration (résolution n° 13).
- Pouvoirs à donner en vue des formalités (résolution n° 14).

PROJETS DE RÉSOLUTIONS ASSEMBLÉE GÉNÉRALE EXTRAORDINAIRE

PREMIÈRE RÉSOLUTION (*Délégation de compétence consentie au Conseil d'administration pour émettre des actions, des titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que des valeurs mobilières donnant accès à des titres de capital à émettre de la Société, avec maintien du droit préférentiel de souscription des actionnaires*). — L'Assemblée générale, connaissance prise du rapport du Conseil d'administration et du rapport spécial des Commissaires aux comptes, après avoir constaté la libération intégrale du capital social et statuant conformément aux articles L. 225-129 à L. 225-129-6, L. 225-132 à L. 225-134, L. 22-10-49, L. 22-10-51, L. 228-91 et L. 228-92 du Code de commerce :

1. Délégué au Conseil d'administration sa compétence pour décider, en une ou plusieurs fois, à l'époque ou aux époques qu'il fixera, dans les proportions qu'il appréciera, tant en France qu'à l'étranger, en euros ou en devises étrangères, l'émission, avec maintien du droit préférentiel de souscription, d'actions, de titres de capital donnant accès à d'autres titres de capital ou donnant droit à l'attribution de titres de créances ainsi que de toutes autres valeurs mobilières donnant accès à des titres de capital de la Société à émettre, lesdites actions conférant les mêmes droits que les actions anciennes sous réserve de leur date de jouissance ; étant précisé que la souscription des actions, titres de capital et autres valeurs mobilières donnant accès à des titres de capital pourra être opérée soit en espèces, soit par compensation avec des créances certaines, liquides et exigibles ; le Conseil d'administration pouvant déléguer au Directeur général, ou en accord avec ce dernier, à un ou plusieurs directeurs généraux délégués, dans les conditions permises par la loi, tous les pouvoirs nécessaires pour décider de l'augmentation de capital ;
2. Décide qu'est expressément exclue toute émission d'actions de préférence et de valeurs mobilières donnant accès à des actions de préférence ;
3. Décide que le montant nominal des augmentations de capital social susceptibles d'être réalisées immédiatement et/ou à terme en vertu de la présente délégation, le cas échéant tel qu'augmenté en application de la cinquième résolution, ne pourra excéder un montant nominal global de € 20 000 000, étant précisé que ce montant nominal global ne tient pas compte des ajustements susceptibles d'être opérés conformément aux dispositions légales et réglementaires applicables, et le cas échéant, aux stipulations contractuelles prévoyant d'autres cas d'ajustement, pour préserver les droits des porteurs de valeurs mobilières ou autres droits donnant accès au capital ;
4. Décide que le montant nominal global des valeurs mobilières représentatives de titres de créance susceptibles d'être émises en vertu de la présente délégation sera au maximum de € 100 millions ou la contre-valeur de ce montant en cas d'émission en monnaie étrangère ou en unités de comptes fixées par référence à plusieurs monnaies ;
5. Décide que les actionnaires pourront exercer, dans les conditions prévues par la loi, leur droit préférentiel de souscription à titre irréductible. En outre, le Conseil d'administration aura la faculté de conférer aux actionnaires le droit de souscrire à titre réductible un nombre de valeurs mobilières supérieur à celui qu'ils pourraient souscrire à titre irréductible, proportionnellement aux droits de souscription dont ils disposent et, en tout état de cause, dans la limite de leur demande ;

Si les souscriptions à titre irréductible et, le cas échéant, à titre réductible, n'ont pas absorbé la totalité d'une émission d'actions ou de valeurs mobilières telles que définies ci-dessus, le Conseil d'administration pourra utiliser, conformément à l'article L. 225-134 du Code de commerce, dans l'ordre qu'il déterminera, l'une ou l'autre des facultés ci-après :

- offrir au public tout ou partie des titres non souscrits ;
 - répartir librement tout ou partie des titres non souscrits entre les personnes de son choix ;
 - limiter l'émission au montant des souscriptions reçues sous la condition que ce montant atteigne au moins les trois-quarts de l'émission décidée ;
6. Constate que cette délégation emporte de plein droit au profit des porteurs de valeurs mobilières émises au titre de la présente résolution et donnant accès au capital de la Société, renonciation des actionnaires à leur droit préférentiel de souscription aux titres de capital auxquelles ces valeurs mobilières donnent droit ;

7. Décide que la somme revenant ou devant revenir à la Société pour chacune des actions émises dans le cadre de la présente délégation sera au moins égale à la valeur nominale de l'action à la date d'émission desdites valeurs mobilières ;
8. décide que le Conseil d'administration ne pourra, sauf autorisation préalable par l'Assemblée générale, faire usage de la présente autorisation à compter du dépôt par un tiers d'un projet d'offre publique visant les titres de la Société et ce, jusqu'à la fin de la période d'offre ;
9. Décide que la présente délégation prive d'effet la délégation de même nature consentie par l'Assemblée générale extraordinaire des actionnaires du 28 avril 2021 dans sa première résolution à hauteur de la partie non utilisée de cette délégation.

La délégation ainsi conférée au Conseil d'administration est valable pour une durée de 26 mois à compter de la présente Assemblée.

DEUXIÈME RÉSOLUTION (*Délégation de compétence consentie au Conseil d'administration pour émettre des actions, des titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que des valeurs mobilières donnant accès à des titres de capital à émettre, avec suppression du droit préférentiel de souscription des actionnaires et par offre au public, autre que celles visées à l'article L. 411-2 1° du Code monétaire et financier*). — L'Assemblée générale, connaissance prise du rapport du Conseil d'administration et du rapport spécial des Commissaires aux comptes, après avoir constaté la libération intégrale du capital social et statuant conformément aux articles L. 225-129 à L. 225-129-6, L. 225-135, L. 225-136, L. 22-10-49, L. 22-10-51, L. 22-10-52, L. 22-10-54, L. 228-91 à L. 228-94 du Code de commerce :

1. Délègue au Conseil d'administration sa compétence pour décider, par une offre au public, autre que celles visées à l'article L. 411-2 1° du Code monétaire et financier, en une ou plusieurs fois, dans les proportions et aux époques qu'il appréciera, tant en France qu'à l'étranger, en euros ou en devises étrangères, l'émission, sans droit préférentiel de souscription :

(a) d'actions de la Société, de titres de capital donnant accès à d'autres titres de capital ou donnant droit à l'attribution de titres de créances ainsi que de toutes autres valeurs mobilières donnant accès à des titres de capital de la Société à émettre, (b) d'actions de la Société, de titres de capital donnant accès à d'autres titres de capital ou donnant droit à l'attribution de titres de créances ou de toutes autres valeurs mobilières donnant accès à des titres de capital de la Société à émettre, à la suite de l'émission par une société dont la Société possède directement ou indirectement plus de la moitié du capital de titres de capital ou de toutes valeurs mobilières donnant accès à des titres de capital de la Société à émettre, (c) d'actions, de titres de capital donnant accès à d'autres titres de capital ou donnant droit à l'attribution de titres de créances ou de valeurs mobilières par la Société donnant accès à des titres de capital à émettre d'une société dont elle possède directement ou indirectement plus de la moitié du capital et (d) de valeurs mobilières donnant accès à des titres de capital existants ou donnant droit à l'attribution de titres de créances d'une autre société dont la Société ne possède pas directement ou indirectement plus de la moitié du capital ;

étant précisé que (a) les actions de la Société à émettre conféreront les mêmes droits que les actions anciennes sous réserve de leur date de jouissance et (b) la souscription des actions, titres de capital et autres valeurs mobilières donnant accès à des titres de capital pourra être opérée soit en espèces, soit par compensation avec des créances liquides et exigibles ; le Conseil d'administration pouvant déléguer au Directeur général, ou en accord avec ce dernier, à un ou plusieurs directeurs généraux délégués, dans les conditions permises par la loi, tous les pouvoirs nécessaires pour décider des émissions susceptibles d'être réalisées en vertu de la présente délégation ;

2. Décide qu'est expressément exclue toute émission d'actions de préférence et de valeurs mobilières donnant accès à des actions de préférence ;

3. Décide que le montant nominal maximal des augmentations de capital susceptibles d'être réalisées immédiatement et/ou à terme en vertu de la présente délégation, le cas échéant tel qu'augmenté en application de la cinquième résolution, ne pourra excéder un montant de € 15 000 000, étant précisé que ce montant s'imputera sur le plafond nominal global d'augmentation de capital de € 20 000 000 fixé par la première résolution de la présente Assemblée et que ce montant ne tient pas compte des actions supplémentaires à émettre pour préserver les droits des porteurs de valeurs mobilières donnant accès au capital conformément aux dispositions légales et réglementaires applicables ainsi que, le cas échéant, aux stipulations contractuelles prévoyant d'autres cas d'ajustement ; ce montant de € 15 000 000 constituant un sous-plafond nominal global d'augmentation de capital sur lequel s'imputeront toutes émissions réalisées en application des deuxième, troisième, quatrième, septième et huitième résolutions de la présente Assemblée ;
4. Décide que le montant nominal global des valeurs mobilières représentatives de titres de créances susceptibles d'être émises en vertu de la présente délégation ne pourra excéder un montant de € 100 millions ou la contre-valeur de ce montant en cas d'émission en monnaie étrangère ou en unité de compte fixée par référence à plusieurs monnaies, étant précisé que ce montant s'imputera sur le plafond de € 100 millions prévu à la première résolution de la présente Assemblée ;
5. Décide de supprimer le droit préférentiel de souscription des actionnaires aux actions, titres de capital et autres valeurs mobilières à émettre au titre de la présente délégation. Le Conseil d'administration pourra conférer aux actionnaires une faculté de souscription par priorité sur tout ou partie de l'émission, pendant le délai et selon les conditions qu'il fixera conformément à l'article L. 22-10-51 du Code de commerce ;
6. Constate que la présente délégation emporte de plein droit, au profit des porteurs de valeurs mobilières donnant accès au capital de la Société, renonciation des actionnaires à leur droit préférentiel de souscription aux titres de capital auxquels ces valeurs mobilières donnent droit ;
7. Décide que la somme revenant, ou devant revenir, à la Société pour chacune des actions émises ou à émettre dans le cadre de la présente délégation sera au moins égale à la valeur minimale fixée par les dispositions légales et réglementaires applicables au moment où il est fait usage de la présente délégation, soit actuellement à la moyenne pondérée des cours de l'action de la Société sur le marché réglementé d'Euronext à Paris lors des trois dernières séances de bourse précédant le début de l'offre au public au sens du règlement (UE) n° 2017/1129 du 14 juin 2017, éventuellement diminuée d'une décote maximale de 10 %, après correction, s'il y a lieu, de ce montant pour tenir compte de la différence de date de jouissance ; étant précisé à toutes fins utiles que le prix d'émission des valeurs mobilières donnant accès au capital sera tel que la somme perçue immédiatement par la Société, majorée le cas échéant de celle susceptible d'être perçue ultérieurement par elle, soit, pour chaque action émise en conséquence de l'émission de ces valeurs mobilières, au moins égale à la valeur minimale susmentionnée ;
8. Décide que la présente délégation pourra être utilisée à l'effet de rémunérer des titres apportés à une offre publique d'échange initiée par la Société, dans les limites et sous les conditions prévues par l'article L. 22-10-54 du Code de commerce.
9. Décide que si les souscriptions n'ont pas absorbé la totalité d'une émission d'actions ou de valeurs mobilières telles que définies ci-dessus, le Conseil d'administration pourra, dans le cadre des augmentations de capital qu'il pourrait décider dans le cadre de la présente résolution, limiter l'émission au montant des souscriptions reçues
10. Décide que le Conseil d'administration ne pourra, sauf autorisation préalable par l'Assemblée générale, faire usage de la présente autorisation à compter du dépôt par un tiers d'un projet d'offre publique visant les titres de la Société et ce, jusqu'à la fin de la période d'offre ;
11. Décide que la présente délégation prive d'effet la délégation de même nature consentie par l'Assemblée générale extraordinaire des actionnaires du 28 avril 2021 dans sa deuxième résolution à hauteur de la partie non utilisée de cette délégation.

La délégation conférée au Conseil d'administration est valable pour une durée de 26 mois à compter de la présente Assemblée.

TROISIÈME RÉSOLUTION (*Délégation de compétence consentie au Conseil d'administration pour émettre des actions, des titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que des valeurs mobilières donnant accès à des titres de capital à émettre, avec suppression du droit préférentiel de souscription des actionnaires et dans le cadre d'une offre au public visée à l'article L. 411-2 1° du Code monétaire et financier*). — L'Assemblée générale, connaissance prise du rapport du Conseil d'administration et du rapport spécial des Commissaires aux comptes, après avoir constaté la libération intégrale du capital social et statuant conformément aux articles L. 225-129 à L. 225-129-6, L. 225-135, L. 225-136, L. 22-10-49, L. 22-10-51, L. 22-10-52, L. 228-91 à L. 228-94 du Code de commerce :

1. Délégué au Conseil d'administration sa compétence pour décider, par une offre au public visée à l'article L. 411-2 1° du Code monétaire et financier, en une ou plusieurs fois, dans les proportions et aux époques qu'il appréciera, tant en France qu'à l'étranger, en euros ou en devises étrangères, l'émission sans droit préférentiel de souscription :

(a) d'actions de la Société, de titres de capital donnant accès à d'autres titres de capital de la société ou donnant droit à l'attribution de titres de créances ainsi que de toutes autres valeurs mobilières donnant accès à des titres de capital de la Société à émettre, (b) d'actions de la Société, de titres de capital donnant accès à d'autres titres capital de la société ou donnant droit à l'attribution de titres de créances ou de toutes autres valeurs mobilières donnant accès à des titres de capital de la Société à émettre, à la suite de l'émission par une société dont la Société possède directement ou indirectement plus de la moitié du capital de titres de capital ou toutes valeurs mobilières donnant accès à des titres de capital de la Société à émettre, (c) d'actions, de titres de capital donnant accès à d'autres titres capital de la société ou donnant droit à l'attribution de titres de créances ou de valeurs mobilières par la Société donnant accès à des titres de capital à émettre d'une société dont elle possède directement ou indirectement plus de la moitié du capital et (d) de valeurs mobilières donnant accès à des titres de capital existants ou donnant droit à l'attribution de titres de créances d'une autre société dont la Société ne possède pas directement ou indirectement plus de la moitié du capital ;

étant précisé que (a) les actions de la Société à émettre conféreront les mêmes droits que les actions anciennes sous réserve de leur date de jouissance et (b) la souscription des actions, titres de capital et autres valeurs mobilières donnant accès à des titres de capital pourra être opérée soit en espèces, soit par compensation avec des créances liquides et exigibles ; le Conseil d'administration pouvant déléguer au Directeur général, ou en accord avec ce dernier, à un ou plusieurs directeurs généraux délégués, dans les conditions permises par la loi, tous les pouvoirs nécessaires pour décider des émissions susceptibles d'être réalisées en vertu de la présente délégation ;

2. Décide qu'est expressément exclue toute émission d'actions de préférence et de valeurs mobilières donnant accès à des actions de préférence ;
3. Décide que le montant nominal maximal des augmentations de capital susceptibles d'être réalisées immédiatement et/ou à terme en vertu de la présente délégation, le cas échéant tel qu'augmenté en application de la cinquième résolution, ne pourra excéder un montant de € 15 000 000, étant précisé que ce montant s'imputera sur le sous-plafond nominal global d'augmentation de capital de € 15 000 000 fixé par la deuxième résolution et sur le plafond nominal global d'augmentation de capital de € 20 000 000 fixé par la première résolution de la présente Assemblée et que ce montant ne tient pas compte des actions supplémentaires à émettre pour préserver les droits des porteurs de valeurs mobilières donnant accès au capital conformément aux dispositions légales et réglementaires applicables ainsi que, le cas échéant, aux stipulations contractuelles prévoyant d'autres cas d'ajustement ; le montant des augmentations de capital décidées en application de la présente délégation ne pourra en outre excéder 20 % du capital social par an ;
4. Décide que le montant nominal global des valeurs mobilières représentatives de titres de créances susceptibles d'être émises en vertu de la présente délégation ne pourra excéder un montant de € 100 millions ou la contre-valeur de ce montant en cas d'émission en monnaie étrangère ou en unité de compte fixée par référence à plusieurs monnaies, étant précisé que ce montant s'imputera sur le plafond de € 100 millions prévu à la première résolution de la présente Assemblée ;
5. Décide de supprimer le droit préférentiel de souscription des actionnaires aux actions, titres de capital et autres valeurs mobilières à émettre au titre de la présente délégation. Le Conseil d'administration pourra conférer aux actionnaires une faculté de souscription par priorité sur tout ou partie de l'émission, pendant le délai et selon les conditions qu'il fixera conformément à l'article L. 22-10-51 du Code de commerce ;

6. Décide que si les souscriptions n'ont pas absorbé la totalité d'une émission d'actions ou de valeurs mobilières telles que définies ci-dessus, le Conseil d'administration pourra, dans le cadre des augmentations de capital qu'il pourrait décider dans le cadre de la présente résolution, limiter l'émission au montant des souscriptions reçues ;
7. Constate que la présente délégation emporte de plein droit, au profit des porteurs de valeurs mobilières donnant accès au capital de la Société, renonciation des actionnaires à leur droit préférentiel de souscription aux titres de capital auxquelles ces valeurs mobilières donnent droit ;
8. Décide que la somme revenant, ou devant revenir, à la Société pour chacune des actions émises ou à émettre dans le cadre de la présente délégation sera au moins égale à la valeur minimale fixée par les dispositions légales et réglementaires applicables au moment où il est fait usage de la présente délégation, soit actuellement à la moyenne pondérée des cours de l'action de la Société sur le marché réglementé d'Euronext à Paris lors des trois dernières séances de bourse précédant le début de l'offre au public au sens du règlement (UE) n° 2017/1129 du 14 juin 2017, éventuellement diminuée d'une décote maximale de 10 %, après correction, s'il y a lieu, de ce montant pour tenir compte de la différence de date de jouissance ; étant précisé à toutes fins utiles que le prix d'émission des valeurs mobilières donnant accès au capital sera tel que la somme perçue immédiatement par la Société, majorée le cas échéant de celle susceptible d'être perçue ultérieurement par elle, soit, pour chaque action émise en conséquence de l'émission de ces valeurs mobilières, au moins égale à la valeur minimale susmentionnée ;
9. Décide que le Conseil d'administration ne pourra, sauf autorisation préalable par l'Assemblée générale, faire usage de la présente autorisation à compter du dépôt par un tiers d'un projet d'offre publique visant les titres de la Société et ce, jusqu'à la fin de la période d'offre ;
10. Décide que la présente délégation prive d'effet la délégation de même nature consentie par l'Assemblée générale extraordinaire des actionnaires du 28 avril 2021 dans sa troisième résolution à hauteur de la partie non utilisée de cette délégation.

La délégation conférée au Conseil d'administration est valable pour une durée de 26 mois à compter de la présente Assemblée.

QUATRIEME RÉSOLUTION (*Autorisation consentie au Conseil d'administration pour fixer le prix d'émission des titres à émettre dans le cadre des émissions réalisées en application des deuxième et troisième résolutions dans la limite de 10% du capital social par an*). — L'Assemblée générale, connaissance prise du rapport du Conseil d'administration et du rapport spécial des Commissaires aux comptes, après avoir constaté la libération intégrale du capital social et statuant conformément à l'article L. 22-10-52 du Code de commerce :

1. Autorise le Conseil d'administration, avec faculté de subdélégation au Directeur Général, ou en accord avec ce dernier, à un ou plusieurs directeurs généraux délégués, dans les conditions permises par la loi, dans la limite de 10 % du capital social par an, à déroger aux conditions de fixation du prix prévues par les deuxième et troisième résolutions de la présente Assemblée pour les titres à émettre dans le cadre des résolutions précitées et à fixer le prix d'émission desdits titres selon les pratiques de marché habituelles, étant précisé que la somme revenant, ou devant revenir, à la Société pour chacune des actions émises dans le cadre de la présente délégation sera au moins égale à la moyenne pondérée des cours de l'action de la Société sur le marché réglementé d'Euronext à Paris lors des trois dernières séances de bourse précédant la fixation du prix d'émission, cette moyenne pouvant le cas échéant être corrigée pour tenir compte des différences de date de jouissance et être éventuellement diminuée d'une décote maximum de 15 % ; étant précisé à toutes fins utiles que le prix d'émission des valeurs mobilières donnant accès au capital sera tel que la somme perçue immédiatement par la Société, majorée le cas échéant de celle susceptible d'être perçue ultérieurement par elle, soit, pour chaque action émise en conséquence de l'émission de ces valeurs mobilières, au moins égale au prix minimum susmentionné ;
2. Décide que le montant nominal maximal des augmentations de capital susceptibles d'être réalisées en vertu de la présente autorisation s'imputera sur le plafond nominal d'augmentation de capital de € 15 000 000 fixé par les deuxième et troisième résolutions de la présente Assemblée ;
3. Décide que le Conseil d'administration ne pourra, sauf autorisation préalable par l'Assemblée générale, faire usage de la présente autorisation à compter du dépôt par un tiers d'un projet d'offre publique visant les titres de la Société et ce, jusqu'à la fin de la période d'offre ;

L'autorisation conférée au Conseil d'administration en vertu de la présente résolution est valable pour une durée de 26 mois à compter de la présente Assemblée.

CINQUIEME RÉSOLUTION (*Autorisation consentie au Conseil d'administration pour augmenter le nombre de titres à émettre dans le cadre des émissions, avec ou sans droit préférentiel de souscription, réalisées en application des première, deuxième, troisième, quatrième et huitième résolutions*). — L'Assemblée générale, connaissance prise du rapport du Conseil d'administration et du rapport spécial des Commissaires aux comptes, après avoir constaté la libération intégrale du capital social et statuant conformément aux articles L. 225-135-1 et R. 225-118 du Code de commerce :

1. Autorise le Conseil d'administration, avec faculté de subdélégation au Directeur Général, ou en accord avec ce dernier, à un ou plusieurs directeurs généraux délégués, dans les conditions permises par la loi, à augmenter le nombre de titres à émettre pour chacune des émissions avec ou sans droit préférentiel de souscription décidées en vertu des première, deuxième, troisième et septième résolutions de la présente Assemblée, dans les trente jours de la clôture de la souscription dans la limite de 15 % de l'émission initiale et au même prix que celui retenu pour l'émission initiale ;
2. Décide que le montant nominal maximal des augmentations de capital susceptibles d'être réalisées en vertu de la présente autorisation s'imputera sur le plafond nominal d'augmentation de capital fixé par chacune des résolutions au titre de laquelle l'émission initiale a été décidée, soit € 20 000 000 pour la première résolution de la présente Assemblée et € 15 000 000 pour les deuxième, troisième, quatrième et huitième résolutions de la présente Assemblée ;
3. Décide que le Conseil d'administration ne pourra, sauf autorisation préalable par l'Assemblée générale, faire usage de la présente autorisation à compter du dépôt par un tiers d'un projet d'offre publique visant les titres de la Société et ce, jusqu'à la fin de la période d'offre ;
4. Décide que la présente délégation prive d'effet la délégation de même nature consentie par l'Assemblée générale extraordinaire des actionnaires du 28 avril 2021 dans sa quatrième résolution à hauteur de la partie non utilisée de cette délégation.

L'autorisation conférée au Conseil d'administration en vertu de la présente résolution est valable pour une durée de 26 mois à compter de la présente Assemblée.

SIXIEME RÉSOLUTION (*Délégation de compétence consentie au Conseil d'administration pour augmenter le capital par incorporation de réserves, bénéfices, primes ou autres sommes dont la capitalisation serait admise*). — L'Assemblée générale, connaissance prise du rapport du Conseil d'administration, après avoir constaté la libération intégrale du capital social et statuant conformément aux articles L. 225-129 à L. 225-129-6, L. 225-130 et L. 22-10-50 du Code de commerce :

1. Délégué au Conseil d'administration sa compétence pour augmenter le capital social en une ou plusieurs fois, dans la proportion et aux époques qu'il appréciera, par incorporation de réserves, bénéfices, primes ou autres sommes dont la capitalisation serait admise, et sous forme d'attributions d'actions gratuites ou d'augmentation de la valeur nominale des actions existantes, soit en combinant les deux opérations ; étant précisé que le Conseil d'administration pourra déléguer au Directeur général, ou en accord avec ce dernier, à un ou plusieurs directeurs généraux délégués, dans les conditions permises par la loi, tous les pouvoirs nécessaires pour décider de l'augmentation de capital ;
2. Décide que le montant des augmentations de capital social susceptibles d'être réalisées en vertu de la présente délégation ne pourra excéder le montant des sommes pouvant être incorporées au capital à la date du Conseil d'administration faisant usage de la présente délégation, étant précisé que ce montant ne s'imputera pas sur le plafond nominal global d'augmentation de capital de € 20 000 000 fixé par la première résolution de la présente Assemblée et que ce montant ne tient pas compte des ajustements susceptibles d'être opérés conformément aux dispositions législatives et réglementaires applicables et, le cas échéant, aux stipulations contractuelles prévoyant d'autres cas d'ajustement, pour préserver les droits des porteurs de valeurs mobilières ou autres droits donnant accès au capital ;
3. Décide que les droits formant rompus ne seront ni négociables ni cessibles et que les actions correspondantes seront vendues. Les sommes provenant de la vente seront allouées aux titulaires des droits au plus tard 30 jours après la date d'inscription à leur compte du nombre entier d'actions attribuées.

4. Décide que le Conseil d'administration ne pourra, sauf autorisation préalable par l'Assemblée générale, faire usage de la présente autorisation à compter du dépôt par un tiers d'un projet d'offre publique visant les titres de la Société et ce, jusqu'à la fin de la période d'offre ;
5. Décide que la présente délégation prive d'effet la délégation de même nature consentie par l'Assemblée générale extraordinaire des actionnaires du 28 avril 2021 dans sa cinquième résolution.

La délégation ainsi conférée au Conseil d'administration est valable pour une durée de 26 mois à compter de la date de la présente Assemblée générale.

SEPTIEME RÉSOLUTION (*Délégation de pouvoirs consentie au Conseil d'administration pour augmenter le capital dans la limite de 10 % du capital social en vue de rémunérer des apports en nature consentis à la Société en dehors d'une offre publique d'échange*). — L'Assemblée générale connaissance prise du rapport du Conseil d'administration et du rapport spécial des Commissaires aux comptes, après avoir constaté la libération intégrale du capital social et statuant conformément à l'article L. 22-10-53 du Code de commerce :

1. Délègue au Conseil d'administration les pouvoirs nécessaires pour augmenter le capital social, en une ou plusieurs fois, dans la limite de 10 % du capital social, par émission d'actions, de titres de capital donnant accès à d'autres titres de capital ou donnant droit à l'attribution de titres de créances de la Société ainsi que de toutes autres valeurs mobilières donnant accès à des titres de capital de la Société à émettre, sur le rapport du ou des Commissaires aux apports, en vue de rémunérer des apports en nature consentis à la Société et constitués de titres de capital ou de valeurs mobilières donnant accès au capital, lorsque les dispositions de l'article L. 22-10-54 du Code de commerce ne sont pas applicables ;
2. Décide que le Conseil d'administration aura tous pouvoirs pour mettre en œuvre la présente délégation, notamment à l'effet de statuer sur le rapport du ou des Commissaires aux apports, d'arrêter toutes les modalités et conditions des opérations autorisées et notamment évaluer les apports ainsi que l'octroi, le cas échéant, d'avantages particuliers, de fixer le nombre de titres à émettre en rémunération des apports ainsi que la date de jouissance des titres à émettre, de procéder le cas échéant, à toute imputation sur la ou les primes d'apport, et notamment celles des frais entraînés par la réalisation des émissions, de constater la réalisation de l'augmentation de capital et modifier les statuts en conséquence, et de prendre plus généralement toutes les dispositions utiles et conclure tous accords, procéder à toutes formalités requises pour l'admission aux négociations des actions émises et procéder à toutes formalités de publicité requises ;
3. Prend acte, en tant que de besoin, que la présente délégation emporte renonciation des actionnaires à leur droit préférentiel de souscription aux titres de capital de la Société auxquelles les valeurs mobilières qui seraient émises sur le fondement de la présente délégation pourront donner droit ;
4. Décide que le montant nominal maximal des augmentations de capital susceptibles d'être réalisées en vertu de la présente délégation s'imputera sur le sous-plafond nominal global d'augmentation de capital de € 15 000 000 fixé par la deuxième résolution de la présente Assemblée, qui lui-même s'impute sur le plafond nominal global d'augmentation de capital de € 20 000 000 fixé par la première résolution de la présente Assemblée ;
5. Décide que le Conseil d'administration ne pourra, sauf autorisation préalable par l'Assemblée générale, faire usage de la présente autorisation à compter du dépôt par un tiers d'un projet d'offre publique visant les titres de la Société et ce, jusqu'à la fin de la période d'offre ;
6. Décide que la présente délégation prive d'effet la délégation de même nature consentie par l'Assemblée générale extraordinaire des actionnaires du 28 avril 2021 dans sa sixième résolution à hauteur de la partie non utilisée de cette délégation.

La délégation ainsi conférée au Conseil d'administration est valable pour une durée de 26 mois à compter de la date de la présente Assemblée générale.

HUITIEME RÉSOLUTION (*Délégation de compétence consentie au Conseil d'administration pour augmenter le capital au bénéfice d'une catégorie de bénéficiaires, avec suppression du droit préférentiel de souscription des actionnaires à leur profit*). — L'Assemblée générale, connaissance prise du rapport du Conseil d'administration et du rapport spécial des Commissaires aux comptes, après avoir constaté la libération intégrale du capital social et statuant conformément aux articles L. 225-129-2 et L. 225-138 du Code de commerce :

1. Délégué au Conseil d'administration sa compétence pour décider d'augmenter le capital social, en une ou plusieurs fois, par l'émission d'actions, de titres de capital donnant accès à d'autres titres de capital ou donnant droit à l'attribution de titres de créances de la Société ainsi que de toutes autres valeurs mobilières donnant accès à des titres de capital de la Société à émettre, lesdites actions conférant les mêmes droits que les actions anciennes, sous réserve de leur date de jouissance ; étant précisé que la souscription des actions, titres de capital et autres valeurs mobilières donnant accès à des titres de capital pourra être opérée soit en espèces, soit par compensation avec des créances certaines, liquides et exigibles ; le Conseil d'administration pouvant déléguer au Directeur général, ou en accord avec ce dernier, à un ou plusieurs directeurs généraux délégués, dans les conditions permises par la loi, tous les pouvoirs nécessaires pour décider de l'augmentation de capital ;
2. Décide que le montant nominal des augmentations de capital susceptibles d'être réalisées immédiatement ou à terme en vertu de la présente délégation, le cas échéant tel qu'augmenté en application de la cinquième résolution, ne pourra excéder un montant nominal maximum de € 15 000 000, étant précisé que ce montant s'imputera sur le sous-plafond nominal global d'augmentation de capital de € 15 000 000 fixé par la deuxième résolution de la présente Assemblée, qui lui-même s'impute sur le plafond nominal global d'augmentation de capital de € 20 000 000 fixé par la première résolution de la présente Assemblée et que ce montant ne tient pas compte des actions supplémentaires à émettre pour préserver les droits des porteurs de valeurs mobilières donnant accès au capital conformément aux dispositions légales et réglementaires applicables ainsi que, le cas échéant, aux stipulations contractuelles prévoyant d'autres cas d'ajustement ;
3. Décide qu'est expressément exclue toute émission d'actions de préférence et de valeurs mobilières donnant accès à des actions de préférence ;
4. Décide que le montant nominal maximal des valeurs mobilières représentatives de titres de créances susceptibles d'être émises en vertu de la présente délégation ne pourra être supérieur à € 50 millions ou à la contre-valeur de ce montant en monnaies étrangères ou unités de compte fixées par référence à plusieurs monnaies, étant précisé que ce montant s'imputera sur le plafond de € 100 millions prévu à la première résolution ;
5. Décide de supprimer le droit préférentiel de souscription des actionnaires aux actions, titres de capital ou autres valeurs mobilières faisant l'objet de la présente résolution et de réserver le droit de les souscrire, pour une émission donnée, à :
 - (i) une ou plusieurs sociétés ou fonds gestionnaire d'épargne collective de droit français ou de droit étranger investissant dans le secteur pharmaceutique/biotechnologique ;
 - (ii) des personnes physiques investissant à titre habituel dans le secteur pharmaceutique/biotechnologique ;
 - (ii) un ou plusieurs établissements de crédit ou tout prestataire de services d'investissement habilité s'engageant à les acquérir pour les revendre aux personnes visées au (i) et (ii) ci-dessus ;
6. Constate que la présente délégation emporte, au profit des porteurs de valeurs mobilières donnant accès au capital de la Société, renonciation des actionnaires à leur droit préférentiel de souscription aux titres de capital auxquels les valeurs mobilières émises donnent droit ;

7. Décide que le Conseil d'administration arrêtera les caractéristiques, montant et modalités de toute émission ainsi que les modalités de libération des titres émis. Notamment, il déterminera le nombre de titres à émettre au profit de chaque bénéficiaire et fixera, compte tenu des indications contenues dans son rapport, le prix de souscription desdits titres, leur date de jouissance, étant précisé que la somme revenant, ou devant revenir, à la Société pour chacune des actions émises dans le cadre de la présente délégation sera au moins égale à la moyenne pondérée des cours de l'action de la Société sur le marché réglementé d'Euronext à Paris lors des trois dernières séances de bourse précédant la fixation du prix d'émission, cette moyenne pouvant le cas échéant être corrigée pour tenir compte des différences de date de jouissance et être éventuellement diminuée d'une décote maximum de 15 % ; étant précisé à toutes fins utiles que le prix d'émission des valeurs mobilières donnant accès au capital sera tel que la somme perçue immédiatement par la Société, majorée le cas échéant de celle susceptible d'être perçue ultérieurement par elle, soit, pour chaque action émise en conséquence de l'émission de ces valeurs mobilières, au moins égale au prix minimum susmentionné ;
8. Décide que le Conseil d'administration ne pourra, sauf autorisation préalable par l'Assemblée générale, faire usage de la présente autorisation à compter du dépôt par un tiers d'un projet d'offre publique visant les titres de la Société et ce, jusqu'à la fin de la période d'offre ;
9. Décide que la présente délégation prive d'effet la délégation de même nature consentie par l'Assemblée générale extraordinaire des actionnaires du 28 avril 2021 dans sa septième résolution.

La délégation ainsi conférée au Conseil d'administration est valable pour une durée de 18 mois à compter de la présente Assemblée.

NEUVIEME RÉOLUTION (*Délégation de compétence consentie au Conseil d'administration pour augmenter le capital au profit des adhérents à un plan d'épargne d'entreprise avec suppression du droit préférentiel de souscription des actionnaires à leur profit*). — L'Assemblée générale, connaissance prise du rapport du Conseil d'administration et du rapport spécial des Commissaires aux comptes, dans le cadre des dispositions des articles L. 3332-1 et suivants du Code du travail et des articles L. 225-129-2, L. 225-138-1, et L. 228-91 et L. 228-92 du Code de commerce et conformément à l'article L. 225-129-6 de ce même Code :

1. Délègue au Conseil d'administration sa compétence pour décider d'augmenter, en une ou plusieurs fois, le capital social de la Société d'un montant nominal maximum de € 60 000, par émission d'actions ou d'autres titres donnant accès au capital de la Société, réservée aux adhérents à un plan d'épargne entreprise de la Société et des entreprises françaises ou étrangères qui lui sont liées dans les conditions de l'article L. 225-180 du Code de commerce et de l'article L. 3344-1 du Code du travail ;
2. Décide que le prix de souscription des actions nouvelles sera au moins égal à 70 % de la moyenne pondérée des cours de l'action de la Société sur le marché réglementé d'Euronext à Paris lors des 20 séances de bourse précédant le jour de la décision fixant la date d'ouverture des souscriptions lorsque la durée d'indisponibilité prévue par le plan d'épargne est inférieure à 10 ans, et à 60 % de cette moyenne lorsque ladite durée d'indisponibilité est supérieure ou égale à 10 ans. Toutefois, l'Assemblée générale autorise expressément le Conseil d'administration, s'il le juge opportun, à réduire ou supprimer les décotes susmentionnées, dans les limites légales et réglementaires, afin de tenir compte, inter alia, des régimes juridiques, comptables, fiscaux et sociaux applicables dans les pays de résidence des adhérents à un plan d'épargne bénéficiaires de l'augmentation de capital ;
3. Le Conseil d'administration en application de l'article L. 3332-21 du Code du travail pourra également décider de substituer tout ou partie de la décote par l'attribution gratuite d'actions ou d'autres titres donnant accès au capital de la Société, existants ou à émettre, l'avantage total résultant de cette attribution et, le cas échéant, de la décote mentionnée ci-dessus, ne pouvant excéder l'avantage total dont auraient bénéficié les adhérents au plan d'épargne si cet écart avait été de 30 % ou de 40 % lorsque la durée d'indisponibilité prévue par le plan est supérieure ou égale à 10 ans ;

4. Décide en application de l'article L. 3332-21 du Code du travail que le Conseil d'administration pourra également décider l'attribution, à titre gratuit, d'actions à émettre ou déjà émises ou d'autres titres donnant accès au capital de la Société à émettre ou déjà émis, au titre de l'abondement, sous réserve que la prise en compte de leur contre-valeur pécuniaire, évaluée au prix de souscription, n'ait pour effet de dépasser les limites prévues à l'article L. 3332-11 du Code du travail ;
5. Décide de supprimer le droit préférentiel de souscription des actionnaires aux actions nouvelles à émettre ou autres titres donnant accès au capital et aux titres auxquels donneront droit ces titres émis en application de la présente résolution en faveur des adhérents à un plan d'épargne entreprise défini au premier paragraphe ;
6. Décide que les caractéristiques des autres titres donnant accès au capital de la Société seront arrêtées par le Conseil d'administration dans les conditions fixées par la réglementation ;
7. Décide que Conseil d'administration aura tous pouvoirs, avec faculté de délégation ou de subdélégation, conformément aux dispositions légales et réglementaires, pour mettre en œuvre la présente résolution et notamment pour fixer les modalités et conditions des opérations et arrêter les dates et les modalités des émissions qui seront réalisées en vertu de la présente autorisation, fixer les dates d'ouverture et de clôture des souscriptions, les dates de jouissance des titres émis, les modalités de libération des actions et des autres titres donnant accès au capital de la Société, consentir des délais pour la libération des actions et, le cas échéant, des autres titres donnant accès au capital de la Société, demander l'admission en bourse des titres créés partout où il avisera, constater la réalisation des augmentations de capital à concurrence du montant des actions qui seront effectivement souscrites, accomplir, directement ou par mandataire, toutes opérations et formalités liées aux augmentations du capital social et sur sa seule décision et, s'il le juge opportun, imputer les frais des augmentations de capital sur le montant des primes afférentes à ces augmentations et prélever sur ce montant les sommes nécessaires pour porter la réserve légale au dixième du nouveau capital après chaque augmentation ;
8. Décide que le montant nominal maximal des augmentations de capital susceptibles d'être réalisées en vertu de la présente délégation s'imputera sur le plafond nominal global d'augmentation de capital de € 20 000 000 fixé par la première résolution de la présente Assemblée ;
9. Décide que la présente délégation prive d'effet la délégation de même nature consentie par l'Assemblée générale extraordinaire des actionnaires du 28 avril 2021 dans sa huitième résolution.

La délégation ainsi conférée au Conseil d'administration est valable pour une durée de 26 mois à compter de la présente Assemblée.

DIXIEME RÉOLUTION (*Autorisation donnée au Conseil d'administration pour procéder à des attributions gratuites d'actions existantes ou à émettre, emportant de plein droit renonciation des actionnaires à leur droit préférentiel de souscription*). — L'Assemblée générale, connaissance prise du rapport du Conseil d'administration et du rapport spécial des Commissaires aux comptes, conformément aux articles L. 225-197-1 et suivants, L. 22-10-59 et L. 22-10-60 du Code de commerce :

1. Autorise le Conseil d'administration à procéder, en une ou plusieurs fois, à des attributions gratuites d'actions existantes ou à émettre de la Société, au profit des membres du personnel ou de certaines catégories d'entre eux qu'il déterminera parmi les salariés et les mandataires sociaux éligibles de la Société ou des sociétés liées au sens de l'article L. 225-197-2 Code de commerce ;
2. Décide que le Conseil d'administration déterminera l'identité des bénéficiaires des attributions ainsi que les conditions et les critères d'attribution des actions, étant précisé que l'acquisition définitive des actions sera soumise à des conditions de performance qui seront fixées par le Conseil d'administration au moment de leur attribution ;

3. Décide que les attributions gratuites d'actions effectuées en vertu de cette autorisation ne pourront excéder 1 000 000 actions existantes ou nouvelles d'une valeur nominale de un euro, étant par ailleurs précisé que le montant nominal maximum des augmentations de capital susceptibles d'être réalisées immédiatement ou à terme en vertu de la présente résolution ne pourra excéder € 1 000 000, ces montants ne tenant pas compte des éventuels ajustements susceptibles d'être opérés conformément aux dispositions législatives et réglementaires applicables et, le cas échéant, aux stipulations contractuelles prévoyant d'autres cas d'ajustement, pour préserver les droits des porteurs de valeurs mobilières ou autres droits donnant accès au capital. A cette fin, l'Assemblée générale autorise, en tant que de besoin, le Conseil d'administration à augmenter le capital social par incorporation de réserves à due concurrence ;
4. Décide que l'attribution des actions à leurs bénéficiaires deviendra définitive au terme d'une période d'acquisition dont la durée sera fixée par le Conseil d'administration, étant entendu que cette durée ne pourra être inférieure à un an, et que les bénéficiaires devront, si le Conseil d'administration l'estime utile ou nécessaire, conserver lesdites actions pendant une durée librement fixée par le Conseil d'administration, étant précisé que la durée cumulée des périodes d'acquisition, et le cas échéant de conservation, ne pourra être inférieure à deux ans ;
5. Décide par ailleurs que dans l'hypothèse de l'invalidité du bénéficiaire correspondant au classement dans la deuxième ou troisième des catégories prévues à l'article L. 341-4 du Code de la sécurité sociale, les actions lui seront attribuées définitivement avant le terme de la période d'acquisition restant à courir. Lesdites actions seront librement cessibles à compter de leur livraison ;
6. La présente autorisation emporte de plein droit au profit des bénéficiaires renonciation des actionnaires à leur droit préférentiel de souscription aux actions qui seraient émises en vertu de la présente résolution ;
7. Décide d'autoriser le Conseil d'administration à prendre toutes mesures qu'il jugera utiles destinées à protéger les droits des bénéficiaires de droits à l'attribution gratuite d'actions pendant la période d'acquisition ;
8. Délègue tous pouvoirs au Conseil d'administration, avec faculté de délégation dans les conditions légales et réglementaires, pour mettre en œuvre la présente autorisation, dans les conditions ci-dessus et dans les limites autorisées par les textes en vigueur et notamment, fixer, le cas échéant, les modalités et conditions des émissions qui seraient réalisées en vertu de la présente autorisation, les dates de jouissance des actions nouvelles, constater la réalisation des augmentations de capital, modifier les statuts en conséquence, et plus généralement, accomplir toutes les formalités utiles à l'émission, à la cotation et au service financier des titres émis en vertu de la présente résolution et faire tout ce qui sera utile et nécessaire dans le cadre des lois et règlements en vigueur ;
9. Décide que la présente autorisation prive d'effet pour sa partie non utilisée l'autorisation ayant le même objet consentie par l'Assemblée générale extraordinaire des actionnaires du 28 avril 2021 dans sa dixième résolution ;
10. Décide que la présente autorisation est valable pour une durée de 38 mois à compter de la présente Assemblée.

Le Conseil d'administration informera chaque année l'Assemblée générale ordinaire, dans les conditions légales et réglementaires, en particulier l'article L. 225-197-4 du Code de commerce, des opérations réalisées dans le cadre de la présente autorisation.

ONZIEME RÉSOLUTION (Autorisation donnée au Conseil d'administration pour consentir des options donnant droit à la souscription d'actions nouvelles de la Société ou à l'achat d'actions existantes, emportant de plein droit renonciation des actionnaires à leur droit préférentiel de souscription). — L'Assemblée générale, connaissance prise du rapport du Conseil d'administration et du rapport spécial des Commissaires aux comptes, conformément aux articles L. 225-177 et suivants, L. 22-10-56 à L. 22-10-58 du Code de commerce :

1. Autorise le Conseil d'administration à consentir, en une ou plusieurs fois, aux salariés et mandataires sociaux, ou à certaines catégories d'entre eux, de la Société et des sociétés qui lui seraient liées au sens de l'article L. 225-180 du Code de commerce, détenant moins de 10 % du capital de la Société, des options donnant droit à la souscription d'actions nouvelles de la Société ou à l'achat d'actions existantes, dans la limite d'un nombre maximum de 2 500 000 actions existantes ou nouvelles, d'une valeur nominale de un euro chacune, étant par ailleurs précisé que le montant nominal maximum des augmentations de capital susceptibles d'être réalisées immédiatement ou à terme en vertu de la présente résolution ne pourra excéder € 2 500 000, ces montants ne tenant pas compte des éventuels ajustements susceptibles d'être opérés conformément aux dispositions législatives et réglementaires applicables et, le cas échéant, aux stipulations contractuelles prévoyant d'autres cas d'ajustement, pour préserver les droits des porteurs de valeurs mobilières ou autres droits donnant accès au capital ;
2. Décide que le prix de souscription des actions nouvelles ou d'achat des actions existantes par exercice des options sera déterminé par le Conseil le jour de l'attribution des options de la façon suivante :
 - Le prix de souscription des actions nouvelles ne pourra être inférieur à 80 % de la moyenne pondérée des cours de l'action de la Société sur le marché réglementé d'Euronext à Paris lors des 20 séances de bourse précédant la séance du Conseil ;
 - Le prix d'achat des actions existantes ne pourra être inférieur au plus élevé des deux montants suivants : (a) 80 % de la moyenne pondérée des cours de l'action de la Société sur le marché réglementé d'Euronext à Paris lors des 20 séances de bourse précédant la séance du Conseil et (b) le cours moyen d'achat des actions détenues par la Société au titre de l'article L. 22-10-62 du Code de commerce ;
 - Si les actions de la Société cessaient d'être admises aux négociations sur un marché réglementé, le prix de souscription ou d'achat des actions par exercice des options sera déterminé par le Conseil conformément à l'article L. 225-177 du Code de commerce. Dans la seule hypothèse des options d'achat d'actions, le prix ainsi déterminé par le Conseil ne pourra en aucun cas être inférieur au prix moyen d'achat des actions éventuellement détenues par la Société ;

Le prix d'exercice des options, tel que déterminé ci-dessus, ne pourra être modifié sauf en cas de mise en œuvre, conformément à l'article L. 225-181 du Code de commerce, des mesures nécessaires à la protection des intérêts des bénéficiaires des options dans les conditions légales et réglementaires.

3. Prend acte qu'aucune option ne pourra être consentie moins de vingt séances de bourse après le détachement des actions d'un coupon donnant droit à un dividende ou à une augmentation de capital ;
4. Prend acte qu'aucune option ne pourra être consentie (i) dans le délai de dix séances de bourse précédant la date à laquelle les comptes consolidés annuels et intermédiaires ou, à défaut, les comptes annuels et semestriels de la société sont rendus publics ainsi que le jour de la publication et (ii) dans le délai compris entre la date à laquelle les organes sociaux ont connaissance d'une information privilégiée au sens de l'article 7 du règlement (UE) n° 596/2014 du Parlement européen et du Conseil du 16 avril 2014 sur les abus de marché et la date à laquelle cette information est rendue publique ;
5. Prend acte de ce que la présente autorisation comporte, au profit des bénéficiaires des options de souscription d'actions, renonciation expresse des actionnaires à leur droit préférentiel de souscription aux actions qui seraient émises au fur et à mesure des levées d'options ;
6. Décide que les options devront être exercées dans un délai maximum de huit ans à compter de leur attribution par le Conseil d'administration, celui-ci pouvant toutefois réduire ce délai pour les bénéficiaires résidents de pays dans lesquels une durée inférieure est prévue par la loi ;

7. Délègue tous pouvoirs au Conseil d'administration à l'effet de mettre en œuvre la présente autorisation et notamment de :
- arrêter la liste des bénéficiaires et le nombre d'options consenties à chacun d'eux ;
 - fixer les modalités et conditions des options et, notamment ;
 - la durée de validité des options dans la limite fixée ci-dessus ;
 - la ou les dates ou période d'exercice des options, étant entendu que le Conseil d'administration pourra (a) anticiper les dates ou périodes d'exercice des options, (b) maintenir le caractère exerçable des options, ou (c) modifier les dates ou périodes pendant lesquelles les actions obtenues par l'exercice des options ne pourront être cédées ou mises au porteur ;
 - des clauses éventuelles d'interdiction de revente immédiate de tout ou partie des actions sans que le délai imposé pour la conservation des titres puisse excéder trois ans à compter de la levée de l'option sans préjudice des dispositions prévues par l'article L. 225-185 alinéa 4 du Code de commerce ;
 - le cas échéant, limiter, suspendre, restreindre ou interdire l'exercice des options ou la cession ou la mise au porteur des actions obtenues par l'exercice des options, pendant certaines périodes ou à compter de certains événements, sa décision pouvant porter sur tout ou partie des options ou des actions ou concerner tout ou partie des bénéficiaires ;
 - arrêter les conditions d'exercice et de suspension temporaire d'exercice des options consenties, réaliser toutes les opérations qui seront nécessaires, arrêter la date de jouissance des actions nouvelles provenant de l'exercice des options, constater la réalisation des augmentations de capital à concurrence des actions souscrites par exercice des options, modifier les statuts en conséquence, le cas échéant, imputer les frais des augmentations de capital sur le montant des primes qui y sont afférentes et prélever sur ce montant les sommes nécessaires pour porter la réserve légale au dixième du nouveau capital après chaque augmentation de capital, et plus généralement, accomplir toutes les formalités utiles à l'émission, à la cotation et au service financier des titres émis en vertu de la présente résolution et faire tout ce qui sera utile et nécessaire dans le cadre des lois et règlements en vigueur.
8. Décide que l'exercice des options sera, s'agissant des bénéficiaires qui sont membres du Comité de direction ou mandataire social, soumis à des conditions de performance qui seront fixées par le Conseil d'administration au moment de leur attribution ;
9. Décide que la présente autorisation prive d'effet pour sa partie non utilisée l'autorisation ayant le même objet consentie par l'Assemblée générale extraordinaire du 28 avril 2021 sous sa onzième résolution.
10. Décide que la présente autorisation est valable pour une durée de 38 mois à compter de la présente Assemblée.

Le Conseil, conformément à l'article L. 225-184 du Code de commerce, informera chaque année l'Assemblée générale ordinaire des opérations réalisées dans le cadre de la présente résolution.

DOUZIEME RÉOLUTION (*Autorisation à conférer au Conseil d'administration à l'effet de réduire le capital social par annulation d'actions précédemment rachetées dans le cadre d'un programme de rachat d'actions*). — L'Assemblée générale, connaissance prise du rapport du Conseil d'administration et du rapport spécial des Commissaires aux comptes, conformément aux articles L. 22-10-62 et suivants du Code de commerce, autorise le Conseil d'administration à :

- réduire le capital social par voie d'annulation, en une ou plusieurs fois, de tout ou partie des actions acquises par la Société dans le cadre d'un programme de rachat de ses propres actions, et ce dans la limite de 10 % du capital par périodes de 24 mois ; et
- imputer la différence entre la valeur de rachat des actions annulées et leur valeur nominale sur les postes de primes et réserves disponibles.

L'Assemblée générale donne, plus généralement, à cet effet tous pouvoirs au Conseil d'administration pour fixer les conditions et modalités de cette ou de ces réductions de capital, constater la réalisation de la ou des réductions du capital consécutives aux opérations d'annulations autorisées par la présente résolution, modifier, le cas échéant, les statuts de la Société en conséquence, effectuer toutes déclarations auprès de l'Autorité des marchés financiers ou tout autre organisme, remplir toutes formalités et plus généralement faire le nécessaire à la bonne fin de cette opération.

Cette autorisation est donnée pour cinq ans et expire à l'issue de l'Assemblée générale ordinaire annuelle appelée à statuer sur les comptes de l'exercice clos le 31 décembre 2025. Elle prive d'effet pour sa partie non utilisée l'autorisation ayant le même objet consentie par l'Assemblée générale extraordinaire du 28 avril 2021 sous sa douzième résolution.

TREIZIEME RÉSOLUTION (*Modification des statuts pour porter à 75 ans la limite d'âge du Président du Conseil d'administration*). — L'Assemblée générale, connaissance prise du rapport du Conseil d'administration, décide de modifier l'article 14 des statuts de la Société comme suit :

« Le Conseil d'administration élit parmi ses membres un Président qui est, à peine de nullité de la nomination, une personne physique.

Il détermine sa rémunération et la durée de ses fonctions sans qu'elle puisse excéder celle de son mandat d'administrateur.

Le Président du Conseil d'administration doit être âgé de moins de 75 ans. Lorsqu'en cours de mandat cette limite d'âge aura été atteinte, le Président du Conseil d'administration sera réputé démissionnaire d'office.

Son mandat se prolonge cependant jusqu'à la réunion la plus prochaine du Conseil d'administration au cours de laquelle il sera procédé à la désignation d'un nouveau Président dans les conditions prévues au présent article.

Le Président organise et dirige les travaux du Conseil d'administration dont il rend compte à l'Assemblée Générale.

Il veille au bon fonctionnement des organes de la société et s'assure que les administrateurs sont en mesure de remplir leur mission. »

QUATORZIEME RÉSOLUTION (*Pouvoirs à donner en vue des formalités*). — L'Assemblée générale donne tous pouvoirs au porteur d'une copie ou d'un extrait du procès-verbal des présentes en vue de l'accomplissement des formalités légales.

1. Formalités préalables à effectuer pour participer à l'Assemblée générale

Tout actionnaire, quel que soit le nombre d'actions qu'il possède, peut participer à l'Assemblée générale. Les actionnaires peuvent choisir entre l'une des trois modalités suivantes de participation :

- Assister personnellement à l'Assemblée générale ;
- Donner procuration à toute personne de leur choix dans les conditions légales et réglementaires applicables ou adresser une procuration à la Société sans indication de mandataire ;
- Voter par correspondance **ou par Internet via le site VOTACCESS** ou à adresser une procuration à la **Société sans indication de mandataire.**

Pour pouvoir assister à l'Assemblée générale, s'y faire représenter ou voter par correspondance ou à distance, les actionnaires devront justifier de l'inscription des titres à leur nom ou à celui de l'intermédiaire inscrit pour leur compte le deuxième jour ouvré précédant l'Assemblée générale, soit le jeudi 7 juillet 2022 à zéro heure (heure de Paris, France), soit dans les comptes de titres nominatifs tenus par la Société, soit dans les comptes de titres au porteur tenu par l'intermédiaire habilité.

L'inscription en compte des titres dans les comptes de titres au porteur tenus par l'intermédiaire habilité devra être constatée par une attestation de participation délivrée par ce dernier, jointe au formulaire de vote à distance ou de procuration de vote ou à la demande de carte d'admission établie au nom de l'actionnaire ou pour le compte de l'actionnaire représenté par l'intermédiaire inscrit.

Une attestation sera également délivrée à l'actionnaire souhaitant participer personnellement à l'Assemblée générale et qui n'a pas reçu sa carte d'admission le deuxième jour ouvré précédant l'Assemblée générale, soit le jeudi 7 juillet 2022 à zéro heure (heure de Paris, France),

2. Mode de participation à l'Assemblée générale

Les actionnaires désirant assister personnellement à l'Assemblée générale peuvent demander leur carte d'admission soit par voie postale, soit par voie électronique.

2.1 Demande de carte d'admission par voie postale

- **Pour l'actionnaire au nominatif (pur et administré)** : il convient d'adresser le formulaire unique dûment rempli et signé, à la Société Générale à l'aide de l'enveloppe de réponse prépayée jointe à la convocation.

Les demandes de cartes d'admission devront, pour être prises en compte, parvenir à Nicox ou à la Société Générale, au plus tard le vendredi 8 juillet 2022.

- **Pour l'actionnaire au porteur** : il convient d'adresser une demande à l'intermédiaire habilité qui assure la gestion de son compte titres.

2.2 Demande de carte d'admission par voie électronique

- **Pour l'actionnaire au nominatif (pur et administré)** : il convient d'adresser la demande en se connectant sur le site internet www.sharinbox.societegenerale.com grâce aux identifiants préalablement reçus avec ses codes habituels.

Pour l'actionnaire au porteur : il appartient à l'actionnaire au porteur de se renseigner afin de savoir si son intermédiaire financier teneur de compte est connecté ou non au site Votaccess et, le cas échéant, si cet accès est soumis à des conditions d'utilisation particulière.

Si l'établissement teneur de compte de l'actionnaire est connecté au site Votaccess, l'actionnaire au porteur devra s'identifier sur le portail internet de son établissement teneur de compte avec ses codes d'accès habituels. Il devra ensuite cliquer sur l'icône qui apparaît sur la ligne correspondant à ses actions Nicox et suivre les indications données à l'écran afin d'accéder au site Votaccess et demander une carte d'admission.

Tout actionnaire ayant déjà exprimé son vote à distance, envoyé un pouvoir ou demandé sa carte d'admission ou une attestation de participation (dans les conditions définies au paragraphe II de l'article R.225 -85), ne peut plus choisir un autre mode de participation à l'Assemblée.

3. Vote par correspondance ou par procuration

3.1 Vote par correspondance ou par procuration par voie postale

Les actionnaires n'assistant pas personnellement à l'Assemblée générale et souhaitant voter par correspondance ou être représentés en donnant pouvoir au Président de l'Assemblée générale ou à un mandataire pourront renvoyer le formulaire unique de vote par correspondance ou par procuration. Ledit formulaire sera transmis sur demande par lettre simple adressé à Nicox, Drakkar D, 2405 route des Dolines, 06560 Valbonne, Sophia-Antipolis ou à Société Générale, Service des Assemblées, CS 30812 - 44308 Nantes Cedex 3. Par exception, les actionnaires au nominatif recevront directement le formulaire unique de vote par correspondance ou par procuration dans le pli de convocation qui leur sera adressé.

Il est rappelé que, conformément à la loi et aux statuts :

- la demande du formulaire unique devra avoir été reçue par la Société ou la Société Générale six jours au moins avant la réunion de l'Assemblée générale, soit le mardi 5 juillet 2022 au plus tard ;
- les votes par correspondance ou par procuration ne seront pris en compte que pour les formulaires dûment remplis et incluant, le cas échéant, l'attestation de participation, parvenus à la Société ou à Société Générale trois jours au moins avant la réunion de l'Assemblée générale, soit le vendredi 8 juillet 2022 au plus tard.

Les actionnaires peuvent révoquer leur mandataire, étant précisé que la révocation, qui devra être communiquée à la Société, devra être faite dans les mêmes formes que celles requises pour la désignation du mandataire conformément à l'article R. 225-79, alinéa 5 du Code de commerce.

Afin que les désignations ou révocations de mandats par courrier postal puissent être prises en compte, les confirmations devront être réceptionnées au plus tard le vendredi 8 juillet 2022.

3.2 Vote par correspondance ou par procuration par voie électronique

Les actionnaires ont également la possibilité de transmettre leurs instructions de vote et désigner ou révoquer un mandataire par internet avant l'Assemblée générale, dans les conditions décrites ci-après :

Conformément aux dispositions de l'article R. 225-61 du Code de commerce, la Société met à la disposition de ses actionnaires un site sécurisé dédié au vote par internet préalable à l'Assemblée générale dans les conditions suivantes :

- **Pour l'actionnaire au nominatif (pur et administré) :** il convient de se connecter sur le site sécurisé www.sharinbox.societegenerale.com accessible à l'aide du code d'accès et du mot de passe adressés par courrier lors de l'entrée de l'actionnaire en relation avec Société Générale Securities Services. Après s'être connecté, l'actionnaire au nominatif devra suivre les indications données à l'écran afin d'accéder au site Votaccess et voter ou désigner ou révoquer un mandataire.
- **Pour l'actionnaire au porteur :** il convient de se connecter sur le portail de son intermédiaire financier à l'aide de ses identifiants habituels pour accéder au site. L'actionnaire au porteur devra ensuite cliquer sur l'icône qui apparaît sur la ligne correspondant à ses actions Nicox et suivre les indications données à l'écran afin d'accéder au site Votaccess et voter ou désigner ou révoquer un mandataire. Il est précisé que seuls les titulaires d'actions au porteur dont l'établissement teneur de compte a adhéré au système Votaccess pourront accéder.

Le site internet Votaccess sera ouvert du mercredi 22 juin 2022 à 9 heures au dimanche 10 juillet 2022 à 15 heures (heure de Paris, France). Afin d'éviter toute saturation éventuelle du site internet dédié, il est recommandé aux actionnaires de ne pas attendre cette date ultime pour se connecter au site.

Conformément aux dispositions de l'article R. 22-10-24 du Code de commerce, si l'établissement teneur de compte n'a pas adhéré au système Votaccess, la notification de la désignation et de la révocation d'un mandataire peut être faite par voie électronique. Les envois par email sont assimilés à des envois papier, le délai de réception devrait être J-3 soit le vendredi 8 juillet, en envoyant un courriel signé électroniquement à l'aide d'un procédé de signature électronique résultant d'un procédé fiable d'identification de l'actionnaire garantissant son lien avec le contenu du courriel auquel elle s'attache (l'actionnaire faisant son affaire de l'obtention des certificats ou clefs de signature électronique), à l'adresse ag2022nicox@nicox.com et incluant les informations suivantes :

- **Pour l'actionnaire au nominatif (pur et administré) :** nom, prénom, adresse et l'identifiant Société Générale pour l'actionnaire au nominatif pur (information disponible en haut et à gauche de leur relevé de compte) ou l'identifiant auprès de l'intermédiaire habilité pour l'actionnaire au nominatif administré, ainsi que les nom, prénom et adresse du mandataire désigné ou révoqué ;
- **Pour l'actionnaire au porteur :** nom, prénom, adresse, et références bancaires complètes, ainsi que les nom, prénom et adresse du mandataire désigné ou révoqué. L'actionnaire au porteur devra impérativement demander à son intermédiaire financier qui assure la gestion de son compte titres

d'envoyer une confirmation à Nicox SA, Drakkar D, 2405 route des Dolines, 06560 Valbonne, Sophia-Antipolis.

L'adresse électronique ci-dessus ne pourra traiter que les demandes de désignation ou de révocation de mandataires, toute autre demande ne pourra pas être prise en compte.

4. Faculté d'inscription à l'ordre du jour de points ou de projets de résolutions

Les demandes d'inscription à l'ordre du jour de points ou de projets de résolution doivent être envoyés par lettre recommandée avec demande d'avis de réception au siège social de la Société, à l'attention du Président du Conseil d'administration, et reçues au plus tard le vingt-cinquième jour qui précède la date de l'Assemblée générale, soit au plus tard le jeudi 16 juin 2022, pour les actionnaires remplissant les conditions de l'article R.225-71 du Code de commerce (c'est-à-dire représentant un pourcentage minimum de capital).

La demande d'inscription d'un point à l'ordre du jour doit être motivée.

La demande d'inscription de projets de résolution est accompagnée du texte des projets de résolution assortis d'un bref exposé des motifs.

Ces demandes doivent être accompagnées d'une attestation d'inscription en compte. Il est en outre rappelé que l'examen par l'Assemblée générale des points ou des résolutions qui seront présentés est subordonné à la transmission par les intéressés, au plus tard le deuxième jour ouvré précédant l'Assemblée générale, soit le jeudi 7 juillet 2022 à zéro heure (heure de Paris, France), d'une nouvelle attestation justifiant de l'inscription de leurs titres dans les mêmes conditions que celles indiquées ci-dessus.

Le texte des points et des projets de résolution ajoutés à l'ordre du jour présentés par les actionnaires seront publiés sans délai sur le site internet de la Société susmentionné.

5. Questions écrites

Les actionnaires peuvent adresser des questions écrites au plus tard le quatrième jour ouvré précédant la date de l'Assemblée générale, soit au plus tard le mardi 5 juillet 2022, par lettre recommandée avec demande d'avis de réception au siège social de la Société, ou à l'adresse ag2022nicox@nicox.com à l'attention du Président du Conseil d'administration. Elles doivent impérativement être accompagnées d'une attestation d'inscription en compte.

6. Prêt-emprunt de titres

Conformément aux dispositions de l'article L. 22-10-48 du Code de commerce, il est rappelé que toute personne qui détient seule ou de concert, au titre d'une ou plusieurs opérations de cession temporaire portant sur les actions de la Société ou de toute opération lui donnant le droit ou lui faisant obligation de revendre ou de restituer ces actions au cédant, un nombre d'actions représentant plus du deux-centième (0,5 %) des droits de vote, doit informer la Société et l'Autorité des marchés financiers, au plus tard le deuxième jour ouvré précédant l'Assemblée générale, soit le jeudi 7 juillet 2022 à zéro heure (heure de Paris, France), et lorsque le contrat organisant cette opération demeure en vigueur à cette date, du nombre total d'actions qu'elle possède à titre temporaire. A défaut d'information dans les conditions qui précèdent, les actions sont privées de droit de vote pour l'Assemblée générale concernée et toute autre assemblée d'actionnaires qui se tiendrait jusqu'à la revente ou la restitution desdites actions.

7. Informations et documents mis à disposition

Les informations visées à l'article R. 22-10-23 du Code de Commerce, notamment les documents destinés à être présentés à l'Assemblée générale, seront publiées sur le site internet de la Société www.nicox.com, au plus tard le vingt-et-unième jour précédant l'Assemblée générale, soit le lundi 20 juin 2022 au plus tard. Ils seront également disponibles et consultables au siège social de la Société.

Le Conseil d'administration

NICOX SA

AGENDA AND SUMMARY OF THE DRAFT RESOLUTIONS

EXTRAORDINARY SHAREHOLDER MEETING

CONVENED ON JULY 11, 2022
(AND ON SECOND CALL ON JULY 28, 2022)

Agenda of the extraordinary meeting

- Delegation of competence to the Board of Directors to issue shares, equity securities giving right to other equity securities or debt securities and other securities giving access to newly issued equity securities of the Company, with preferential right of subscription of the shareholders (resolution 1).
- Delegation of competence to the Board of Directors to issue shares, equity securities giving right to other equity securities or debt securities and other securities giving access to newly issued equity securities, without preferential right of subscription of the shareholders and by way of public offering (other than the public offering pursuant to Article L. 411-2 1° of the French Financial and Monetary Code) (resolution 2).

Delegation of competence to the Board of Directors to issue shares, equity securities giving right to other equity securities or debt securities and other securities giving access to newly issued equity securities, without preferential right of subscription of the shareholders and by way of a public offering pursuant to Article L 411-2 1° of the French Financial and Monetary Code (private placement) (resolution 3).

- Authorization to the Board of Directors to set the issue price of securities to be issued in the context of an issuance carried out pursuant to the second and third resolutions within the limit of 10% of the share capital (resolution 4).
- Authorization to the Board of Directors to increase the number of securities to be issued in the context of an issuance carried out pursuant to the first, second, third, fourth and eighth resolutions, with or without preferential right of subscription of the shareholders (resolution 5).
- Delegation of competence to the Board of Directors to increase the share capital by capitalization of reserves, provisions, premiums or other sums the capitalization of which would be permitted (resolution 6).
- Delegation of powers to the Board of Directors to increase the share capital in consideration for capital contributions in kind out of the scope of a public exchange offer, within the limit of 10% of the share capital (resolution 7).
- Delegation of competence to the Board of Directors to increase the share capital for the benefit of a category of investors without preferential right of subscription of the shareholders (resolution 8).
- Delegation of competence to the Board of Directors to increase the share capital in connection with a profit sharing plan reserved for the Company's employees without preferential right of subscription of the shareholders (resolution 9).

- Authorization to the Board of Directors to grant free shares, existing or to be issued, without preferential right of subscription of the shareholders (resolution 10).
- Authorization to the Board of Directors to grant stock-options to subscribe new shares or purchase existing shares without preferential right of subscription of the shareholders (resolution 11).
- Authorization to the Board of Directors to reduce the share capital by cancellation of previously repurchased shares in the context of a share repurchase plan (resolution 12).
- Amendment of article 14 of the by-laws (resolution 13).
- Power of attorney to complete the formalities (resolution 14).

SUMMARY OF THE RESOLUTIONS EXTRAORDINARY SHAREHOLDER MEETING

First resolution

Delegation of competence to the Board of Directors to proceed with increases in share capital (issuance of shares, equity securities giving right to other equity securities or debt securities and securities giving right to newly issued equity securities – in euro or other currencies) up to a maximum nominal amount of € 20,000,000 for a period of 26 months. Under this resolution, shareholders keep their preferential rights of subscription to the newly issued securities. This resolution includes the possibility of issuing debt securities giving right to shares up to a maximum amount € 100,000,000.

Second resolution

Delegation of competence to the Board of Directors to proceed with increases in share capital (issuance of shares, equity securities giving right to other equity securities or debt securities and securities giving right to newly issued equity securities – in euro or other currencies) by way of public offering (except public offerings within the meaning of Article L. 411-2 1° of the French Commercial Code), subject to the maximum nominal amount of € 15,000,000 (and to the global nominal amount of € 20,000,000 provided for in resolution 1) for a period of 26 months. Under this resolution, shareholders waive their preferential rights of subscription to the newly issued securities. Accordingly, the price per equity security to be issued hereunder shall be equal to no less than a 10% discount on the last three trading days weighted average price (VWAP) of the Nicox share prior to the beginning of the public offering. This resolution also includes the possibility of issuing debt securities giving right to shares up to a maximum amount € 100,000,000, subject to the global nominal amount of € 100,000,000 provided for in resolution 1. This resolution can also be used to issue securities in connection with a public exchange offer initiated by the Company on the securities of another company pursuant to Article L. 22-10-54 of the French Commercial Code.

(The maximum nominal amount of € 15,000,000 under this resolution applies globally to all the authorizations under resolutions 2, 3, 4, 7 and 8)

Third resolution

Delegation of competence to the Board of Directors to proceed with increases in share capital (issuance of shares, equity securities giving right to other equity securities or debt securities and securities giving right to newly issued equity securities – in euros or other currencies) by

way of a private placement (qualified as a public offering within the meaning of Article L. 411-2 1° of the French Commercial Code, since the entry into force of the new EU prospectus regulation in July 2019), subject to the maximum nominal amount of € 15,000,000 and a maximum of 20% of the share capital per year (as well as to both (i) the nominal amount of € 15,000,000 provided for in resolution 2 and (ii) the global nominal amount of € 20,000,000 provided for in resolution 1) for a period of 26 months. Under this resolution, shareholders waive their preferential rights of subscription to the newly issued securities. Accordingly, the price per equity security to be issued hereunder shall be equal to no less than a 10% discount on the last three trading days weighted average price (VWAP) of the Nicox share prior to the beginning of the public offering. This resolution also includes the possibility of issuing debt securities giving right to shares up to a maximum amount € 100,000,000, subject to the global nominal amount of € 100,000,000 provided for in resolution 1.

(The maximum nominal amount of € 15,000,000 applies globally to all the authorizations under resolutions 2, 3, 4, 7 and 8)

Fourth resolution

Authorization to the Board of Directors, for a period of 26 months, to set the issue price of securities to be issued in the context of an increase of the share capital under resolutions 2 and 3 with pricing conditions deviating from the conditions set forth in such resolutions and within the limit of 10% of the share capital. Under this resolution, the price per equity security to be issued shall be equal to no less than a 15% discount on the last three trading days weighted average price (VWAP) of Nicox share prior to pricing.

Fifth resolution

(overallotment) Authorization to the Board of Directors, for a period of 26 months, to increase the number of securities to be issued in the context of an increase of the share capital (with or without shareholders preferential rights of subscription) under resolutions 1, 2, 3 and 7, subject to the maximum nominal amounts of:

- € 20,000,000 with respect to share capital increases under resolution 1
- € 15,000,000 with respect to share capital increases under resolutions 2, 3 and 7, within 30 days of the end of the subscription period of the initial increase and within the limit of 15% of the amount thereof and under identical pricing conditions.

Sixth resolution

Delegation of competence to the Board of Directors, for a period of 26 months, to increase the share capital by incorporation of reserves, profits, premiums or other distributable amounts subject to the amount available for incorporation.

Seventh resolution

Delegation of powers to the Board of Directors, for a period of 26 months, to increase the share capital (issuance of shares, equity securities giving right to other equity securities or debt securities and securities giving right to newly issued equity securities), within the limit of 10% of said share capital and subject to both (i) the nominal amount of € 15,000,000 provided for in resolution 2 and (ii) the global nominal amount of € 20,000,000 provided for in resolution 1) for a period of 26 months, to remunerate capital contributions in kind consisting in securities of another entity. This resolution can be used in transactions where there is no public exchange offer within the meaning of Article L. 22-10-54 of the French Commercial Code.

(The maximum nominal amount of € 15,000,000 applies globally to all the authorizations under resolutions 2, 3, 4, 7 and 8)

Eighth resolution

(PIPE) Delegation of competence to the Board of Directors, subject to the maximum nominal amount of € 15,000,000 and for a period of 18 months, to increase the share capital (issuance of shares, equity securities giving right to other equity securities or debt securities and securities giving right to newly issued equity securities), for the benefit of (i) one or several companies, investment funds investing in the pharmaceutical/biotech sector, either French or foreign, or (ii) natural persons that invest on a routine basis in the pharmaceutical/ biotech sector or (iii) one or several credit institutions or authorized investment services providers committing to purchase such securities with a view to resell them to legal entities falling with the category defined in (i) and (ii) above.

- reference price: last three trading days weighted average price (VWAP) prior to pricing;
- maximum authorized discount: 15%.

This resolution is subject to the maximum nominal amount of € 20,000,000 provided for in resolution 1 and to the maximum nominal amount of € 15,000,000 provided for in resolution 2.

Under this resolution, shareholders waive their preferential rights of subscription to the newly issued securities. This resolution also includes the possibility of issuing debt securities giving right to shares up to a maximum amount € 50,000,000, subject to the global nominal amount of € 100,000,000 provided for in resolution 1.

(The maximum nominal amount of € 15,000,000 applies globally to all the authorizations under resolutions 2, 3, 4, 7 and 8)

Ninth resolution

Delegation of competence to the Board of Directors, for a period of 26 months, to proceed with increases in share capital up to a maximum nominal amount of € 60,000 in connection with profit sharing plans reserved for the Company's employees and waiver of the shareholders' preferential subscription rights.

This resolution is subject to the maximum nominal amount of € 20,000,000 provided for in resolution 1.

Tenth resolution

Authorization granted to the Board of Directors, for a period of 38 months, to grant to employees and corporate officers of the Group free shares within the limit of 1,000,000 new or existing shares, it being specified that nominal increases in share capital under this resolution may not exceed € 1,000,000. The obtaining of the shares will be subject to the achievement of performance criteria to be fixed by the Board.

The Board may choose between two possibilities:

- the attribution of shares to the beneficiaries would only become firm at the expiry of a minimum one year period and, subsequently, the shares may not be sold before an additional minimum one year period;
- the attribution of shares to the beneficiaries would only become firm at the expiry of a minimum two year period in which case the shares may then be sold immediately.

These time limits may be extended by the Board of Directors.

This resolution replaces the resolution voted by the April 28, 2021 shareholder meeting.

Eleventh resolution

Authorization granted to the Board of Directors for a period of 38 months to grant to employees and corporate officers of the group, stock options giving right to subscribe up to 2,500,000 new or existing shares, it being specified that nominal increase in share capital under this resolution may not exceed € 2,500,000. The subscription price of the shares may not be less than 80% of the weighted average price of the Nicox share over the 20 trading days preceding the date of the decision of the board to grant the stock-options. The exercise of stock-options granted to Executive Committee members and to the CEO will be subject to the achievement of performance criteria to be fixed by the Board.

This resolution replaces the resolution voted by the April 28, 2021 shareholder meeting.

Twelfth resolution

Authorization to the Board of Directors to reduce the share capital by cancelling shares that have been repurchased up to a limit of 10% of the share capital over a 24-month period. This authorization is granted for a five year period.

Thirteenth resolution

Amendment of article 14 of the by-laws to extend the age-limit for the Chairman of the Board from 70 to 75.

Fourteenth resolution

Power for legal formality requirements.

* * *

How to participate in the July 11, 2022, extraordinary shareholder meeting

All Nicox shareholders are entitled to take part in the shareholder meeting. You may:

- attend the shareholder meeting in person,
- be represented by any person or legal entity,
- give power of attorney to the Chairman,
- vote by correspondence.

Shareholders may vote by correspondence or by internet, through the website VOTACCESS or give proxy to the Company. The arrangements for physical participation in the shareholder meeting could be subject to modification in relation with the pandemic. Shareholders are invited to regularly consult the section dedicated to the 2022 shareholder meeting on the Company's website www.nicox.com.

These options are offered to you both in the attached proxy form and in a dedicated internet platform, as explained hereafter.

We are available to help you should you have any additional question regarding the shareholder meetings:

- Nicox's Investor Relations: ag2022nicox@nicox.com - +33 (0)4 97 24 53 28
-

If your shares are in REGISTERED form, please fill in the proxy form as explained below and send it in the prepaid return envelope sent with your personal notice of convening.

If your shares are in BEARER form, please fill in the proxy form as explained below and send it to the financial institution holding the shares who will in turn send it, with a share certificate to Société Générale Securities Services - Service Assemblée Générale - 32 rue du Champ de Tir - CS 30812 - 44312 NANTES Cedex 3.

IF YOUR SHARES ARE IN BEARER FORM, A SHARE CERTIFICATE ISSUED BY YOUR BANK MENTIONING THE SHAREHOLDER MEETINGS OF JULY 11, 2022, MUST ACCOMPANY YOUR PROXY FORM.

The proxy form (together with the share certificate if your shares are in bearer form) must be received on or before July 08, 2022 (or July 25, 2022, on second call if the quorum is not reached) by Société Générale Securities Services - Service Assemblée Générale - 32 rue du Champ de Tir - CS 30812 - 44312 NANTES Cedex 3.

1. How to participate using the enclosed proxy form

Please send back this proxy form to your bank, completed as explained below.

1.1. If you wish to attend the shareholder meeting in person

- Tick the corresponding box of the proxy form.
- Add your name and address or check that they are correct if they are already included.
- Date and sign the proxy form.
- Send back the proxy form to your bank (for the holders of bearer shares) or to Société Générale (if you hold registered shares).

You will receive an admission card*.

* If you have not received your admission card in the 2 days preceding the shareholders meetings, please contact us at ag2022nicox@nicox.com.

1.2. If you wish to vote without attending the shareholder meeting in person

TO GIVE PROXY TO THE CHAIRMAN	TO VOTE BY CORRESPONDENCE	TO GIVE PROXY TO ANY PERSON OR LEGAL ENTITY
<ul style="list-style-type: none"> • Tick box 2 of the proxy form. • Add your name and address or check that they are correct if they are already included. • Date and sign the proxy form. • Send back the proxy form to your bank who will send it in turn to Société Générale (with the share certificate if necessary) <u>by July 08, 2022 (or July 25, 2022 on second call)</u>. <p>Your vote will follow the Chairman's vote.</p> <p>You have voted.</p>	<ul style="list-style-type: none"> • Tick box 1 of the proxy form. • Fill in the box on the left to indicate your vote for each resolution (darkening the little box in front of each resolution number means voting against the resolution or abstention from voting). • Do not darken the little box if you wish to vote 'in favor' of a resolution. • Add your name and address or check that they are correct if they are already included. • Date and sign the proxy form. • Send back the proxy form to your bank who will send it in turn to Société Générale (with the share certificate if necessary) <u>by July 08, 2022 (or July 25, 2022 on second call)</u>. <p>You have voted.</p>	<ul style="list-style-type: none"> • Tick box 3 of the proxy form. • Add the identity and contact details of the person or legal entity that will represent you. • Add your name and address or check that they are correct if they are already included. • Date and sign the proxy form. • Send back the proxy form to your bank who will send it in turn to Société Générale (with the share certificate if necessary) <u>by July 08, 2022 (or July 25, 2022 on second call)</u>. <p>You have given proxy.</p>

The proxy form (together with the share certificate if your shares are in bearer form) must be received on or before July 08, 2022 (or July 25, 2022, on second call if the quorum is not reached) by Société Générale Securities Services - Service Assemblée Générale - 32 rue du Champ de Tir - CS 30812 - 44312 NANTES Cedex 3

1.3 How to fill in your proxy form

**TO ATTEND THE MEETING
IN PERSON - Tick box**

**TO VOTE BY CORRESPONDENCE
Tick box
Then vote as per the instructions**

**TO GIVE PROXY TO THE CHAIRMAN
Tick box**

**TO GIVE PROXY TO ANY PERSON OR
LEGAL ENTITY
Tick box**

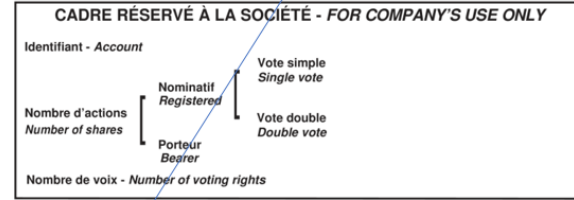
Important : Avant d'exercer votre choix, veuillez prendre connaissance des instructions situées au verso - **Important :** Before selecting please refer to instructions on reverse side
Quelle que soit l'option choisie, noircir comme ceci ■ la ou les cases correspondantes, dater et signer au bas du formulaire - **Whichever option is used, shade box(es) like this ■, date and sign at the bottom of the form**

JE DÉSIRE ASSISTER À CETTE ASSEMBLÉE et demande une carte d'admission : dater et signer au bas du formulaire / **I WISH TO ATTEND THE SHAREHOLDER'S MEETING and request an admission card: date and sign at the bottom of the form**

NICOX SA
DRAKKAR D - 2405 ROUTE DES DOLINES
06560 VALBONNE SOPHIA ANTIPOLIS

Au Capital de 43 223 135 EUR
403 942 642 R.C.S. GRASSE

ASSEMBLEE GENERALE EXTRAORDINAIRE
Du Lundi 11 Juillet 2022 à 14H00
EXTRAORDINARY GENERAL MEETING
On Monday the 11th of July 2022 at 2.00 p.m.



JE VOTE PAR CORRESPONDANCE / I VOTE BY POST
Cf. au verso (2) - See reverse (2)

Sur les projets de résolutions non agréés, je vote en noircissant la case correspondant à mon choix.
On the draft resolutions not approved, I cast my vote by shading the box of my choice.

Je vote **OUI** à tous les projets de résolutions présentés ou agréés par le Conseil d'Administration ou le Directoire ou la Gérance, à l'EXCEPTION de ceux que je signale en noircissant comme ceci ■ l'une des cases "Non" ou "Abstention". / I vote **YES** all the draft resolutions approved by the Board of Directors, EXCEPT those indicated by a shaded box, like this ■, for which I vote No or I abstain.

	1	2	3	4	5	6	7	8	9	10		A	B
Non / No	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Oui / Yes	<input type="checkbox"/>
Abs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Non / No	<input type="checkbox"/>
	11	12	13	14	15	16	17	18	19	20		C	D
Non / No	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Oui / Yes	<input type="checkbox"/>
Abs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Non / No	<input type="checkbox"/>
	21	22	23	24	25	26	27	28	29	30		E	F
Non / No	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Oui / Yes	<input type="checkbox"/>
Abs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Non / No	<input type="checkbox"/>
	31	32	33	34	35	36	37	38	39	40		G	H
Non / No	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Oui / Yes	<input type="checkbox"/>
Abs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Non / No	<input type="checkbox"/>
	41	42	43	44	45	46	47	48	49	50		J	K
Non / No	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Oui / Yes	<input type="checkbox"/>
Abs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>		Non / No	<input type="checkbox"/>
												Abs.	<input type="checkbox"/>

Si des amendements ou des résolutions nouvelles étaient présentés en assemblée, je vote **NON** sauf si je signale un autre choix en noircissant la case correspondante :
In case amendments or new resolutions are proposed during the meeting, I vote **NO** unless I indicate another choice by shading the corresponding box:

- Je donne pouvoir au Président de l'assemblée générale. / I appoint the Chairman of the general meeting

- Je m'abstiens. / I abstain from voting

- Je donne procuration [cf. au verso renvoi (4)] à M., Mme ou Mlle, Raison Sociale pour voter en mon nom

I appoint [see reverse (4)] Mr, Mrs or Miss, Corporate Name to vote on my behalf

Pour être pris en considération, tout formulaire doit parvenir au plus tard :
To be considered, this completed form must be returned no later than:

à la banque / to the bank 08/07/2022

JE DONNE POUVOIR AU PRÉSIDENT DE L'ASSEMBLÉE GÉNÉRALE
Cf. au verso (3)

I HEREBY GIVE MY PROXY TO THE CHAIRMAN OF THE GENERAL MEETING
See reverse (3)

JE DONNE POUVOIR À : Cf. au verso (4) pour me représenter à l'Assemblée
I HEREBY APPOINT: See reverse (4) to represent me at the above mentioned Meeting
M. Mme ou Mlle, Raison Sociale / Mr, Mrs or Miss, Corporate Name

Adresse / Address

ATTENTION : Pour les titres au porteur, les présentes instructions doivent être transmises à votre banque.

CAUTION: As for bearer shares, the present instructions will be valid only if they are directly returned to your bank.

Nom, prénom, adresse de l'actionnaire (les modifications de ces informations doivent être adressées à l'établissement concerné et ne peuvent être effectuées à l'aide de ce formulaire). Cf au verso (1)
Surname, first name, address of the shareholder (Change regarding this information have to be notified to relevant institution, no changes can be made using this proxy form). See reverse (1)

**Add your name and address
Or check that they are correct if they are already registered (whatever your choice)**

**DATE and SIGN here
(whatever your choice)**

Date & Signature

* Si le formulaire est renvoyé daté et signé mais qu'aucun choix n'est coché (carte d'admission / vote par correspondance / pouvoir au président / pouvoir à mandataire), cela vaut automatiquement pouvoir au Président de l'assemblée générale -
If the form is returned dated and signed but no choice is checked (admission card / postal vote / power of attorney to the President / power of attorney to a representative), this automatically applies as a proxy to the Chairman of the General Meeting

2. How to participate in the shareholder meeting via Internet platform Votaccess

Nicox has set up a dedicated on-line voting website ahead of the shareholder meetings, as explained below.

Votaccess will be open from June 22, 2022 at 9:00 am until July 10, 2022 at 3:00 pm (CET) (and from July 13, 2022 at 9:00 am until July 27, 2022 at 3:00 pm (CET) in case of second call). To avoid overloading the site, we recommend that you do not wait until the last day to vote.

2.1 Attend the shareholder meetings in person

Registered shares

If you hold registered shares, you should log onto the secure website www.sharinbox.societegenerale.com by entering the identification numbers sent to you by post when you were first in contact with Société Générale Securities Services. On the home page, click on the “Answer” button in the “shareholder meetings” box, then click on “Participate”. You will be automatically redirected to the voting site.

Bearer shares

If you hold bearer shares you should log onto the web portal of your bank or broker, with your usual user name and password, to connect to the VOTACCESS site and vote. You simply click on the icon displayed on the line corresponding to your Nicox shares. You will only be able to connect in this way if your bank or broker is a member of the VOTACCESS system.

2.2 Vote through Internet

Registered shares

If you hold registered shares, you should log onto the secure website www.sharinbox.societegenerale.com by entering the identification numbers sent to you by post when you were first in contact with Société Générale Securities Services. On the home page, click on the “Answer” button in the “shareholder meetings” box, then click on “Participate”. You will be automatically redirected to the voting site.

Bearer shares

If you hold bearer shares you should log onto the web portal of your bank or broker, with your usual user name and password, to connect to the VOTACCESS site and vote. You simply click on the icon displayed on the line corresponding to your Nicox shares. You will only be able to vote in this way if your bank or broker is a member of the VOTACCESS system.

2.3 Give proxy to the Chairman or to any other person of your choice through internet

In accordance with Article R. 225-79 of the French Commercial Code, you may give proxy or withdraw a proxy (to the chairman of the meeting or to any other person) electronically by logging onto the website www.sharinbox.societegenerale.com if you hold registered shares, or onto the website of your bank or broker if you hold bearer shares, with your usual username and password, in order to connect to the VOTACCESS site as described above.

If your bank or broker is not a member of the VOTACCESS system, the notification of the designation or revocation of a proxy can be done electronically until July 8, 2022 11:59 pm CET (or until July 25, 2022 11:59 pm in the event of a second call) by sending an email find electronically through an accredited certification service provider in accordance with applicable laws and regulations to ag2022nicox@nicox.com including the following information: name, first name, address and bank details as well as the name and first name of the designated or revoked proxy. The shareholder must request his bank or broker to send a confirmation to Nicox SA; - Drakkar D, 2405 routes de Dolines – 05650 Valbonne – France.

If you give proxy to the Chairman, he will vote in favor of all of the resolutions presented or supported by the Board of Directors and against all resolutions not supported by the Board.

NICOX SA

Société anonyme au capital social de € 43 223 135

Siège social : Drakkar D - 2405 route des Dolines
06560 Valbonne, Sophia Antipolis
403 942 642 R.C.S. Grasse

N° d'immatriculation Insee : 403 942 642 00055

RAPPORT DU CONSEIL D'ADMINISTRATION SUR LES RESOLUTIONS PROPOSEES

A L'ASSEMBLEE GENERALE EXTRAORDINAIRE

CONVOQUEE LE 11 JUILLET 2022 SUR PREMIERE CONVOCATION

(ET LE 28 JUILLET 2022 SUR SECONDE CONVOCATION)

Chers Actionnaires,

Nous vous présentons ci-après les résolutions soumises à votre approbation dans le cadre de l'Assemblée générale extraordinaire appelées à se réunir le 11 juillet 2022, sur première convocation.

L'ordre du jour de cette assemblée est le suivant :

- Délégation de compétence consentie au Conseil d'administration pour émettre des actions, des titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que des valeurs mobilières donnant accès à des titres de capital à émettre de la Société, avec maintien du droit préférentiel de souscription des actionnaires (résolution n° 1).
- Délégation de compétence consentie au Conseil d'administration pour émettre des actions, des titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que des valeurs mobilières donnant accès à des titres de capital à émettre, avec suppression du droit préférentiel de souscription des actionnaires et par offre au public autre que celles visées à l'article L. 411-2 1° du Code monétaire et financier (résolution n° 2).
- Délégation de compétence consentie au Conseil d'administration pour émettre des actions, des titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que des valeurs mobilières donnant accès à des titres de capital à émettre, avec suppression du droit préférentiel de souscription des actionnaires et dans le cadre d'une offre au public visée à l'article L.411-2 1° du Code monétaire et financier (résolution n° 3).

- Autorisation consentie au Conseil d'administration pour fixer le prix d'émission des titres à émettre dans le cadre des émissions réalisées en application des deuxième et troisième résolutions dans la limite de 10% du capital social par an (résolution n° 4).
- Autorisation consentie au Conseil d'administration pour augmenter le nombre de titres à émettre dans le cadre des émissions, avec ou sans droit préférentiel de souscription, réalisées en application des première, deuxième, troisième, quatrième et huitième résolutions (résolution n° 5).
- Délégation de compétence consentie au Conseil d'administration pour augmenter le capital par incorporation de réserves, bénéfices, primes ou autres sommes dont la capitalisation serait admise (résolution n° 6).
- Délégation de pouvoirs consentie au Conseil d'administration pour augmenter le capital dans la limite de 10 % du capital social en vue de rémunérer des apports en nature consentis à la Société en dehors d'une offre publique d'échange (résolution n° 7).
- Délégation de compétence consentie au Conseil d'administration pour augmenter le capital au bénéfice d'une catégorie de bénéficiaires, avec suppression du droit préférentiel de souscription des actionnaires à leur profit (résolution n° 8).
- Délégation de compétence consentie au Conseil d'administration pour augmenter le capital au profit des adhérents à un plan d'épargne d'entreprise avec suppression du droit préférentiel de souscription des actionnaires à leur profit (résolution n° 9).
- Autorisation donnée au Conseil d'administration pour procéder à des attributions gratuites d'actions existantes ou à émettre, emportant de plein droit renonciation des actionnaires à leur droit préférentiel de souscription (résolution n° 10).
- Autorisation donnée au Conseil d'administration pour consentir des options donnant droit à la souscription d'actions nouvelles de la Société ou à l'achat d'actions existantes, emportant de plein droit renonciation des actionnaires à leur droit préférentiel de souscription (résolution n° 11).
- Autorisation à conférer au Conseil d'administration à l'effet de réduire le capital social par annulation d'actions précédemment rachetées dans le cadre d'un programme de rachat d'actions (résolution n° 12).
- Modification des statuts pour étendre à 75 ans la limite d'âge du Président du Conseil d'administration (résolution n° 13).
- Pouvoirs à donner en vue des formalités (résolution n° 14).

1. Délégations générales de compétence au Conseil d'administration en vue de l'émission d'actions, de titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que de valeurs mobilières donnant accès à des titres de capital à émettre, avec ou sans droit préférentiel de souscription des actionnaires (résolutions n° 1, 2, 3 et 8) ou par incorporation de réserves (résolution n° 6), et autorisation d'ajuster certaines caractéristiques desdites émissions dans certaines conditions (résolutions n° 4 et 5).

Nous vous proposons de consentir des délégations de compétence au Conseil d'administration afin de lui permettre d'émettre des actions, des titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que des valeurs mobilières donnant accès à des titres de capital à émettre, avec (résolution n° 1) ou sans droit préférentiel de souscription des actionnaires (résolutions n° 2, 3 et 8), pour une durée de 18 mois (résolution n° 8) à 26 mois (résolutions n° 1, 2 et 3), dans la limite d'un plafond nominal global d'augmentation de capital de € 20.000.000 et d'un sous plafond cumulatif de € 15.000.000 s'agissant des autorisations sans droit préférentiel de souscription prévues aux résolutions n° 2, 3 et 8.

Nous vous proposons également d'autoriser le Conseil d'administration à fixer le prix d'émission des titres à émettre dans le cadre des augmentations de capital sans droit préférentiel de souscription et par voie d'offre au public (résolutions n° 2 et 3) en dérogeant au prix minimum légal dans la limite de 10% du capital social par an pour permettre au Conseil une plus grande flexibilité pour tenir compte des conditions de marché (résolution n° 4).

Nous vous proposons enfin d'autoriser le Conseil d'administration à augmenter le nombre de titres à émettre dans la limite de 15 % de l'émission initiale dans tous les cas en cas de demande excédentaire (résolution n° 5).

Si vous approuvez ces résolutions, le Conseil aurait la possibilité :

- (1) de décider l'émission d'actions, de titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que de valeurs mobilières donnant accès à des titres de capital à émettre, avec maintien du droit préférentiel de souscription des actionnaires (résolution n° 1) :
 - le montant nominal global des augmentations de capital serait limité à € 20.000.000,
 - la somme revenant ou devant revenir à la Société pour chacune des actions émises serait au moins égale à la valeur nominale de l'action à la date d'émission desdites valeurs mobilières,
 - le montant nominal global des valeurs mobilières représentatives de titres de créance donnant accès au capital ou droit à l'attribution de titres de créance serait au maximum de € 100 millions ou la contre-valeur de ce montant en cas d'émission en monnaie étrangère ou en unités de comptes fixées par référence à plusieurs monnaies,
 - les actionnaires bénéficieraient d'un droit préférentiel de souscription à titre irréductible et le Conseil d'administration aurait en outre la faculté de leur conférer un droit de souscrire à titre réductible ; étant précisé que la souscription pourrait être opérée soit en espèces, soit par compensation avec des créances certaines, liquides et exigibles,

- si les souscriptions à titre irréductible et, le cas échéant, à titre réductible, n’absorbent pas la totalité d’une émission d’actions ou de valeurs mobilières, le Conseil pourrait offrir au public tout ou partie des titres non souscrits, les répartir librement, totalement ou partiellement et/ou limiter le montant de l’augmentation de capital au montant des souscriptions à condition qu’il atteigne au moins 75 % de l’augmentation de capital décidée.
- (2) de procéder à l’émission d’actions, de titres de capital donnant accès à d’autres titres de capital de la Société ou donnant droit à l’attribution de titres de créances ainsi que de valeurs mobilières donnant accès à des titres de capital à émettre, avec suppression du droit préférentiel de souscription des actionnaires (résolutions n° 2, 3, 4 et 8) :
- le placement des titres serait effectué soit par voie d’une offre au public, exceptées les formes d’offres au public visées par l’article L. 411-2 1° du Code monétaire et financier (résolution n° 2), soit, comme le permet l’article L. 411-2 1° du Code monétaire et financier, par voie d’une offre au public auprès notamment d’investisseurs qualifiés et de gérants de portefeuille (résolution n° 3), soit à catégorie de personnes conformément à l’article L. 225-138 du Code de commerce (résolution n° 8). Nous vous précisons que depuis l’entrée en vigueur en juillet 2019 du règlement européen sur les prospectus (n° 2017/1129 du 14 juin 2017 (le "Règlement Prospectus"), toutes les offres sont désormais qualifiées d’offres au public, y compris ce qui était auparavant défini comme un placement privé. Néanmoins, il existe différents types d’offres au public, dont l’un reprend les contours de ce qui précédemment qualifié de placement privé, d’où la persistance de deux résolutions distinctes.
 - le droit préférentiel de souscription des actionnaires serait supprimé mais le Conseil pourrait leur conférer un droit de priorité sur tout ou partie de l’émission, à l’exception du cas d’une augmentation de capital réservée, pour une émission donnée, à l’une des catégories de personnes visées à la résolution n° 8, à savoir
 - (i) une ou plusieurs sociétés ou fonds gestionnaire d’épargne collective de droit français ou de droit étranger investissant dans le secteur pharmaceutique/biotechnologique ;
 - (ii) des personnes physiques investissant à titre habituel dans le secteur pharmaceutique/biotechnologique ;
 - (iii) un ou plusieurs établissements de crédit ou tout prestataire de services d’investissement habilité s’engageant à les acquérir pour les revendre aux personnes visées au (i) et (ii) ci-dessus ;
 - s’agissant des émissions par voie d’offres au public (résolutions n° 2 et 3), elles pourront également porter sur (a) des valeurs mobilières donnant accès à des titres de capital à émettre par la Société à la suite de l’émission par une société dont la Société possède directement ou indirectement plus de la moitié du capital de valeurs mobilières donnant accès à des titres de capital à émettre par la Société, (b) des valeurs mobilières donnant accès à des titres de capital à émettre par une société dont la Société possède directement ou indirectement plus de la moitié du capital et (c) de valeurs mobilières donnant accès à des titres de capital existants ou donnant droit à l’attribution de titres de créances d’une autre société dont la Société ne possède pas directement ou indirectement plus de la moitié du capital ;
 - la somme revenant ou devant revenir à la Société pour chacune des actions émises (la souscription pouvant être opérée soit en espèces, soit par compensation avec des créances

certaines, liquides et exigibles) serait au moins égale à la valeur minimum fixée par la loi et les règlements applicables au moment où il est fait usage de la délégation, soit actuellement à la moyenne pondérée des cours de l'action de la Société sur le marché réglementé d'Euronext à Paris lors des trois dernières séances de bourse précédant le début de l'offre au public au sens du Règlement Prospectus, éventuellement diminuée d'une décote maximale de 10 %, après correction s'il y a lieu, de ce montant pour tenir compte de la différence de date de jouissance (résolutions n° 2 et 3),

- par dérogation aux conditions de fixation du prix susmentionnée, dans la limite de 10% du capital social par an, la somme revenant ou devant revenir à la Société pour chacune des actions émises serait au moins égale à la moyenne pondérée des cours de l'action de la Société sur le marché réglementé d'Euronext à Paris lors des trois dernières séances de bourse précédant la fixation du prix d'émission, éventuellement diminuée d'une décote maximale de 15 %. Ces modalités distinctes permettraient au Conseil de faciliter une levée de fonds par offre au public en fonction des circonstances de marché et de l'appétit des investisseurs (résolution n° 4) ; elles sont identiques à celles proposées pour les émissions réservées à catégorie de personnes visées ci-après,
- s'agissant des émissions à catégorie de personnes (résolution n° 8), pour lesquelles le Conseil d'administration fixerait la liste précise des bénéficiaires au sein, pour une émission donnée, de l'une des catégories susmentionnées au profit de laquelle le droit préférentiel de souscription aurait été supprimé, la somme revenant ou devant revenir à la Société pour chacune des actions émises serait au moins égale à la moyenne pondérée des cours de l'action de la Société sur le marché réglementé d'Euronext à Paris lors des trois dernières séances de bourse précédant la fixation du prix d'émission, éventuellement diminuée d'une décote maximale de 15 % ; la possibilité d'une décote pouvant aller jusqu'à 15 % visant à faciliter l'opération en fonction des conditions de marché,
- dans chaque cas (résolutions n° 2, 3, 4 et 8), le montant nominal des augmentations de capital social susceptibles d'être réalisées immédiatement ou à terme ne pourrait excéder un montant nominal global pour toutes les autorisations de € 15.000.000 (ni 20 % du capital par an, s'agissant d'une offre au public régie par l'article L. 411-2 1° du Code monétaire et financier – résolution n° 3), étant précisé que ce montant s'imputerait sur le plafond nominal global de € 20.000.000,
- de la même façon, dans chaque cas (résolutions n° 2, 3, 4 et 8), le montant nominal global des valeurs mobilières représentatives de titres de créance donnant accès au capital ou à l'attribution de titres de créance, susceptibles d'être émises serait au maximum de € 100 millions (résolutions 2, 3 et 4) ou € 50 millions (résolution 8) ou la contre-valeur de ce montant en cas d'émission en monnaie étrangère ou en unités de compte fixées par référence à plusieurs monnaies, étant précisé que ce montant s'imputerait sur le plafond de € 100 millions prévue par la résolution n° 1,
- le Conseil d'administration pourrait faire usage de la délégation consentie aux termes de la résolution n° 2 à l'effet de rémunérer des titres apportés à une offre publique d'échange initiée par la Société répondant aux conditions fixées par l'article L. 22-10-54 du Code de commerce,

- dans le cadre d'une offre au public (résolutions n° 2 et 3), si les souscriptions n'absorbent pas la totalité d'une émission d'actions ou de valeurs mobilières, le Conseil pourrait limiter l'émission au montant des souscriptions reçues.
- (3) d'augmenter le nombre de titres à émettre en cas d'augmentation de capital avec ou sans droit préférentiel de souscription (résolution n° 5, en application des résolutions n° 1, 2, 3, 4 et 8) :
- dans les trente jours de la clôture de la souscription dans la limite de 15 % de l'émission initiale et au même prix que celui retenu pour l'émission initiale,
 - le Conseil aurait ainsi la possibilité d'accroître le volume de l'augmentation de capital en cas de succès de l'opération,
 - le montant nominal maximal des augmentations de capital susceptibles d'être réalisées s'imputerait sur le plafond nominal d'augmentation de capital fixé par chacune des résolutions au titre de laquelle l'émission initiale a été décidée, soit € 20.000.000 pour la première résolution et € 15.000.000 pour les deuxième, troisième, quatrième et huitième résolutions.

Si vous approuvez ces résolutions, le Conseil d'administration établirait à chaque usage de ces autorisations, conformément aux dispositions réglementaires applicables, un rapport destiné aux actionnaires décrivant les conditions définitives de l'opération et indiquant (1) l'effet dilutif potentiel de l'émission des valeurs mobilières sur la situation de chaque actionnaire, (2) l'incidence potentielle de l'émission des valeurs mobilières sur la quote-part des capitaux propres par action et (3) l'incidence théorique potentielle de l'émission des valeurs mobilières sur la valeur boursière de l'action de la Société.

Nous vous demandons également de consentir une autorisation au Conseil d'administration pour lui permettre de réaliser une augmentation du capital social de la Société par incorporation de réserves, primes, bénéfices ou autres sommes dont la capitalisation serait admise dans la limite des sommes pouvant être incorporées au capital. Le montant des augmentations de capital à ce titre serait indépendant du plafond global d'augmentation de capital de € 20.000.000 fixé par la première résolution. Cette délégation serait valable pour une durée de 26 mois (résolution n° 6).

Nous vous précisons que le Conseil d'administration ne pourrait faire usage d'aucune de ces délégations en période d'offre publique sur les titres de la Société.

2. Délégation de pouvoir au Conseil d'administration en vue d'augmenter le capital afin de rémunérer des apports en nature consentis à la Société (résolution n° 7)

Nous vous invitons à déléguer au Conseil d'administration les pouvoirs nécessaires pour augmenter le capital social, en une ou plusieurs fois, dans la limite de 10 % du montant du capital social au jour d'utilisation de la délégation, par émission d'actions, de titres de capital donnant accès à d'autres titres de capital de la Société ou donnant droit à l'attribution de titres de créances ainsi que de valeurs mobilières donnant accès à des titres de capital à émettre, sur le rapport du ou des Commissaires aux apports, en vue de rémunérer des apports en nature consentis à la Société et constitués de titres de capital ou de valeurs mobilières donnant accès au capital, lorsque les dispositions de l'article L. 22-10-54 du Code de commerce ne sont pas applicables.

Cette délégation permettrait au Conseil d'administration de financer dans les meilleurs délais, par émission de titres, des acquisitions de titres d'une société, soit dont les actions ne sont pas cotées, soit dont les actions sont cotées (i) si elles ne le sont pas sur un marché réglementé de l'EEE ou de l'OCDE ou (ii) si l'opération n'est pas réalisée dans le cadre d'une offre publique d'échange.

La délégation ainsi conférée au Conseil serait valable pour une durée de 26 mois à compter de la présente Assemblée générale et ne pourrait être utilisée par le Conseil d'administration en période d'offre publique sur les titres de la Société.

3. Augmentation de capital au profit des adhérents à un plan d'épargne d'entreprise (résolution n° 9)

Nous vous rappelons qu'aux termes des dispositions de l'article L. 225-129-6 du Code de commerce, il est obligatoire de soumettre à toute Assemblée générale appelée à se prononcer sur une augmentation de capital un projet de résolution tendant à réaliser une augmentation de capital dans les conditions prévues aux articles L. 3332-1 et suivants du Code du travail et de l'article L. 225-138-1 du Code de commerce, à savoir réservée aux adhérents d'un plan d'épargne entreprise.

En conséquence, nous vous proposons de déléguer votre compétence au Conseil d'administration afin d'augmenter le capital, par émission d'actions ou d'autres titres donnant accès au capital de la Société, avec suppression du droit préférentiel de souscription des actionnaires au profit des salariés de la Société ou des entreprises françaises ou étrangères qui lui sont liées au sens de l'article L. 225-180 du Code de commerce et de l'article L. 3344-1 du Code du travail qui adhèrent ou adhèreront à un plan d'épargne entreprise. Dans ce cadre :

- le montant nominal des augmentations de capital social susceptibles d'être réalisées immédiatement ou à terme ne pourrait excéder un montant nominal global de € 60.000, étant précisé que ce montant s'imputerait sur le plafond nominal global de € 20.000.000 prévu à la résolution n° 1,
- le prix de souscription des actions nouvelles serait égal à 70 % ou 60 % de la moyenne pondérée des cours de l'action de la Société sur le marché règlementé d'Euronext à Paris lors des 20 séances de bourse précédant le jour de la décision fixant la date d'ouverture des souscriptions, selon la durée d'indisponibilité prévue par le plan d'épargne entreprise, le Conseil pouvant toutefois réduire ou supprimer cette décote,
- le Conseil d'administration pourrait, en application de l'article L. 3332-21 du Code du travail, substituer tout ou partie de la décote par l'attribution gratuite d'actions ou d'autres titres donnant accès au capital de la Société, existants ou à émettre, l'avantage total résultant de cette attribution et, le cas échéant, de la décote mentionnée ci-dessus, ne pouvant excéder l'avantage total dont auraient bénéficié les adhérents au plan d'épargne si cet écart avait été de 20 % ou de 30 % selon la durée d'indisponibilité prévue par le plan,
- le Conseil d'administration pourrait également décider l'attribution, à titre gratuit, d'actions à émettre ou déjà émises ou d'autres titres donnant accès au capital de la Société à émettre ou déjà émis, au titre de l'abondement.

La délégation ainsi conférée au Conseil d'administration serait valable pour une durée de 26 mois à compter de la présente Assemblée générale.

Si vous approuvez cette résolution, le Conseil d'administration établirait, conformément aux dispositions réglementaires applicables, lors de chaque émission, un rapport complémentaire destiné aux actionnaires décrivant les conditions définitives de l'opération et indiquant (1) l'effet dilutif potentiel de l'émission des valeurs mobilières sur la situation de chaque actionnaire, (2) l'incidence potentielle de l'émission des valeurs mobilières sur la quote-part des capitaux propres par action et (3) l'incidence théorique potentielle de l'émission des valeurs mobilières sur la valeur boursière de l'action de la Société.

4. Autorisation donnée au Conseil d'administration pour procéder à l'attribution gratuite d'actions existantes ou à émettre (résolution n° 10)

Nous vous demandons d'autoriser le Conseil d'administration, conformément aux articles L. 225-197-1 et suivants, L. 22-10-59 et L. 22-10-60 du Code de commerce, à procéder, en une ou plusieurs fois, à des attributions gratuites d'actions existantes ou à émettre de la Société, au profit des membres du personnel ou de certaines catégories d'entre eux qu'il déterminerait parmi les salariés et les mandataires sociaux éligibles de la Société ou des sociétés liées au sens de l'article L. 225-197-2 du Code de commerce.

Cette attribution gratuite d'actions aurait pour objectif d'offrir au Conseil d'administration un dispositif attractif dans le cadre de la politique de recrutement de la Société, favorisant la fidélisation des salariés et des mandataires sociaux bénéficiaires et suscitant chez ceux-ci une motivation supplémentaire.

Le Conseil d'administration déterminerait l'identité des bénéficiaires des attributions ainsi que les conditions et les critères d'attribution des actions, étant précisé que l'acquisition définitive des actions serait soumise à des conditions de performance qui seront fixées par le Conseil d'administration au moment de leur attribution.

Les attributions gratuites d'actions effectuées en vertu de cette autorisation ne pourraient excéder 1.000.000 actions existantes ou nouvelles d'une valeur nominale d'un euro, le montant nominal maximum des augmentations de capital susceptibles d'être réalisées immédiatement ou à terme en vertu de la présente résolution ne pouvant excéder € 1.000.000. A cette fin, l'Assemblée générale autoriserait, en tant que de besoin, le Conseil d'administration à augmenter le capital social par incorporation de réserves à due concurrence. Le nombre total d'actions attribués gratuitement ne pourra excéder 10 % du capital social de la Société à la date de la décision d'attribution, conformément à l'article L. 225-197-1 I du Code de commerce

L'autorisation serait consentie pour une durée de 38 mois à compter de la présente Assemblée générale. Elle mettrait fin pour la partie non utilisée à la précédente autorisation ayant le même objet consentie par l'Assemblée du 28 avril 2021.

Le Conseil informerait chaque année l'Assemblée générale, dans les conditions légales et réglementaires, des opérations réalisées dans le cadre de la présente autorisation.

5. Autorisation donnée au Conseil d'administration pour consentir des options donnant droit à la souscription d'actions nouvelles ou à l'achat d'actions existantes (résolution n° 11)

Nous vous demandons d'autoriser le Conseil à consentir, en une ou plusieurs fois, aux salariés et mandataires sociaux détenant moins de 10 % du capital de la Société, ou à certaines catégories d'entre eux, de la Société et des sociétés qui lui seraient liées au sens de l'article L. 225-180 du Code de commerce, des options donnant droit à la souscription d'actions nouvelles de la Société ou à l'achat d'actions existantes, dans la limite de 2.500.000 actions existantes ou nouvelles, d'une valeur nominale de un euro chacune.

Cette attribution d'options de souscription ou d'achat d'actions aurait pour objectif d'attirer et de fidéliser les salariés et mandataires sociaux, de leur donner une motivation supplémentaire et en conséquence de promouvoir la réussite de la Société.

L'autorisation serait consentie pour une durée de 38 mois à compter de la présente Assemblée générale.

Le Conseil d'administration déterminerait l'identité des bénéficiaires des attributions ainsi que les conditions et les critères d'exercice des options, étant précisé que, s'agissant des bénéficiaires qui sont membres du Comité de direction ou mandataire social, l'exercice des options serait soumis à des conditions de performance qui seraient fixées par le Conseil d'administration au moment de leur attribution.

Le prix de souscription des actions nouvelles ou d'achat des actions existantes par exercice des options serait déterminé par le Conseil le jour de l'attribution des options de la façon suivante :

- Le prix de souscription des actions nouvelles ne pourra être inférieur à 80 % de la moyenne pondérée des cours de l'action de la Société sur le marché réglementé d'Euronext à Paris lors des 20 séances de bourse précédant la séance du Conseil.
- Le prix d'achat des actions existantes ne pourra être inférieur au plus élevé des deux montants suivants : (a) 80 % de la moyenne pondérée des cours de l'action de la Société sur le marché réglementé d'Euronext à Paris lors des 20 séances de bourse précédant la séance du Conseil et (b) le cours moyen d'achat des actions détenues par la Société au titre de l'article L. 22-10-62 du Code de commerce.
- Si les actions de la Société cessaient d'être admises aux négociations sur un marché réglementé, le prix de souscription ou d'achat des actions par exercice des options sera déterminé par le Conseil conformément à l'article L. 225-177 du Code de commerce. Dans la seule hypothèse des options d'achat d'actions, le prix ainsi déterminé par le Conseil ne pourra en aucun cas être inférieur au prix moyen d'achat des actions éventuellement détenues par la Société.

Les options devraient être exercées dans un délai maximum de huit ans à compter de leur attribution par le Conseil d'administration, celui-ci pouvant toutefois réduire ce délai pour les bénéficiaires résidents de pays dans lesquels une durée inférieure est prévue par la loi.

L'autorisation serait consentie pour une durée de 38 mois à compter de la présente Assemblée générale. Elle mettrait fin pour la partie non utilisée à la précédente autorisation ayant le même objet consentie par l'Assemblée du 28 avril 2021.

Le Conseil informerait chaque année l'Assemblée générale, dans les conditions légales et réglementaires, des opérations réalisées dans le cadre de la présente autorisation.

6. Annulation d'actions rachetées dans le cadre d'un programme de rachat d'actions (résolution n° 12)

Nous vous proposons d'autoriser le Conseil d'administration, le cas échéant, à annuler tout ou partie des actions qu'il aura rachetées et à réduire corrélativement le capital social dans la limite de 10 % du capital de la Société par périodes de 24 mois. Cette autorisation sera valable pour une période de cinq années expirant lors de l'Assemblée générale appelée à approuver les comptes annuels au 31 décembre 2025. Cette résolution priverait d'effet pour sa partie non utilisée l'autorisation ayant le même objet consentie par l'Assemblée du 28 avril 2021.

7. Modification des statuts pour porter à 75 ans la limite d'âge du Président du Conseil d'administration (résolution n°13)

Le 13 mai 2022, le Conseil d'administration a décidé des changements dans la gouvernance de la Société, en particulier de dissocier les fonctions de Directeur Général et de Président du Conseil d'administration. Le Conseil d'administration souhaite confier la présidence du Conseil d'administration à Jean-François Labbé, administrateur et Président du Comité d'audit.

Cette nomination nécessite l'approbation d'une modification statutaire pour porter la limite d'âge du Président du Conseil de 70 à 75 ans.

Il est donc proposé à l'assemblée de modifier la rédaction de l'article 14 des statuts pour porter la limite d'âge du Président du Conseil d'administration à 75 ans.

8. Pouvoirs en vue des formalités (résolution n° 14)

Nous vous proposons de donner tous pouvoirs au porteur d'une copie ou d'un extrait du procès-verbal des présentes en vue de l'accomplissement des formalités légales.

Au cours de l'Assemblée générale vous seront présentés, notamment, les rapports des Commissaires aux comptes qui vous donneront leur avis sur la proposition de suppression du droit préférentiel de souscription des actionnaires au titre des différentes délégations de compétence ou de pouvoirs aux fins d'augmentation du capital social sur lesquelles nous vous demandons de vous prononcer aujourd'hui.

Nous vous remercions de faire confiance au Conseil d'administration pour toutes décisions à prendre concernant les modalités d'exécution des opérations que nous vous avons présentées.

C'est dans ces conditions que nous vous demandons d'approuver les résolutions qui vous sont soumises par le Conseil d'administration.

Le Conseil d'administration

Nicox's Extraordinary Shareholder Meeting convened for July 11, 2022

Summary of the situation during the financial year 2021

- Extract of the 2021 Annual Report (Registration Document, Rapport Financier Annuel, Rapport de Gestion) filed with the French Autorité des Marchés Financiers (AMF) on April 29, 2022 – Chapters 3-4 and 5 (free translation of the documents in French)
- Press releases including the 2021 annual results issued from April 29, 2022

3. RISK FACTORS AND INTERNAL CONTROL

Under the provisions of article 16 of Regulation(UE) 2017/1129 of the European Parliament and the Council, this section presents the key risks which on the date of this universal registration document could have a material adverse effect on its business, financial status, operating results, or ability to achieve its objectives. However, the occurrence of risks unknown on the date of this universal registration document or not considered likely to have a material adverse effect on the date of this universal registration document cannot be excluded. Each year the Board of Directors reviews the risks to which the Company is exposed and issues an opinion as to their importance.

The key risks to which the Company considers it is exposed are presented according to the following categories, without any order of importance: (i) risks relating to the Company's financial position and capital requirements, (ii) risks relating to the products developed by the Company, regulatory authorizations and sale, (iii) risks relating to a dependence on third parties, (iv) risks relating to the Company's intellectual property, (iv) risks relating to the Company's organization, structure and operations, and (vi) risks relating to legal and administrative proceedings.

Within each of these categories, these risks are ranked according to both their adverse effect and probability of occurrence, while taking into account the risk management measures adopted by the Company on the date of this universal registration document. The following table summarizes the key risks identified by the Company and indicates for each, the probability of their occurrence and their adverse effect on the Company on the filing date of this universal registration document. The probability of occurrence is ranked according to three classifications ("low", "moderate" and "high") and the severity of their adverse effect is ranked according to four classifications ("low", "moderate", "high" and "critical").

Ref.	Risk factors	Probability	Adverse effect
3.1	Risks relating to the Company's financial position and capital requirements		
3.1.1	Risks relating to cash burn which could impede or jeopardize the Company's continuing operations should it be unable to obtain the necessary financing	High	Critical
3.1.2	Specific risks relating to the COVID-19 pandemic which could impact in particular the number of visits to doctors and therefore the amount of sales of VYZULTA and ZERVIA, the recruitment of patients in clinical trials, and therefore the financial situation of the Company	High	Critical
3.1.3	Risks relating to the history of losses and the risk of future losses that have affected and	High	High

CHAPTER 3 RISK FACTORS OF 2021 DOCUMENT D'ENREGISTREMENT UNIVERSEL
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Ref.	Risk factors	Probability	Adverse effect
	may affect the financial position, cash flows and working capital of the Company and its ability to distribute dividends one day to its shareholders		
3.1.4	Risks relating to commitments incurred in connection with bond financing obtained from Kreos Capital	Moderate	Critical
3.1.5	Risks associated with income and exchange rate fluctuations, reliability of investments	Moderate	High
3.1.6	Market risks	Low	Low
3.2	Risks relating to products developed by the Company, regulatory authorizations and their commercialization		
3.2.1	Specific risks relating to NCX 470 and NCX 4251 whose development cannot be guaranteed	High	Critical
3.2.2	Specific risks relating to NCX 470, NCX 4251 and ZERVIAE development in Chinese region and other ex-China and ex-US geographies	High	Critical
3.2.3	Risks relating to clinical and non-clinical trials affecting mainly NCX 470 and NCX 4251 which could significantly impact the Company's activity in the event of failure or delays	High	Critical
3.2.4	Risks relating to new products whose development or sale could be disrupted impacting mainly NCX 470 and NCX 4251 and which could significantly affect the Company's outlook and financial position	High	Critical
3.2.5	Risks relating to competition and rapid technological developments which could render the products developed by the Company obsolete	High	Critical

CHAPTER 3 RISK FACTORS OF 2021 DOCUMENT D'ENREGISTREMENT UNIVERSEL
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Ref.	Risk factors	Probability	Adverse effect
3.2.6	Uncertainty surrounding pricing and reimbursement schemes and reform of health insurance schemes	High	Critical
3.2.7	Risks relating to the market launch of pharmaceutical products	High	Critical
3.2.8	Risks relating to regulatory constraints which could impact the sale and or profitability of the Company's products, in the event of the refusal of an authorization or significant restrictions	Moderate	Critical
3.2.9	Specific risks relating to VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024%, commercialized by Bausch + Lomb, whose commercial success depends on a number of factors and remains uncertain	Moderate	High
3.2.10	Specific risks relating to ZERVIAE® (cetirizine ophthalmic solution), 0.24%, commercialized in the U.S. by Eyevance Pharmaceuticals, whose commercial success depends on a number of factors and remains uncertain	High	Moderate
3.2.11	Product liability and coverage from insurance policies	High	Moderate
3.2.12	Environmental and industrial risks, financial risks linked to the effects of climate change	Moderate	Low
3.3	Risks relating to dependence on third parties		
3.3.1	Dependence on third parties for carrying out clinical and non-clinical trials	High	Critical
3.3.2	Dependence on partners of collaboration agreements and outside consultants to effectively execute plans for development, obtain regulatory approvals and the marketing of products.	High	Critical

Ref.	Risk factors	Probability	Adverse effect
3.3.3	Risks associated with manufacturers, the manufacturing costs of products, the price of raw materials and reliance on third party manufacturers	High	Critical
3.4	Risks relating to the Company's intellectual property		
3.4.1	Infringement and potential infringement of patents and by other intellectual property rights covering our products and product candidates	Moderate	Critical
3.4.2	Scope, validity and enforceability of patents	Moderate	Critical
3.4.3	Litigation and defense of patent rights	Moderate	Critical
3.4.4	Possible infringements of third-party patents	Moderate	Critical
3.4.5	Products not protected by intellectual property rights, trade secrets for which the commercial potential could be affected	Moderate	Critical
3.4.6	Risk relating to the protection of trademarks the use of which could be subject to disputes	Moderate	Critical
3.4.7	Confidentiality agreements relating to employees, consultants and subcontractors	Moderate	Critical
3.5	Risks relating to the Company's organization, structure and operations		
3.5.1	Reliance on qualified personnel	High	Critical
3.5.2	Risks associated with potential future acquisitions of products or companies and with potential future in-licensing transactions	Moderate	Moderate
3.6	Risks relating to legal and administrative proceedings	Moderate	Moderate

3.1 Risks relating to the Company's financial position and capital requirements

3.1.1 Risks associated with cash burn

At December 30, 2021 Nicox Group had cash and cash equivalents in the amount of €42.0 million compared to €47.1 million at December 31, 2020.

Based on a specific review of its liquidity risk, Nicox considers that on the date of this universal registration document the Company has sufficient net working capital to meet its cash requirements until Q4 2023, based on the development of NCX 470 alone.

Nicox anticipates significant capital requirements to complete the following projects:

- the development program for NCX 470 (a novel nitric oxide (NO)-donating prostaglandin analog based on Nicox's internally-developed NO-donating research platform) for lowering of intra-ocular pressure (IOP) in patients with open angle glaucoma or ocular hypertension;
- the development program for NCX 4251 (a novel patented ophthalmic suspension of fluticasone propionate nanocrystals) for dry eye disease; and
- the preclinical development program focused on NCX 1728 selected from a new class of compounds (non-PGA related) based entirely on NO-mediated activity, being investigated for lowering IOP and for applications in retinal diseases. NCX 1728 is an NO-donating PDE5 inhibitor. Formal pre-IND tests are under preparation.

Developments and the cost of clinical and non-clinical trials, as well as costs relating to research and development programs, filing patents and concluding collaboration or product manufacturing agreements also give rise to significant capital requirements that must be met by Nicox.

To date, limited revenues are generated from royalties derived from the direct sales of products. Nicox expects sales for 2022 will not be sufficient to reach profitability. Furthermore, Nicox cannot guarantee that its choices in terms of cash utilization will prove appropriate. Nicox will need to raise additional funds in amounts that will depend on many factors, including the cost of developing or registering new products and, if appropriate, their commercialization. The Company might therefore have to seek other sources of funding:

- either through capital increases, it being specified that as a result of the volatility of the Nicox share price and constraints imposed in connection with capital increases entailing the cancellation of preferential subscription rights, this source of financing could be considered limited; or
- in the form of a debt; or
- by signing strategic partnership agreements with a view to generating new revenue from patent licenses, or to sharing operating costs with partners; or

Nicox cannot guarantee that its future capital requirements will be met or that additional funding will be available on acceptable terms. Turmoil affecting the stock markets has generally made it more difficult to obtain financing by equity securities and could have a materially adverse effect on Nicox's ability to obtain sufficient funding. If the Group were unable to obtain the necessary funding, it could be forced to

delay, reduce or eliminate expenses related to certain projects that are under development, to seek funding through partnerships, to grant licenses for the development or marketing of products that the Group would have preferred to develop or market itself, which would have the effect of reducing the added value that the Group might ultimately draw from these products. Such a situation could even jeopardize the continuation of the Company's activities.

3.1.2 Specific risks relating to the COVID-19 pandemic which could impact in particular the number of visits to doctors and therefore the amount of sales of VYZULTA and ZERVIATE, the recruitment of patients in clinical trials, and therefore the financial situation of the Company

The sales of VYZULTA and ZERVIATE depend on the number of prescriptions which itself depends on the number of visits to doctors. A decrease in the number of visits would result in a decrease in the number of prescriptions and therefore a decrease in revenue for Nicox.

The duration and schedule of the Company's clinical trials depend on the number of patients recruited. If the recruitment is impacted by the COVID-19 pandemic and is no longer in line with the Company's estimates, the trials could take longer than expected and generate additional costs.

The coronavirus pandemic, as well as any other comparable health situation, can have a strong impact on the financial markets, on Nicox's share price, as well as on the Company's ability to finance itself and to advance its development programs on the expected timelines. This could have a significant negative effect on the Company, its business, financial situation and results, as well as on its development and prospects.

There is a risk that the COVID-19 pandemic will disrupt the activities of the Company, its partners and / or subcontractors and therefore have consequences on the development of its product candidates and on its funding needs.

No direct future impacts on the Group's financial situation have been noted following the Russia / Ukraine conflict, which was declared during the month of February 2022. Indeed, to date, the Group has no customers in these territories and did not plan to develop a significant activity there in the short or medium term. The Group also has no direct exposure in terms of research and development. Nevertheless, although this conflict has no significant impact on the performance of the Group, the latter cannot, at this stage, predict the macroeconomic consequences of this geopolitical situation and its evolution, on its future performance.

3.1.3 Risks relating to the history of losses and the risk of future losses

To date, the Company has not yet generated significant revenues. The Company has not yet generated profit and has incurred operating losses each year since the commencement of its operations in 1996, and notably net losses for the periods ended December 31, 2021 and December 31, 2020 of (€43.1) million and (€18.1) million respectively.

Almost all the operating losses of the Company resulted from costs incurred in connection with research and development programs and the manufacture of products in preparation for their commercial launch,

including activities in clinical and pre-clinical development phases, general and administrative costs linked to the Company's activities.

The payments that Nicox might receive from strategic partners under collaboration agreements might not be sufficient to cover its operating expenses and there is no guarantee, moreover, that the Group will receive additional payments under its collaboration agreements.

Nicox may be expected to continue to incur significant expenses and its operating losses should increase in the near future as a consequence of the significant investments carried out in connection with the development of product candidates and the development of the selected candidate in a new class of NO-mediated IOP lowering agents.

These operating losses have had and may have a material unfavorable effect on the Company's financial position, cash flows and working capital. For that reason, no assurance can be given that the Company may one day be able to distribute dividends to its shareholders.

3.1.4 Risks relating to commitments incurred in connection with bond financing obtained from Kreos Capital

Nicox has obtained financing of €20 million from Kreos Capital structured as bonds accessible as 3 tranches. The financing was structured into 3 tranches of senior secured bonds, the second tranche being divided into two sub-tranches. The first tranche of €8 million was drawn down on February 1st, 2019, the first sub-tranche of €4 million was paid on November 1st, 2019, the second sub-tranche of €3 million and the last tranche of €5 million were both drawn down on December 12, 2019 and paid on January 2, 2020. In January 2021 Nicox amended its bond financing agreement with Kreos Capital, introducing an additional one-year period of interest-only payments on the outstanding principal starting on February 1st, 2021, and an extension of the overall period of the loan by 6 months to July 2024. The new one-year interest-only period is expected to provide approximately €5.5 million of additional flexibility for investment in development activities in 2021.

On November 30, 2021 a new amendment to the bond financing agreement was signed, whereby the interest-only period will be increased by 18 months to July 2023 (against January 2022 previously) and the maturity date of the loan increased by 18 months to January 1st, 2026. In addition, the Company has the option to further extend the interest-only period and the maturity date by 6 additional months, to respectively January 2024 and July 2026, if the Mont Blanc Phase 3 NCX 470 clinical trial meets the primary endpoint of non-inferiority compared to latanoprost. These changes apply to 70% of the outstanding principal, excluding pre-payments of €0.6 million (the "Term Loan"). The interest rate remains unchanged.

€3.3 million of the remaining capital was issued as convertible bonds (the "Convertible Loan"). The term is January 1st, 2026 with the same interest rate of 9.25% per annum, payable in cash. The Convertible Loan is secured against the same securities already in place for the Term Loan. This portion of the debt can be converted into shares at Kreos's discretion at any time (after an initial 60-day period) up to the maturity date of January 1st, 2026. The conversion price is €3.67. If Kreos has not converted the Convertible Loan by the end of the repayment period of the Term Loan, the entire amount of the Convertible Loan remaining is due as a single payment at that time.

The remaining €1.8 million was issued as a new non-convertible bonds with an interest rate of 9.25%, a term the same as the Convertible Loan and with an additional premium payable at repayment such that the total return to Kreos is 1.75 times the original amount.

This financing includes standard early repayment clauses. A breach of Nicox's obligations under this contract could constitute a default event under these clauses and in consequence result in its early repayment. There can be no assurance that Nicox will have the resources required for the early repayment of this bond issue.

For additional information about the bond financing agreement with Kreos Capital, refer to section 20.2 of this universal registration document.

There can also be no assurance that cash flows generated by Nicox will be sufficient to pay the bonds at their maturity which could have a material adverse effect on its business, with security interests having been granted over certain tangible and intangible assets of Nicox S.A., and notably patents relating to the approved product VYZULTA (with the pledge having no impact on the exclusive worldwide license agreement with Bausch + Lomb), securities of the subsidiary Nicox Ophthalmics Inc. as well as a pledge of bank account balances and all receivables of more than €100,000.

3.1.5 Risks associated with income and exchange rate fluctuations, reliability of investments

To date the Group's recurring revenue consist of royalties on sales of VYZULTA and ZERVIAE. The Group considers that there exists an uncertainty about the evolution and stability of this revenue which could potentially impact its sources of funds.

The majority of the Group's expenses are denominated in US dollars. In fiscal year 2021, approximately 66.40 % of operating expenses were in US dollars (55.8% in 2020).

Foreign exchange fluctuations in the value of the euro in relation to the US dollar may result in a material impact on the Group's operating results, notably with respect to the worldwide license for VYZULTA granted to Bausch + Lomb and the license for ZERVIAE for the U.S. market granted to Eyevance for which the Group may receive milestone payments respectively for an amount of up to US\$165 million for VYZULTA and \$37.5 million for Eyevance in addition to up 6% to 12% in net royalties for VYZULTA and to up 8% to 15% for ZERVIAE. For VYZULTA, the first sales milestone (\$5 million, net of payments to Pfizer – see Section 5.2.1) is due upon reaching \$100 million of net sales and there is not guarantee that this milestone or any other milestone will be met. For ZERVIAE, \$30 million of these milestones are triggered by annual sales targets of \$100 million or more.

The Group does not have significant receivables subject to foreign exchange risks.

The Group also holds US dollar bank accounts that are translated into euros in the consolidated financial statements at the year-end exchange rate. Cash amounted to €13 487 149 at December 31, 2021 (or 32% of cash and cash equivalents) and may be materially impacted by the Euro/US Dollar exchange rates. This risk is however mitigated by the fact that cash is exclusively destined to cover the Group's expenses denominated in US dollars resulting from its research and development activities in the United States over the medium term.

3.1.6 Market risks

For additional information, refer to note 25.3 "Market risk" to the consolidated financial statements for the period ended December 31, 2021.

3.2 Risks relating to products developed by the Company, regulatory authorizations and their commercialization

3.2.1 Specific risks relating to NCX 470 and NCX 4251 whose development cannot be guaranteed

NCX 470 is a novel nitric oxide (NO)-donating prostaglandin analog (PGA) in development for the lowering of IOP in patients with open-angle glaucoma and ocular hypertension. Another Nicox product candidate, which leverages an established molecule, is NCX 4251, a novel patented ophthalmic suspension of fluticasone propionate nanocrystals which is being developed for dry eye disease.

The Company has completed a Phase 2 clinical trial, Dolomites, for NCX 470. The first Phase 3 clinical trial, Mont Blanc, necessary for U.S. regulatory approval was initiated in the U.S. in June 2020 following a successful End-of-Phase 2 meeting with the FDA. The second Phase 3 clinical trial, Denali, was initiated in November 2020 and, together with the Mont Blanc trial, is designed to fulfill the regulatory requirements for Phase 3 safety and efficacy trials to support New Drug Application (NDA) filings of NCX 470 both in the U.S. and China. The Denali trial is financed jointly and in equal parts by Nicox and our Chinese partner Ocumension and includes clinical sites in both the U.S. and China, with approximately 80% of the patients to be recruited in the U.S. and the remaining 20% of the patients to be recruited in China. The management of a multi-country clinical trial is more complex than in one country alone. The Denali trial includes a long-term safety extension with participation of patients from the U.S. and China.

Certain additional clinical and non-clinical data will be required to support NDA submissions. The requirements for a complete Chinese NDA submission may be different from those in the U.S. Changes in the regulatory environment in one country may impact Nicox's products or product candidates in other countries.

The Company has also completed a Phase 2b clinical trial of NCX 4251, Mississippi, initiated in December 2020 for the treatment of acute exacerbations of blepharitis, whose results were announced in September 2021. The Mississippi trial did not meet the primary efficacy endpoint of demonstrating complete resolution of the signs (eyelid margin redness and eyelid debris) and symptom (eyelid discomfort) of blepharitis, or secondary efficacy endpoints. Following the encouraging post hoc results from the Mississippi trial and a subsequent positive meeting with the U.S. FDA the Company took the decision to focus the future development of NCX 4251 on dry eye disease. The future development of NCX 4251 in the U.S. will require initial manufacturing scale-up followed by two additional efficacy clinical trials, both evaluating one sign and one symptom of dry eye disease, long term safety data, and certain additional clinical and non-clinical data to support an NDA submission in the U.S. The remaining pharmaceutical, non-clinical and clinical development of NCX 4251 is not yet financed and therefore the Company has not planned yet the start of this last phase of development.. The requirements for a Chinese NDA submission may be different from those in the U.S., and if Ocumension develops NCX 4251 for a



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different indication, this may require additional clinical and/or non-clinical data, or further pharmaceutical development.

There is a risk that the results of the NCX 470 clinical trials may not be sufficient to move forward with NDA submissions or that additional trials may be necessary to file for approval to commercialize NCX 470.

For NCX 4251, there is a risk that the development required may not lead to a commercially viable business, or that additional trials may be necessary to advance the development or in order to file for approval to commercialize NCX 4251.

Clinical trials or other development activities may be more costly or of longer duration than expected. There is no guarantee that Nicox can file an NDA in the U.S. for NCX 470 or NCX 4251 in the future.

The development of NCX 470 and NCX 4251 could be delayed or fail.

3.2.2 Specific risks relating to NCX 470, NCX 4251 and ZERVATE development in ex-US and ex-China geographies

The Company has multiple collaborations concerning the development and commercialization of its products and product candidates in countries outside of the U.S. and China, and expects to enter into further collaborations in the future. The regulatory requirements in such countries may be different from those in the U.S. and China. If additional clinical or nonclinical studies are required, the Company or its partners may have difficulty finding suitable local contractors.

The development plans for product candidates are currently focused on obtaining regulatory approval in the U.S. initially. For NCX 470, the next expected approval would be in China. Other countries may require additional clinical or non-clinical data to support regulatory approval, which may delay development and launch in those countries. Generating additional data or incorporating the regulatory requirements of those countries into the Company's development plans may result in delay to, or increase the risk of, the development of such product candidates in those countries.

For products which have been approved in the U.S., the FDA approval may, in some cases, be used as a basis for regulatory approval outside of the U.S. However, there is no guarantee that such regulatory approval will be achieved without generation of additional clinical or non-clinical data, or that the product approved in the U.S. will be approved outside of the U.S.

3.2.3 Risks associated with clinical trials and non-clinical studies, affecting mainly NCX 470 and NCX 4251 which could significantly impact the Company's activity in the event of failure or delays

It cannot be guaranteed that the necessary authorizations will be obtained to conduct clinical trials.

There can be no assurance that the authorized trials will be conducted in a timely manner or that they can be conducted without significant additional resources or knowledge. Significant delays in the conduct of clinical trials and non-clinical studies could generate additional costs in connection with the development

of the drug candidates in question. Such delays could also limit the period of exclusivity available to Nicox to commercialize its drug candidates.

Pharmaceutical companies or the regulatory authorities may suspend or terminate clinical trials if they consider that the trial patients are exposed to health risks.

The conduct of clinical trials depends on various factors such as indication, size of the affected population, nature of the clinical protocols followed, proximity between patients and clinical trial sites, eligibility criteria for trials, competition from other companies for the enrollment of patients to conduct clinical trials, availability of sufficient amounts of a compound of appropriate quality, ability to enter into agreements with appropriate subcontractors (and the discharge by them of their contractual obligations), and compliance with the regulatory standards.

The product candidates under development may not have the desired effects or may cause adverse reactions that preclude regulatory approval or limit their marketing potential. It frequently occurs that the favorable results of non-clinical studies and preliminary clinical trials are not confirmed in subsequent clinical trials.

Clinical trials may produce insufficient data to obtain regulatory approval.

This risk concerns mainly NCX 470 and NCX 4251 which are currently under clinical development. The risks related to the development of NCX 470 and NCX 4251 may be different for countries other than the U.S. and China, where development is currently focused.

While VYZULTA and ZERVIATE have been approved in selected territories, they remain subject to risks relating to clinical development in those territories where a marketing authorization is required which remains contingent on the nature of requirements imposed by regulatory authorities in these territories.

For additional information, refer to Section 3.1 of this universal registration document.

3.2.4 Risks relating to new products

The development or sale of new products generates risks associated with their novelty.

New Molecular Entities (NMEs) are compounds whose chemical and pharmacological profile is unknown at the time of their discovery. The product candidates under development covered by patents filed by Nicox relating to our nitric oxide (NO) release technology are NMEs. Each NME must be subjected to studies or extensive testing so that its chemical and pharmacological properties can be studied and investigated in detail. The outcome of these studies can entail a degree of uncertainty. Consequently, there can be no assurance that these compounds will demonstrate the same chemical and pharmacological properties in patients as those observed in the preliminary laboratory and animal studies, nor that these compounds will not interact unpredictably and intolerably with human biological functions.

When a molecule achieves first regulatory approval, it may be considered a NME. This classification allows for certain additional periods of marketing or patent exclusivity.

As new compounds, given that the uncertainties of their development, manufacture and properties are not known at the time of their design, difficulties may arise which might cause the company to terminate their development or their sale, thereby potentially affecting the company's prospects or financial position.

Certain product candidates under development by Nicox may include molecules that have already been approved. If the development data relating to the previous development of these molecules is available, Nicox may use it, but there is a risk that a molecule used in another formulation or for another indication or for another route of administration will present new or different side effects. Additional safety studies and/or efficacy studies on the new indication or formulation or route of administration may be required. NCX 4251 is a product candidate containing a molecule which has already been approved.

Recent changes in FDA regulations now consider NCX 4251 and NCX 470 as drug-led combination products in the U.S. This leads to a requirement to generate additional data and the product candidate will be subject to additional review steps for approval in the U.S., which leads to additional costs and or a longer period for the review and approval of NCX 4251 and/or NCX 470 than would have been expected had it been treated purely as a drug product.

3.2.5 Risks relating to competition and rapid technological developments

The markets in which Nicox operates are highly competitive and rapidly changing. The Company competes with larger companies with development programs that target the same indications, and with greater experience in the development and marketing of products. In addition, these companies have far greater financial and human resources than the Company. As a result, the Company cannot guarantee that its products:

- Will be able to obtain the required regulatory approval or be brought to market more quickly than those of its competitors;
- Will be able to compete with safer, more effective or less expensive existing or future products;
- Will adapt quickly enough to new technologies and scientific progress; and
- Will be accepted and selected by medical centers, physicians or patients to replace or complement existing products.

New developments are expected both in the healthcare industry and in public and private research facilities. In addition to the development of safer, more effective and less costly products than those developed or marketed by Nicox, its competitors may manufacture and market products under better conditions. Furthermore, competitors' rapid technology developments, including new products developed during the development of our product candidates, may render Nicox's products obsolete before they can become commercially viable. In certain therapeutic areas targeted by Nicox products and product candidates, such as dry eye and allergic conjunctivitis, products may switch from prescription only to non-prescription, also known as over-the-counter, which may have a significant impact on the available market for Nicox products and product candidates.

3.2.6 Uncertainty surrounding pricing and reimbursement schemes and reform of health insurance schemes

The ability of Nicox and its partners to secure commercially viable prices for its products that may potentially be marketed in the future depends on several factors, including the profile of its product compared to that of its competitors' products, the price of competing products, the existence of generic products and the targeted geographic area. The Company cannot guarantee that its products will secure pricing agreements for cost-effective marketing within the broader context, where pressure on pricing and reimbursement intensifies (greater control over prices, increased delisting, trend towards the promotion of generics). In some countries, specifically the U.S., the use of Nicox products may be constrained by the need for a patient to try an alternative, generally cheaper, product first before being prescribed a Nicox product. In certain cases, the healthcare prescriber may be required to specifically justify the prescription of the Nicox product in order for the patient to receive reimbursement. Such request can be refused by the company providing the reimbursement.

In fact, the commercial success of the Group's products depends in part on the agreement of the regulatory authorities responsible for health insurance, private insurance companies and other similar organizations in terms of product prices and reimbursement rates. Governments and third-party payers seek to control public health expenditure by limiting the reimbursement of new products. The Group cannot guarantee that it, its partners or its distributors will obtain a high enough reimbursement rate or price for the Company's products and the commercial profitability of these products in the market may consequently be affected.

In addition, pricing and prescribing freedom in some markets are governed and limited by the public authorities. The introduction of more stringent controls on pharmaceutical pricing can have a negative impact on the company's activities, either directly on the products it intends to sell or indirectly on the amount of income that the company can earn through its partnerships and licensing agreements.

3.2.7 Risks relating to the market launch of pharmaceutical products

The market launch of pharmaceutical products of the Company is subject to the following risks which could seriously affect the Company's financial position and prospects:

- Regulatory approvals, including approval of branding, may not be granted in time to secure a commercial return;
- The products may be difficult to produce on an industrial scale or their production on an industrial scale may prove too expensive;
- The products may not be profitable because of their cost of production, distribution and/or sale price as imposed by the relevant regulatory authorities;
- The products may not qualify for reimbursement arrangements in some countries, thereby jeopardizing their commercial potential in certain jurisdictions;
- It may be difficult to achieve acceptable quality standards;

- The company may not find a trading partner for the marketing of its products;
- The products may not be marketable on account of rights held by third parties;
- Third parties may market similar products that offer a higher benefit-risk ratio or a more competitive price; and
- A secondary effect or a manufacturing quality problem may arise at any time for a marketed product, which could lead to the restriction or withdrawal of regulatory authorizations for this product.

A pharmaceutical product can only be introduced on the market after it has successfully completed all phases of development provided for by regulations in force in the territory in question. This risk concerns, in the short term, VYZULTA and ZERVIAE. Specifically, VYZULTA is currently being commercialized by exclusive worldwide partner Bausch+Lomb in the U.S., Canada, Argentina, Hong Kong, Mexico, Taiwan and Ukraine, and has been approved in Brazil, Colombia, Jordan, Qatar, Singapore, South Korea, Thailand, Turkey and United Arab Emirates. However, no assurance can be given that the product will be marketed in other territories. While ZERVIAE has been commercialized in the U.S. by U.S. partner Eyeavance Pharmaceuticals (an affiliate of Santen Pharmaceuticals Ltd, Japan) since March 2020, it is possible that ZERVIAE might never be marketed in other territories. With respect to the other product candidates, the risk associated with marketing will persist until a future date in light of their current stage of development.

3.2.8 Risks relating to regulatory constraints

The regulatory process may give rise to delays or rejections. The U.S. and European, regulatory authorities tend to impose ever more cumbersome requirements, particularly regarding the volume of data required to demonstrate safety and efficacy. Other regulatory authorities, including China, may also change their requirements for the approval of pharmaceutical products.

Pharmaceutical products cannot be marketed in a given jurisdiction until they have been approved by the relevant regulatory authority, and all pharmaceutical development requires non-clinical and clinical trials to demonstrate the safety and efficacy of the compound under evaluation. The unfavorable outcome of clinical trials or applications for regulatory approval of the therapeutic products developed by the Group is likely to have a material adverse effect on its business.

The achievement of primary endpoints of clinical trials, even with statistically significant results, does not guarantee that the drug-candidate will then be approved by the regulatory authorities. Those authorities may argue that the comparator was inadequate, that the number of patients involved was insufficient, or that the results, although statistically significant, are not clinically significant or that there is inadequate benefit-to-risk to approve the product.

Even after they have been approved, drugs and their manufacturers are subject to continuous and permanent review and the uncovering of problems or the inability to comply with the manufacturing and quality control requirements may lead to restrictions in the distribution, sale or use of these products and even to their withdrawal from the market.



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The regulatory authorities have the authority, when approving a product, to impose significant limitations on the product in the form of warnings, precautions and contraindications, or restrictions on the indicated use, conditions for use, labeling, advertising, promotion, marketing, distribution and/or production of the product that could negatively affect its profitability.

The EMA, the U.S. FDA, the Chinese NMPA and similar regulatory bodies may also implement new standards, or change their interpretation and enforcement of existing standards and requirements, for the manufacture, packaging or testing of products at any time. A company that is unable to comply could be subject to regulatory or civil proceedings or be ordered to pay fines.

New regulations may be enacted. Given the disparity of the regulations and procedures, which vary from one country or jurisdiction to another, obtaining authorization in each country within a reasonable time frame cannot be guaranteed.

The Risk Factors addressed here are on the basis of the regulatory environment at the date of this document. Regulatory requirements may be changed by regulatory bodies which may impact either the ability to commercialize already-approved products in the concerned territory, or may increase the costs and the time for development of product candidates. An example is the recent change in the FDA's position on ophthalmic dispensers, which are now considered medical devices, as noted in section 3.2.4. Specifically, FDA has determined that the language in 21 CFR 200.50(c) indicating that eye cups, eye droppers, and ophthalmic dispensers are regulated as drugs when packaged with other drugs is now obsolete, as these articles meet the 'device' definition.

As part of its research and development work Nicox is, or may be, subject to regulations concerning safety standards, good laboratory practice (GLP), good clinical practice (GCP), current good manufacturing practice (cGMP), the experimental use of animals, the use and destruction of hazardous substances, in addition to regulations and market surveillance good practice (including medical device vigilance and pharmacovigilance) where the products are marketed. In the event of non-compliance with the applicable regulations, the company may be subject to penalties which may take the form of temporary or permanent suspension of operations, withdrawal of the product, restrictions on the marketing of the product and civil and criminal penalties.

**3.2.9 Specific risks related to VYZULTA® (latanoprostene bunod ophthalmic solution),
0.024%**

VYZULTA® is a prostaglandin analog with one of its metabolites being NO. VYZULTA was developed for the reduction of IOP in patients with open angle glaucoma or ocular hypertension in the U.S.. The marketing authorization application for VYZULTA, submitted by its exclusive worldwide licensee, Bausch + Lomb (a company of Bausch Health Companies, Inc.) was approved by the U.S. FDA in November 2017 and VYZULTA has been marketed in the U.S. by the licensee since December 2017. VYZULTA is also approved and commercialized in Canada, Argentina, Hong Kong, Mexico, Taiwan and Ukraine, and has been approved in Brazil, Colombia, Jordan, Qatar, Singapore, South Korea, Thailand, Turkey and United Arab Emirates.

The Company has identified the main risks related to VYZULTA below. Moreover, it should be noted that all of the “Risks related to Nicox’s strategy and business: the research, development and marketing of ophthalmic products” apply to VYZULTA.

Outside the United States, Canada, Argentina, Brazil, Colombia, Jordan, Mexico, Hong Kong, Qatar, Singapore, South Korea, Taiwan, Thailand, Turkey, Ukraine and United Arab Emirates, it is still necessary to obtain regulatory approvals before launching VYZULTA on the market. There is no guarantee that Bausch + Lomb will file an application for countries other than the United States, Canada, Argentina, Brazil, Colombia, Jordan, Mexico, Hong Kong, Qatar, Singapore, South Korea, Taiwan, Thailand, Turkey, Ukraine and United Arab Emirates or that if such applications are filed, that they will be successful.

As for marketing authorizations in Europe, a marketing authorization application (MAA) must be filed with the EMA (European Medicines Agency) or – in accordance with the decentralized procedure – with the national regulatory authorities of the European countries covered, which would conduct a validation process and scientific approval to evaluate the safety and efficacy of the drug.

The requirements of the EMA or national regulatory authorities may differ significantly from those of the U.S. FDA and these authorities may request the conduct of different non-clinical and clinical studies.

If VYZULTA has limited or no commercial potential, the Group's activities could be harmed

Nicox is contractually entitled to receive from Bausch + Lomb net royalties on sales of 6 % to 12 % after deduction of payments owed to Pfizer (see Section 5.2.1 for additional information concerning these payments). Royalties received by Nicox depend on sales generated by Bausch + Lomb, which depend on the commercial success of VYZULTA in the United States, Canada, Argentina, Brazil, Colombia, Jordan, Mexico, Hong Kong, Qatar, Singapore, South Korea, Taiwan, Thailand, Turkey, Ukraine and United Arab Emirates and any other territories where it may be commercialized. Nicox cannot guarantee such commercial success. Figures for actual sales may be impacted by the following factors:

- The commercial success of VYZULTA depends on several factors (none of these factors can be guaranteed by the Group), including:
 - Bausch + Lomb's success in obtaining a satisfactory product reimbursement level and sale price after, as applicable, discounts, allowing for viable business development;
 - The maintenance and development of commercial production capabilities at Bausch + Lomb that provide for flexible conditions to ensure enough orders are processed;
 - The continued investment by Bausch + Lomb in medical, marketing and sales support at an appropriate level;
 - VYZULTA's acceptance by the medical community, and, more generally, the success of its launch, commercial sales and distribution.

- Bausch + Lomb's continued ability to manufacture VYZULTA in accordance with applicable regulatory requirements; and
- Bausch + Lomb's ability to obtain marketing approvals in other countries for VYZULTA and its wish to apply for such authorizations.
- In addition, restrictions on the use, promotion or sale of VYZULTA or other post-approval restrictions could limit the market potential and reduce the sales volume of the product and its profitability;

Bausch + Lomb has focused its efforts on the United States and countries which accept U.S. FDA approval or reference to existing studies in support of marketing applications in local countries. To our knowledge, marketing applications have not been filed in Europe or Japan and we are not aware of any such plans. In addition, no assurances can be given that such marketing authorizations would be approved. The absence of a marketing authorization for VYZULTA outside the United States, Canada, Argentina, Brazil, Colombia, Jordan, Mexico, Hong Kong, Qatar, Singapore, South Korea, Taiwan, Thailand, Turkey, Ukraine and United Arab Emirates could limit the commercial success of this product and have a significant effect on the Company's financial position and delay achieving its objectives.

Bausch Health Companies, Inc., has announced their intention to create a spin-off company around Bausch + Lomb. There is a risk this may impact sales of VYZULTA.

3.2.10 Specific risks related to ZERVIA[®] (cetirizine ophthalmic solution), 0.24%

ZERVIA[®] is an innovative and patented cetirizine-based eye-drop developed to treat ocular itching (itchy eyes) associated with allergic conjunctivitis.

The Company has identified the main specific risks associated with ZERVIA and has listed them below.

If ZERVIA has limited or no commercial potential, the Group's activities could be harmed

In September 2017, Nicox entered into an exclusive license agreement with Eyevance Pharmaceuticals (an affiliate of Santen Pharmaceuticals, Ltd., Japan) for the commercialization of ZERVIA in the U.S. All manufacturing and regulatory responsibilities, together with decisions on launch timing, lie with Eyevance. Eyevance launched ZERVIA in a unit-dose presentation in the U.S. in March 2020 and expects a multi-dose presentation in the future. Many countries outside of the U.S. and other major markets base their regulatory approval on FDA approvals. Consequently, the development programs outside of the U.S. may be negatively impacted by the delayed availability of the multi-dose trade unit product presentation and their development risks may increase.

In March 2019, the Company entered into an exclusive license agreement with Ocumension Therapeutics for the development and commercialization of ZERVIA for a territory comprising mainland China, Hong Kong, Macau and Taiwan or the Chinese market. In March 2020 the license agreement was amended to expand Ocumension exclusive rights to the majority of the Southeastern Asian countries. A

Phase 3 clinical trial in China was successfully completed by Ocumension in February 2022 for a submission of an NDA in China.

In December 2019, the Company entered into an exclusive license agreement with Samil Pharmaceutical for the development and commercialization of ZERVIATE in South Korea, which was expanded in February 2022 to include Vietnam.

In August 2020, the Company entered into an exclusive license agreement with ITROM Pharmaceutical Group for the development and commercialization in Gulf and Arab markets.

In May 2021, the Company entered into an exclusive license agreement with Laboratorios Grin for the registration and commercialization in Mexico.

No guarantee exists that the Company or its partners will obtain regulatory authorizations to sell ZERVIATE outside the U.S.

The Company does not plan to commercialize ZERVIATE directly in any country and therefore cannot guarantee commercial success. Potential partners make evaluations of the regulatory and commercial environment concerning products for allergic conjunctivitis, and the potential costs for approving and commercializing ZERVIATE. The Company cannot guarantee that any such evaluations will be positive, and that any positive evaluation will lead to the signature of an agreement.

- Regulatory authorities might impose restrictions on the use or sale of ZERVIATE. These restrictions could limit the potential market, delay the launch and/or reduce the level of sales and profitability of the product.
- The commercial success of ZERVIATE will depend on several factors (none of which can be guaranteed by the Group), including:
 - Availability of the product within the timeframe and in sufficient quantities to support the commercial launch;
 - The maintenance and development of commercial production capacities that provide for flexible conditions to ensure enough orders are processed;
 - In the U.S., Eyevance's success in obtaining a satisfactory reimbursement level and sale price after, as applicable, discounts, allowing for viable business development. This will apply similarly when ZERVIATE is launched in other countries;
 - In the U.S., the continued investment by Eyevance in medical, marketing and sales support at an appropriate level. This will apply similarly when ZERVIATE is launched in other countries; The Company's ability to include new partnerships to develop and market ZERVIATE in other countries;
 - The ability of our partners to obtain regulatory authorizations in other countries; and
 - The acceptance of ZERVIATE by the medical community, and, more generally, the success of the launch, commercial sales and distribution.

- Eyevance was acquired by Santen Pharmaceutical Co., Ltd of Japan in September 2020. There is a risk this may impact sales of ZERVIATE; and,
- The evolution of the allergic conjunctivitis market, for example the launch of cheaper, generic equivalents of branded products and Rx-to-OTC switches, already occurring in the U.S., which may significantly impact the future potential sales.

3.2.11 Product liability and coverage from insurance policies

The use of product candidates under development in clinical trials and the possible sale of drugs may expose the company to liability suits. In the U.S., the approval of a product by the U.S. FDA may only offer limited or indeed no protection against liability claims based on federal state law (federal preemption cannot be invoked), and the obligations imposed on the company may vary from one federal state to another. If the company cannot successfully defend against liability suits, including liability in connection with clinical trials of its product candidates under development or with future commercial sales of its therapeutic products under development, it could incur heavy liability with potentially adverse consequences for the company.

The insurance policies obtained by the Company might not adequately cover the risks of its existing activities.

Whatever the grounds or eventual outcome of any liability suits, they could result in a fall in demand for a product, a reputation loss for the company, the withdrawal of volunteers from clinical trials, the withdrawal of a product from the market and/or loss of revenue.

3.2.12 Environmental and industrial risks, financial risks linked to the effects of climate change

Nicox's research and development activities involve the storage, use and disposal of hazardous radioactive and biological products (see Section 5.6.3 of the 2021 Universal Registration Document). Since 2012, these activities have been outsourced. Although these activities are monitored and involve only small amounts of hazardous materials, they pose a risk of contamination to the environment. Even though the Group believes that its activities and procedures comply with standards laid down by applicable laws and regulations, the risk of accidental contamination or injury due to the storage, use and disposal of these hazardous materials cannot be completely eliminated. Nicox could therefore be held liable for amounts over and above the limits of its insurance policy (see Section 3.7.1 of this universal registration document). The occurrence of such a risk could have a significant negative impact on the Group's financial position.

The Company has not identified any specific risk, in particular financial, linked to the effects of climate change and has therefore not taken any action in this regard, which does not mean that this risk does not exist.

3.3 Risks relating to dependence on third parties

3.3.1 Dependence on third parties for carrying out clinical and non-clinical trials

The Company has recourse to subcontractors, and in particular medical institutions, clinical researchers, clinical research organizations to conduct its clinical trials and non-clinical studies. The Company is able to exercise full control over the activity of its subcontractors.

Should its subcontractors fail to respect the terms of their engagement or not succeed in meeting the deadlines provided for within the framework of the trials to be conducted, the Company might be required to delay the development and sale of certain drug candidates.

In the event of default by subcontractors responsible for conducting clinical trials and non-clinical studies, no assurance can be given that the Company will find an alternative solution with other parties which offer acceptable commercial conditions.

In consequence, the occurrence of one or more of these risks could have a material adverse effect on the Group's business, financial position and prospects.

3.3.2 Dependence on partners of collaboration agreements and on outside consultants

To maximize its chances of success to launch its products on the market, it could be preferable for Nicox to enter into collaboration agreements with third party companies, and notably Bausch + Lomb for VYZULTA, Eyevance Pharmaceuticals, Samil Pharmaceutical, ITROM Pharmaceutical Group and Laboratorios Grin for ZERVIATE, and Ocumension Therapeutics for ZERVIATE, NCX 4251 and NCX 470.

Company cannot guarantee that it will be able to maintain the collaboration agreements in force, enter into new agreements in future on acceptable terms, or that these agreements will produce the desired results.

When the Company enters into a collaboration agreement, it runs the risk that its partner may unilaterally and arbitrarily terminate the agreement or decide not to market the product. If current partners decided to terminate the agreements in place, or the development of selected compounds, the Company would then have to pursue the development of these products itself, seek new partners or cease their development. Such a situation could increase the company's costs and/or adversely affect its business. The termination or non-renewal of a collaboration agreement could also adversely affect the Company's image and share price.

Conflicts could arise with the company's partners. In addition, the Company's partners could seek to compete with it. The existence of non-competition clauses in the company's collaboration agreements may not provide adequate protection.

Nicox also relies on outside consultants and subcontractors (such as academic researchers, medical specialists, and clinical and pre-clinical research organizations) to develop its products. Agreements between the company and such consultants and subcontractors may include limitation of liability clauses in favor of the other contracting party, in which case the company may not be able to secure full compensation for any losses incurred if the other contracting party fails to perform. Competition for access to these consultants is high, and the company cannot guarantee that it will be able to maintain its

existing relationships on commercially acceptable terms. In general, contracting parties may terminate the contract at any time.

The Company depends on the successful execution by its partner licensees of the development plans, regulatory submissions and for obtaining regulatory and marketing approvals for the products. In consequence, the occurrence of one or more of these risks could have a material adverse effect on the Group's business, financial position and prospects.

3.3.3 Risks associated with manufacturers, the manufacturing costs of products, the price of raw materials and reliance on third party manufacturers

Because Nicox's products and drug candidates are manufactured by third parties, it has limited control over manufacturing activities. Nicox has neither the infrastructure nor the experience required to manufacture pharmaceutical products. Nicox's dependency vis-à-vis third parties and its lack of experience in commercial-scale production increases the risk of difficulties or delays since its drug candidates are manufactured by third-party manufacturers, for clinical and non-clinical trials, but also for sale after the products have been approved. Unforeseen manufacturing problems could cause delays in commercial sourcing or the clinical trials.

The manufacture of VYZULTA is the responsibility of Bausch + Lomb worldwide.

The manufacture of ZERVIATE for the U.S. is the responsibility of Eyevance. However, in countries whose regulatory approval depends, or will depend, on the U.S. FDA approval of ZERVIATE, any changes in the approval and status of manufacturing may negatively impact Nicox's development partners and programs in such country. In some cases, a different manufacturer or product presentation may also be required by Nicox's partners. In such case, transfer of manufacturing may result in delays to regulatory approval.

Any decision by the manufacturers to alter the price of the products could negatively affect the margin received by Nicox. Nicox might delay the development or marketing of its products under development if their manufacture is disrupted or stopped.

The manufacture of medicines must comply with the applicable regulations and with good manufacturing practices, which is a complex, time-consuming and expensive process. Manufacturers may be subject to inspections prior to approval by regulatory authorities before obtaining marketing authorizations. Even after product approval, the facilities of manufacturers with whom the Company is associated are subject to periodic inspections by regulatory authorities or administrative authorizations that may be suspended. Nicox cannot guarantee that such inspections would not give rise to compliance issues that may prevent or delay marketing authorization, adversely impact the Group's ability to retain approval of the product or its distribution, or oblige the Group to use additional resources, financial or otherwise. Business would be negatively affected should its manufacturers fail to comply with the applicable regulations and recommendations.

A higher than anticipated cost of manufacturing the products or a significant rise in the cost of the raw materials needed for their manufacture could affect the commercial prospects of these products or the

Group's margin. In these circumstances, the Group may have to halt the development or sale of these products, thereby potentially affecting the Group's financial position or prospects.

In addition, the Group's ability to develop and deliver products in a timely and competitive manner could be significantly affected if, for example, the Group is unable to maintain relations with manufacturers possessing the requisite facilities and expertise, if contract disputes arise, or if other events hinder production.

3.4 Risks relating to the Company's intellectual property

3.4.1 Infringement and potential infringement of patents and by other intellectual property rights covering our products and product candidates

The Company, by the nature of its activity, is highly dependent on the protection of its intellectual property.

As far as patent-protected products are concerned, if the patent or patents relating to a product developed, in-licensed or acquired by the company were invalidated or declared unenforceable, the development and marketing of such compound or product would be directly affected or interrupted. The company may, for budgetary or other reasons, not be able to retain its patent portfolio in full, given the high cost of annuities and of potential lawsuits.

Nicox cannot therefore guarantee that:

- It will develop new patentable inventions, or that its patents will allow it to develop commercially profitable products;
- The filed patent applications will be granted;
- If these patents are granted, they will not be challenged, invalidated or declared unenforceable;
- That third parties will not develop products that are not in the scope of protection of its patents; or
- The products that it develops or might in-license or acquire will not infringe, or will not be alleged to infringe, patents or other intellectual property rights owned by third parties.

3.4.2 Scope, validity and enforceability of patents

The grant of a patent does not guarantee its validity or its enforceability and may not provide exclusive protection or competitive advantages against competitors with similar products.

To ensure the longest possible exclusivity, the company intends to seek an extension of certain of its patents for a period of up to 5 years. Nevertheless, it cannot guarantee that such extensions will be obtained and failure to obtain these extensions is likely to harm the products concerned. The portfolio of patents and patent applications of the Company covers a number of products. The failure to obtain an

extension for patents could have a significant impact for the sale of products concerned and expose the Company to increased competition, which would have consequences on the Company's financial position and prospects.

In particular, the expiration of patents protecting VYZULTA (protection in the U.S. until 2025, which may be subject to extension to 2030), ZERVIAE (protection in the U.S. until 2030 and 2032, in Japan, Canada and Europe until 2030), NCX 470 (worldwide protection until 2029 under a composition of matter patent with potential extensions up to 5 years in the U.S. and EU and formulation patent until 2039 in the U.S., EU, Japan and China), and NCX 4251 (worldwide protection by patents until 2033 and to 2040 by additional patents granted in the EU and Japan) could have a material adverse effect on the Company's business and financial position (for additional information, refer to Sections 5 and 7 of this universal registration document).

3.4.3 Litigation and defense of patent rights

Competitors can or could infringe the patents of products developed or marketed by Nicox or attempt to circumvent them. The company may have to resort to legal action to enforce its rights, to protect its trade secrets or to determine the scope and validity of others' proprietary rights. Furthermore, the ability of the Group to assert its rights under patents depends on its ability to detect infringements. It is difficult to detect infringers who do not advertise the compounds used in their products.

The protection conferred by a patent in practice varies by product and by country, and depends on many factors such as the nature of the patent, the scope of its protection, the possibility of regulatory extensions, the existence of legal remedies in a given country, and the validity and enforceability of the patents. The laws governing patents are constantly changing and vary from one country to another, with potential for rendering protection uncertain. The Company's patent portfolio includes patents issued in various foreign countries which are on that basis at particular risk.

Any litigation to assert or defend the Group's rights under patents, even if the rights of the Company should prevail, may prove costly in resources and time, and would divert the attention of management teams and key employees from carrying out Company business, which could have a material adverse effect on the Company's operations.

3.4.4 Possible infringements of third-party patents

Products developed or in-licensed by the company must not infringe the exclusive rights belonging to third parties. Third parties may also allege infringement by Nicox of their patents or of other intellectual property rights (see Section 3.6 "Risks relating to legal and administrative proceedings"). If a legal action is brought against the company on such grounds, there can be no assurance that the company will win the case. Moreover, even if Nicox conducted prior art searches to determine whether its rights infringe the rights held by third parties, it cannot be certain that all relevant rights have been identified because of the uncertainty inherent in this type of search. Such disputes could divert the attention of management teams and key personnel from their task of managing the Company's operations which could have a material adverse effect on the Company's business.

Any claim of patent infringement whose outcome is unfavorable to Nicox could require it to pay significant damages as well as royalties. As a result of claims by third parties, the company may be forced to change or rename its products to avoid infringement of the intellectual property rights of third parties, which could prove either impossible or costly in resources and time. In these circumstances, the Group may have to halt the development and/or sale of these products which may have adverse effects on the Company's financial condition and prospects.

3.4.5 Products not protected by intellectual property rights; trade secrets;

The Company may be required in connection with its activities to license or sell therapeutics that are not protected, in all or part of the territories concerned, by intellectual property rights. In this case, it is likely that other market participants will market similar or identical products on the same markets, which may seriously affect the commercial prospects of such products as a result of this increased competition, or indeed the financial condition of the Company.

The development new therapies by the Company depends in part on protecting trade secrets in order to preserve the confidentiality of technologies and processes used. Where there exists non-public know-how or other trade secrets concerning a product (whether or not the product is patent-protected), the company cannot be certain that confidentiality will be ensured and that such know-how or trade secrets will not be disclosed. If disclosed, the products covered by such trade secrets could see their commercial potential diminished.

3.4.6 Risks relating to the protection of trademarks

Nicox is exposed to certain risks related to trademarks. Nicox has submitted applications in numerous countries in order to register several trademarks, particularly for its products. These trademark applications may not result in registration or may be canceled following their registration on the grounds of non-use, revocation or infringement. The company may be denied use of the brand name. Some trademark applications filed by the company may be subject to opposition proceedings. There is no guarantee that the company will be able to resolve these trademark-related disputes and similar disputes in the future. Also, trademarks intended to designate products may be rejected by the relevant regulatory authorities.

3.4.7 Employees, consultants and subcontractors

The company cannot guarantee that the confidentiality agreements signed with its employees, consultants and subcontractors will be respected, that it will have adequate remedies for disclosure of confidential information, or that sensitive data will not be brought to the knowledge of third parties in another manner or independently developed by competitors.

Nicox regularly enters into agreements with researchers working in academia or with other public or private entities and, in such cases, the company has entered into intellectual property agreements with these entities. However, the company cannot guarantee that these entities will not claim intellectual property rights over the results of work conducted by their researchers, or that they will grant licenses for such rights to the company on acceptable terms. This would have a significant adverse impact on the company's business and financial condition.

3.5 Risks relating to the Company's organization, structure and operations

3.5.1 Reliance on qualified personnel

The company's activities rely on a number of key managers and scientists, including particularly members of the Executive Committee. Competition for the recruitment of managers and qualified personnel is fierce in the Group's area of activity. The Group's strategy for development and expansion requires the continuing expansion of teams by recruiting qualified personnel. The Group cannot guarantee that it will be able to retain the human resources currently available to it or that it will be able to recruit any new resources it might require. The departure of key managers or scientists could delay the achievement of objectives in terms of research and development and the commercialization of products, which would significantly impact the Group's business and prospects.

In addition, the Group's limited workforce does not allow for replacements in the case of the absence of an employee so that the prolonged leave of an employee can significantly disrupt operations.

3.5.2 Risks associated with potential future acquisitions of products or companies and with potential future in-licensing transactions

In response to competition and the increasing concentration of resources in the pharmaceutical industry, the Group has carried out and may carry out acquisitions in the future. In addition to the portfolio of assets developed in-house, the Group could acquire rights to product candidates through in-licensing transactions, at different stages of advancement. The Group might however be unable to identify appropriate acquisition targets or conduct acquisitions under acceptable terms or could even find itself unable to complete the integration of these acquisitions, which would be likely to disrupt Group operations and have a negative impact on its activities and its results.

Nicox might continue to seek acquisitions with the aim of optimizing its business model, developing its customer base, accessing new markets and achieving economies of scale. Acquisitions entail certain known and unknown risks that could mean that the Group's growth and actual operating results differ from its forecasts. Thus, the Group:

- might not manage to identify suitable acquisition targets under acceptable terms;
- might seek acquisitions in foreign countries, which represents greater risks than those inherent to domestic acquisitions;
- might find itself in competition with other companies for acquiring complementary products and activities, which could be reflected by lesser availability or an increase in the acquisition costs of intended targets;
- might not achieve the necessary financing under favorable terms, or not achieve any financing at all, for all or some of the potential acquisitions; or
- the products or activities acquired might not generate results in line with the Group's forecasts, which would then risk not achieving the anticipated revenue and returns.

Furthermore, such an acquisition strategy could divert Management's attention from its existing activities, resulting in a loss of key employees. This strategy could also expose the management to unexpected problems or liabilities, such as successor liability for contingent or undisclosed liabilities related to the activities or assets acquired.

If the Group fails to conduct effective prior assessment of these potential targets (due diligence), it risks, for example, to not identify the problems of target companies or not identify incompatibilities or other obstacles to successful integration. Its inability to integrate future acquisitions satisfactorily could prevent it from receiving all the benefits of these acquisitions and considerably weaken its operational activities. The process of integration may also disrupt its activity and, if new products or activities are not implemented effectively, prevent the Group from fully achieving the expected returns and prejudice its operating results. Furthermore, the total integration of new products or new activities may cause unexpected problems, expenses, liabilities and reactions from the competition. Difficulties related to the integration of an acquisition include the following:

- difficulties in integrating products or activities of the target company with those of the Group;
- incompatibility between marketing and employee management techniques;
- maintaining staff motivation and retaining key employees;
- integrating the cultures of both companies;
- maintaining important strategic customer relationships;
- consolidating corporate and administrative infrastructures and eliminating duplications; and
- coordinating and integrating geographically separate organizations.

Moreover, even if the integration of an acquisition's operations is successful, the Group may not receive all the anticipated benefits, including in terms of the synergies, cost savings and growth opportunities expected. These benefits might not be obtained within the planned deadlines, or even never be obtained, which would have a material adverse effect on the Company's business, financial position, results of operations and prospects.

Furthermore, as a result of acquisitions, the Group may find itself forced to:

- use a substantial portion of its cash resources;
- increase its expenses and its debt level if the Group has to make additional borrowings to finance an acquisition;
- take on liabilities for which the Group is not indemnified by the former owners, given that indemnification obligations may also be the subject of litigation or concerns in connection with the solvency of the previous owners;

- lose existing or potential contracts owing to conflicts of interests;
- suffer adverse tax consequences or deferred compensation charges;

3.6 Risks relating to legal and administrative proceedings

Teva Pharmaceutical Industries filed a notice of opposition on November 23, 2016 with the European Patent Office (EPO) against the European patent covering latanoprostene bunod and requested the revocation of the patent as a whole, alleging the absence of novelty or an inventive step. The European patent office rejected this notice of opposition and decided to maintain the patent as delivered. Teva Pharmaceuticals appealed this decision of the EPO on September 12, 2018.

At the end of August 2020, the appeals board in a preliminary opinion concluded in favor of the existence of the inventive step of the patent and invited the parties to submit their observations by December 31, 2020. The parties filed their arguments in December 2020 and January 2021. The date of the hearing is set for July 5, 2022.

The Group considers that the risk of invalidity of the patent is low, and in consequence has not recorded a provision for this contingency. However, this procedure is by nature uncertain and an unfavorable decision for the Company by this body would have a material adverse effects on its business and financial position (See Section 18.7 "legal and arbitration proceedings" of this Universal Registration Document)

The Company contests the application of social security contributions on directors' compensation paid to two non-employee directors whose tax residence is in the United States. By judgment of January 24, 2020, the Court of Justice of Nice approved the claims of the Company; URSSAF appealed this judgment, requesting that it be overturned, the social security charge adjustment confirmed and, as a result, that the Company be ordered to pay €95,054 in principal and €2,000 under Article 700 of the French Code of Civil Procedure. The case was struck from the docket due to the failure of URSSAF to perform procedures. After initiating new procedures, the case was reinstated.

3.7 Insurance and risk coverage

3.7.1 Insurance

Civil liability of senior officers

The Company purchased a global directors and officers liability policy for Group's senior officers (including directors) including coverage for defense costs before the civil and criminal courts, with a coverage limit for 2021 of €20 million per period of insurance.

General civil liability: Operational, product and professional civil liability

The Company purchased a master policy to cover the civil liability of Nicox Group companies' operations, with a coverage limit for 2021 of €15 million per claim for damage to third parties arising from their operations. The Company obtained an extension of guarantee for Product and Professional Liability in

the amount of €15 million per claim and per year of insurance with a deductible of €30,000 per claim. Lower limits of coverage exist for the different guarantees.

This Master Policy provides DIC/DIL (difference in conditions/difference in limits) coverage on top of a local civil liability policy obtained by Nicox Ophthalmics Inc. for the civil liability of the latter within a limit of US\$1 million per claim and per insurance year.

Nicox Ophthalmics Inc. took out a compulsory insurance policy to reimburse the wages and medical expenses of employees involved in occupational accidents and diseases (Workers' Compensation) within a limit of US\$500,000 and US\$100,000 per claim.

Nicox Research Institute purchased coverage for civil liability, civil and criminal legal protection, damage to property, products, its premises, occupational accidents, death and disability for certain designated persons.

Premium for 2021 for the above insurance policies amounted to €264,322, including taxes.

3.7.2 Risk coverage

Besides the insurance policies described in the preceding section, the Company has taken precautions to ensure continued operations and to avoid any significant loss in the event of a major incident. The Company's computer data is stored on central servers located in a secure site as well as in a Tier 3 datacenter. Daily, weekly and monthly backups are performed on a five-day-rolling basis. A copy of the weekly backups is transferred to another Tier 3 datacenter located more than 150 km from the first datacenter. The Company entrusts the storage and backup of all materials relating to its clinical studies, its financial data and its human resources data to a specialist company.

3.8 Internal control system

The Company has based the development, implementation and description of its internal control and risk management system on the framework published by the AMF for small and midcap companies.

It should be noted that the procedures described in this report apply to the parent company and all companies included in the Group's consolidated accounts. This report describes the situation as of December 31, 2021.

3.8.1 Group objectives for Internal Audit

3.8.2 The Group is implementing the structuring of its Internal Audit mechanism over time.

In this respect, the Group notes that Internal Audit is a mechanism of the Company defined and implemented under its responsibility, and intended to ensure:

- Application of the instructions and strategies defined by Management;
- The reliability of financial information;
- Compliance with laws and regulations;

- The correct operation of the Group's internal processes, particularly those which help to protect its assets;

and, in general, it contributes to the control of its activities, the effectiveness of its operations and the efficient use of its resources. However, Internal Audit cannot provide an absolute guarantee that the Company's objectives will be met.

3.8.3 Organization of Internal Audit

The Nicox Internal Audit is based on organizational structures and methods responsible for direction and control, but also responsible for risk management.

The Board of Directors and its different committees:

The Board of Directors

The Board of Directors is the leading player in the Group's Internal Audit. It has adopted internal rules that define, among other items, the responsibilities and procedures for the operation of the Audit Committee, the Compensation Committee, and the Corporate Governance Committee.

The Audit Committee

For the work of its Audit Committee, the Group relies on the report of the AMF working group on the Audit Committee (AMF Recommendation of July 22, 2010).

The Audit Committee, whose role is to advise the Board of Directors, is responsible for the following within the framework of the Internal Audit process:

- to monitor the effectiveness of the Internal Audit and risk management systems within the Group;
- to review the controls performed by the Finance Department to evaluate the relevance and effectiveness of the procedures in effect;
- to monitor the implementation of the recommendations developed on the basis of the results of the Finance Department's controls;
- to regularly review the Group's main financial risks and its significant off-balance sheet commitments;
- to take a position on any changes in accounting principles and the determinant financial statements judgments and estimates.

In the context of the missions it has been assigned, the Audit Committee may ask the Chief Executive Officer to provide it with any document or allow the committee to interview any person, particularly the Vice President for Finance and the Statutory Auditors, in order to obtain information about the specific accounting, financial and operational features of the company. The Audit Committee is regularly informed in reports of the progress on the different work being performed as part of the Internal Audit of Group companies.

The Compensation Committee

The Compensation Committee, which has an advisory role with the Board of Directors, is responsible for the following within the Internal Audit process:

- to review annually the compensation, in-kind benefits, stock options and free shares awarded to corporate officers and senior management employees, and the members of the Management Committee;
- to review the plan for long-term allocation of stock options and free shares;
- to review the annual increase in employee payroll.

The Corporate Governance Committee

The Corporate Governance Committee, which has an advisory role with the Board of Directors, is responsible for the following tasks within the Internal Audit process:

- to establish criteria to assess the independence of the members of the Board of Directors;
- to evaluate and monitor corporate governance procedures;
- to verify the appropriate application of the regulations and recommendations on corporate governance;
- to examine candidates for corporate officers and senior management employees.

The Science and Technology Committee

The Science and Technology Committee, which has an advisory role with the Board of Directors, is responsible for the following tasks within the Internal Audit process:

- Assisting the Board in supervising the scientific and technical aspects of the company's activities;
- Examining the progress and performances of Management in achieving the objectives and limiting the associated risks.

The Corporate Social Responsibility Committee

The Committee assists the Board in overseeing the employment, social and environmental dimensions of the Company's activities. Its mission is to examine employment, social and environmental issues and to consider areas for improvement, in particular to help the Board consider how to share value and achieve a balance between the level of employee compensation, compensation for shareholder risk-taking and the investments needed to ensure the company's long-term sustainability.

The Management Committee

In addition to the Board of Directors and its different committees, Internal Audit also relies on an operational committee: the Management Committee.

The Management Committee, led by the Chief Executive Officer is currently composed of five members. The Management Committee monitors the Group's plan, ensures respect for the operating plan and targets assigned by the Board of Directors at all management levels, and debates all organization and operational strategy questions placed on the agenda by its members.

In addition, it is responsible for defining, leading and monitoring the Internal Audit process best adapted to the Group's situation and activities. Within this framework, it is continually informed of any malfunctions, insufficiencies or difficulties in application. The Management Committee ensures the commitment to the correct actions necessary.

Advisory Committees

The Group regularly organizes meetings of Advisory Committees composed of independent experts in order to exchange information on various issues related, in particular, to its business development activities and its new commercial activities. These committees provide an independent opinion and propose recommendations that assist the Group to make strategic and operational choices.

Quality Assurance and Finance Department

Finally, the other players in Internal Audit are Quality Assurance and the Finance Department:

Quality Assurance (QA)

The Quality management system is organized around two pillars:

- Designing, preparing and managing a quality information system as reflected by procedures, instructions, forms and models. QA ensures the distribution of procedures and the homogeneity of formats and media used;
- conducting quality audits to evaluate in an independent manner;
 - Compliance with procedures and internal processes for the purpose of ensuring continuing improvement for operations;
 - The capabilities of suppliers and service providers for the purpose of guaranteeing compliance with applicable requirements.

The Finance Department

The Vice President of Finance (with the support of QA for the document support area) is responsible for maintaining the Internal Audit process which is based on:

- continual update and improvement of the existing administrative and financial procedures;
- the establishment of new procedures, as needed;
- the availability of adapted information tools.

3.8.4 Internal information distribution

Disseminating information for making it possible to implement Internal Audit within the Group through Quality Assurance which directs production and centralizes all standard procedures through a Quality gateway after formal approval. Each newly issued procedure is transmitted in an accompanying email by Quality Assurance in order to:

- Summarize the objectives of the procedure,
- Indicate its application date.

A reply from each recipient is requested to ensure follow-up (confirmation that it has been read).

Each new employee receives an email from Quality Assurance which informs the employee where he can access the procedures for his department.

In addition, certain procedures are covered by internal training sessions in order to explain the content and responsibilities.

3.8.5 Risk management

In its management of risks, the Group relies on three main tools, which complete the Internal Audit process. This approach is moving it toward conformity with the transposition of the 4th and 7th European Directives, primarily by establishing a specific risk management process.

The universal registration document

Nicox prepares each year a universal registration document (URD) that includes a chapter on the risk factors that could have a material negative impact on its activity, financial position and results. This document deals with operational risk factors as well as financial, environmental, commercial and technological risk factors.

Faced with a number of these risks, the Group adopts a policy of precautions for risk insurance and coverage. Nicox believes that, as of this date, its insurance coverage is adequate for all the operations of its Group.

Assessment of risk management

There was no formal review of risk management in 2021.

Statutory Auditors' review of Internal Audit procedures

The Statutory Auditors conduct a yearly review of the Internal Audit Procedures. The conclusions of this work are presented to the Finance Department and allow the Internal Audit teams to enhance the risk identification process. The answers provided by management are reconciled with the correct action plan.

In December 2021, the Auditors' work consisted of individual interviews with managers of the Company and walk-through tests on the functional processes of certain Company operations.

3.8.6 Control activities

3.8.6.1 Internal control procedures relating to the preparation and processing of financial and accounting information

3.8.6.1.1 Accounting and financial management and organization

Parties involved

The Group's company accounts are kept under the direction of the Vice President for Finance. The accounts of Nicox SA and Nicox Research Institute Srl are maintained internally. The accounting for Nicox Ophthalmics Inc. is outsourced, as is the consolidation of the Group's financial results.

As part of their procedures on behalf of the parent company and the publication of its consolidated financial statements, the Statutory Auditors conducted an audit of companies included in the consolidation scope of Nicox SA and considered at December 31, 2021 as significant entities based on the thresholds set by them.

In addition, as of December 31, 2021, the payroll function was outsourced for the entire Group.

Forward-looking management tools

The Business Plan: This is a projected business model prepared for all Group operations over a time horizon of five years (or ten, if necessary). This document is prepared and updated regularly on the basis of the Group's strategic decisions, taking into account the different objectives to be achieved for each operational development, and also taking into consideration changes in the pharmaceutical markets, regulations and the competitive environment. Each update of the Business Plan is presented to the Board of Directors.

The "Annual Budget": Every year in the final quarter of the year, the Group Finance Department prepares an annual Budget, in close collaboration with the operational departments. On the basis of the strategic objectives defined in the Business Plan, the Management Committee defines the Group's objectives for the coming year. These objectives are then approved by the Board of Directors and distributed to the operational departments. The various operational departments assess their detailed needs in terms of operating expenses, investments and equipment, and human resources. This information is centralized by the Vice President of Finance and the Group Management Controller. The Management Committee evaluates the various budget proposals and makes certain decisions. The finalized Budget is presented to the Audit Committee and then to the Board of Directors for approval. Achievements are monitored and analyzed every quarter as part of the annual reporting process and subject to a detailed review by the Audit Committee at the end of each quarter.

The Revised Budget: budget revision process carried out midyear. This process updates budget assumptions for the following six-month period by comparison of the actual figures for the year to date with the initial budget projection. The Revised Budget is presented to the Audit Committee and then to the Board of Directors.

The Business Plan: the Annual Budget and the Revised Budget compose a set of financial documents and statements intended for the operational departments, the Management Committee, the Audit Committee and the Board of Directors of the Group. These financial documents and statements are shared by a defined and limited group of users, for strictly internal use, and are not, under any circumstance or in any form, communicated to the public.

3.8.6.1.2 Preparation of financial and accounting information

The consolidated internal reporting system

The internal reporting system is based on the collection and compilation of local general accounting and Budget data/Revised Budget of all Group entities. The data are returned in the form of detailed reports and consolidated statements which reflect the discrepancies between actual and forecast data. Consolidation adjustments are recognized at the close of each half-year.

Based on this information, the Finance Department produces an operating report every quarter as part of the financial closing procedure. This consists of various cost accounting financial statements, both for the reference month and year to date as well as an analysis of the most significant variances in relation to Budget and the Revised Budget excluding consolidation adjustments.

The operational reporting information is made available to line management departments. This report is presented every quarter to the Audit Committee.

Added to these monthly operational reporting items are an interim and annual consolidated report including in particular consolidation adjustments and a reconciliation table with the operational reporting information. This report is submitted to and discussed by the Audit Committee, and then submitted to the Board of Directors.

The consolidated quarterly, semi-annual and annual reports are a major component of the financial information control system. They are favored by the Executive Committee as a monitoring, control and management tool. The reconciliation of accounting and forecast data, combined with the monthly analysis, ensures that the information produced is of high quality and reliable.

These reporting elements and analytical reviews are strictly for internal use and accessible to a defined and limited group of users. They are in no way and in no manner disclosed to the public.

The consolidated financial statements

The consolidated reporting system described above, and in particular the monthly report produced as part of a monthly closing procedure, is the basis on which the consolidated financial statements are prepared.

The procedures for escalating information from the subsidiaries to the parent company, along with the closing procedures, enable the parent company to prepare the consolidated financial statements. A closure timetable is circulated in the month preceding each closing to allow the various accounting divisions to arrange for all the necessary information to be submitted on time.

The consolidated accounts are closed semi-annually on June 30 and December 31 of each year (statutory accounting year end date). They are subject to an audit by the statutory auditors on December 31 and to

a limited review on June 30. The statutory auditors carry out a review of internal control procedures in the last quarter of each year.

The separate statutory financial statements of each Group company are prepared only as of December 31 of each year. Each subsidiary prepares its own financial statements (except in special cases as indicated above in the paragraph entitled Parties involved) according to the accounting standards applicable locally. For consolidation purposes, the data are restated using the Group's accounting standards (IFRS since January 1, 2005).

3.8.6.1.3 Update of standard procedures relating to the preparation and processing of financial and accounting information

The accounting manual and four (4) procedures dealing with the preparation and processing of accounting and financial information have remained in application since 2018.

3.8.7 Information systems

During 2021, the reporting documents, business plan and budget were prepared using Excel.

3.8.8 Oversight of the Internal Control system

3.8.8.1 Verification or Periodic Control of the proper implementation of procedures

Operational area

Periodic control of operational areas was undertaken by Quality Assurance and is detailed in Section 3.8.6.3.2, which focuses on Quality Assurance work in 2021.

Accounting and financial area

The Group did not update the self-assessment record in 2021, including:

- The application guide for internal control of accounting and financial information;
- General internal control principles with regard to accounting and financial information;
- Questionnaires on internal control of accounting and financial reporting and on risk analysis and management.

3.8.8.2 Reporting of work on Risks and Internal Control operations

The work conducted on Risks and Internal Control operations is submitted by the Finance Department to the Audit Committee and is a major component of the risk management process.

This work involves the following:

Work in relation to the AMF Reference Framework (Selection of control points involving a self-assessment, identification of the scope of existence tests, proposed corrective action plan, selection of working processes for risk mapping);

- Improvement of the Internal Control system to encompass the updating of procedures, improved management tools, improved security and confidentiality of computer data, the conduct of audits by Quality Assurance.

3.8.8.3 Work carried out in 2021 on Internal Control and Quality System management

3.8.8.3.1 Monitoring work undertaken by Quality Assurance

The Quality Group was integrated into the Quality Assurance Organization.

The Quality function covers all Group operations (research and development, manufacturing).

As of 31 December 2021, the quality system was deployed at all sites and subsidiaries.

In 2021 a Quality Manual and a Quality Policy were validated by Management, and are currently available to all employees on the Quality Portal.

Nicox is constantly striving to improve its processes, and is investing to update its procedures and optimize the work of its teams.

3.8.8.3.2 Work undertaken in the field of IT

The work in the IT area in 2021 was limited to maintenance and infrastructure rationalization. Given its size, the Group subcontracts IT services with an objective of ensuring the continuity of service.

3.8.8.4 Areas for improvement in the Internal Control system

3.8.8.4.1 Adaptation of accounting and financial tools to the Group's new environment

In 2021, the Company developed a database to automate the management of stock options and restricted stock units (*actions gratuites attribuées*) or RSUs granted to Group employees. The purpose of this database is to improve the reliability of financial communications about stock options and RSUs. This database was put into service in February 2022 and was used for the accounts closed on 31 December 2021. In 2021, the Company also improved the order management database for goods and services by introducing the notion of a budget code for each expense and by tracking budget expenditures and balances outstanding by order.

3.8.8.4.2 Network architecture and IT security

In 2021, the Group continued to adapt and rationalize the IT infrastructure of Nicox Group: by replacing obsolete equipment to ensure availability, the integrity and confidentiality of Nicox's IT infrastructure; by outsourcing as much as possible IT operations to guarantee continuity of service in the context of a small structure and by educating end users about information systems to assist them in becoming more autonomous with IT procedures and quality documents.

3.8.8.4.3 Audit program conducted by the Quality Assurance

Service providers (for non-clinical development, pharmaceutical development, clinical development, manufacturing for active substances and finished products, secondary packaging) are audited on a routine basis every 2 years, except when a for-cause audit before the anniversary date is required, or when after risk analysis the QA and technical teams decide that the audit may be postponed for a certain period. In this latter case an internal memorandum is issued. Two (2) external audits were performed in 2021 relating to activities outsourced in 2021 by Group subsidiaries.

4. INFORMATION ABOUT THE COMPANY

4.1 Company name and trade name of the Company

The legal name of the Company is Nicox SA.

4.2 Place of registration, registration number and legal identity number (LEI) of the Company

Nicox SA is registered at the 'registre du commerce et des societies' (Company Register) of Grasse, France, (Postal code 06133) under the number 403 942 642. The Nicox SA APE code is 7211Z.

LEI code: 969500EZGEO9W4JXR353

4.3 Date of incorporation and the length of life of the Company

The Company was established on February 15, 1996 and registered on February 27, 1996 for a period expiring on December 12, 2094.

4.4 Registered office and legal form of the Company legislation under which it operates, its country of incorporation, , the address and telephone number of its registered office and website

Nicox SA is a French corporation with a Board of directors subject to the provisions of the Commercial Code. Its corporate headquarters are located at DRAKKAR D 2405 route des Dolines 06560 Valbonne Sophia Antipolis, France. Telephone number: +33 (0)4 97 24 53.00.

Website: www.nicox.com. Information provided on the Company's website does not constitute part of the original French language version of the universal registration document (*document d'enregistrement universel*) that was filed with the French Financial Market Authority, the AMF, with the exception of information expressly incorporated by reference into said document, and on that basis has not been reviewed or approved by the AMF.

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BUSINESS

5.1 Overview

5.1.1 Summary of the main activities of the Company

We are an international ophthalmology company developing innovative solutions to help maintain vision and improve ocular health. Nicox has two programs in late stage clinical development, one in glaucoma (two Phase 3 trials ongoing) and one in dry eye disease (one Phase 2b trial completed in blepharitis, with *post hoc* analysis in dry eye disease), a pre-clinical development candidate, and two out-licensed and commercialized products with exclusive partners.

- NCX 470, a novel nitric oxide (NO) donating prostaglandin analog, is currently in two Phase 3 clinical trials, Mont Blanc and Denali, for the lowering of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. Top-line results from the Mont Blanc trial are currently expected in Q1 2023. The topline results will not be available by the end of 2023 as previously communicated due to several hurdles (including the COVID-19 pandemic situation in the U.S. and China). The Company will announce a new date for availability of the results when we have more visibility on the overall timelines of the trial.
- NCX 4251, a novel and patented ophthalmic suspension of fluticasone propionate nanocrystals, is currently in development for patients with dry eye disease. A Phase 2b clinical trial in blepharitis, Mississippi, has been completed, with a post hoc analysis carried out in dry eye disease. The future development of NCX 4251 in the U.S. will require initial manufacturing scale-up followed by two additional efficacy clinical trials, both evaluating one sign and one symptom of dry eye disease, long term safety data, and certain additional clinical and non-clinical data to support an NDA submission in the U.S. The remaining pharmaceutical, non-clinical and clinical development of NCX 4251 is not yet financed and therefore the Company has not planned yet the start of this last phase of development.

NCX 1728, a pre-clinical development candidate selected from a new class of compounds (non-PGA related) based entirely on NO-mediated activity, being investigated for lowering IOP and for applications in retinal diseases. NCX 1728 is an NO-donating PDE5 inhibitor.

- VYZULTA[®], indicated for the reduction of IOP in patients with open angle glaucoma or ocular hypertension, is exclusively licensed worldwide to Bausch + Lomb, a Bausch Health Companies Inc. company, and commercialized in the U.S., Canada, Argentina, Hong Kong, Mexico, Taiwan and Ukraine. VYZULTA has been also approved in Brazil, Colombia, Jordan, Qatar, Singapore, South Korea, Thailand, Turkey and United Arab Emirates.
- ZERVIAE[®], indicated for the treatment of ocular itching associated with allergic conjunctivitis, is commercialized in the U.S. by our exclusive U.S. licensee Eyeavance Pharmaceuticals or Eyeavance, a wholly-owned subsidiary of Santen Pharmaceutical Co., Ltd. Our exclusive Chinese partner for the development and commercialization of ZERVIAE in China and in the majority of Southeast Asia, Ocumension Therapeutics, has completed a Phase 3 clinical trial in China. ZERVIAE is also exclusively licensed for development and commercialization in other territories.

Our lead product candidate, NCX 470, leverages the same technology as VYZULTA, our product commercialized under license, which leverages our proprietary expertise in generating novel patentable molecules and are new molecular entities (NMEs) that release NO. NO is a well-known, small, naturally-occurring signaling molecule whose target is an intracellular enzyme, soluble guanylate cyclase (sGC). NO, present in ocular tissues, plays a key role in the regulation of intraocular pressure, or IOP. An NO-donating moiety can be linked to other pharmaceutical agents to improve IOP lowering efficacy. Release of NO and the subsequent activation of sGC is one of the mechanisms that is believed to lead to IOP lowering by Nicox's novel molecules. Adding NO to well-known molecules, such as prostaglandin analogs (PGAs), which is the most commonly prescribed class of IOP-lowering drugs, adds a potential second mechanism of action (MOA), and we believe allows certain of our products and product candidates to lower IOP further than the parent molecule alone. We believe that by designing our

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proprietary molecules with a dual MOA, we may be able to achieve greater IOP lowering compared to the parent compound alone.

Product candidates

NCX 470, developed based on our internally-developed NO-donating research platform, is our lead product candidate. NCX 470, an NME, is a novel NO-donating prostaglandin analog formulated as an ophthalmic solution, which is currently in late-stage clinical development for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension.

Following a positive End-of-Phase 2 meeting with the U.S. FDA, we initiated the first Phase 3 clinical trial, Mont Blanc, in the U.S. in June 2020, evaluating NCX 470 for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension. The Mont Blanc trial is a multi-regional, double-masked, 3-month, parallel group trial evaluating the efficacy and safety of NCX 470 ophthalmic solution, 0.1% compared to latanoprost ophthalmic solution, 0.005% in patients with open-angle glaucoma or ocular hypertension. The 0.1% dose was selected through an initial adaptive design portion of the trial, which also included the 0.065% dose. The primary efficacy evaluation is based on time-matched IOP at 8 AM and 4 PM at Week 2, Week 6 and Month 3. The trial is expected to randomize approximately 670 patients at approximately 50 clinical sites, primarily in the U.S. and one clinical site in China. Top-line results from the Mont Blanc trial are currently expected in Q1 2023.

In November 2020 Nicox initiated the second Phase 3 trial in the U.S., Denali, financed in equal parts by Nicox and Ocumension, our exclusive partner for NCX 470 in the Chinese, Korean and Southeast Asian markets. The Chinese part of the trial was initiated in December 2021. Denali is a 3-month Phase 3 trial evaluating the safety and efficacy of NCX 470 ophthalmic solution, 0.1% versus latanoprost ophthalmic solution, 0.005%, for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension. The Denali trial, which includes a long-term safety extension, is expected to randomize 670 patients, at approximately 60 clinical sites in the U.S. and China, with approximately 80% of the patients to be recruited in the U.S and the remaining 20% of the patients to be recruited in China. The Denali trial, together with the Mont Blanc trial, are designed to fulfill the regulatory requirements for Phase 3 safety and efficacy trials to support NDA submissions in the U.S. and China. The topline results will not be available by the end of 2023 as previously communicated due to several hurdles (including the COVID-19 pandemic situation in the U.S. and China). The Company will announce a new date for availability of the results when we have more visibility on the overall timelines of the trial.

In the U.S., a multicenter, dose-response, Phase 2 clinical trial, Dolomites, NCX 470 ophthalmic solution 0.065% demonstrated non-inferiority and statistical superiority, based on the trial's pre-specified statistical analysis plan of diurnal mean IOP reduction at Day 28, to latanoprost ophthalmic solution, 0.005%, the U.S. market leader in prostaglandin analog prescriptions.

The molecules in VYZULTA and NCX 470, discovered using our research platform, are believed to lower IOP through a dual MOA, which combines NO donation, that activates sGC, with PGAs that activate Prostaglandin F, or FP, receptors, to increase the compounds' ability to lower IOP relative to the parent active compounds. In NCX 470, our NO-donating research platform was applied to add an NO-donating group to bimatoprost. Bimatoprost (known by the brand name LUMIGAN) is a PGA and is the current market leader by sales value among all glaucoma therapies in the U.S. and EU, the two largest glaucoma markets worldwide. NCX 470's potential dual MOA is believed to lower IOP by increasing the outflow of fluid from the eye through the primary, or conventional outflow route via trabecular meshwork as well as through secondary, or unconventional outflow route via uveoscleral pathway. The primary outflow is believed to be increased by NO released from NCX 470 via activation of sGC and relaxation of trabecular meshwork while the secondary outflow pathway is believed to be increased by bimatoprost- released from NCX 470 activation of FP receptors. In addition, exploratory studies on NCX 470 in a nonclinical model of retinal cell damage induced by endothelin-1 (ET-1) investigated the potential protective effects of NCX 470 on the retina and the optic nerve head. The results suggest that NCX 470 improves ocular perfusion and retinal function in damaged eyes compared to vehicle and therefore may have therapeutic properties in addition to lowering of IOP.

We are applying key learnings, based on Nicox's stand-alone NO-donors, to NO-donating moieties attached to other non-PGA therapeutic classes of compounds with the goal of enhancing the NO-mediated effects.

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NCX 1728, NO-donating PDE5 inhibitor, is the first in a new class of compounds in which NO-mediated effects are enhanced by concomitant phosphodiesterase-5 (PDE5) inhibition activity within the same molecule. PDE5 inhibition has been shown both to enhance the efficacy and the duration of NO-mediated effects. This class of molecules is being evaluated for development in IOP lowering and in certain retinal diseases.

In addition to our NO-donating product candidates in preclinical and clinical development, our pipeline includes a product candidate based on a novel and proprietary formulation of a well-established molecule that has previously been used in other indications and therapeutic areas, with the potential to offer novel treatments for various eye conditions.

NCX 4251, our novel patented ophthalmic suspension of fluticasone propionate nanocrystals, is in development as a topical treatment, applied to the eyelid margins for patients with dry eye disease. Fluticasone propionate, the active ingredient in NCX 4251, is a well-established corticosteroid which has been marketed for more than 20 years for a number of non-ophthalmic indications, including asthma and allergic rhinitis. Fluticasone propionate has an affinity for the glucocorticoid receptor approximately ten times greater than dexamethasone, a corticosteroid commonly used in ophthalmology. Fluticasone propionate has not been approved previously for topical ophthalmic use. Once-daily NCX 4251, fluticasone propionate ophthalmic suspension 0.1% was evaluated in the Mississippi Phase 2b clinical trial, versus placebo in patients with acute exacerbations of blepharitis. The primary outcome measure in the Mississippi trial was the proportion of patients achieving complete cure in all three hallmark signs and symptoms of blepharitis, eyelid redness, eyelid debris and eyelid discomfort, at Day 15, with two secondary outcome measures focused on signs and symptoms of dry eye. The trial did not meet the primary or secondary efficacy endpoints, however, a *post hoc* analysis of the data suggest that NCX 4251 is effective in reducing dry eye symptoms in patients with higher severity (moderate to severe) of key signs and symptoms of dry eye. The results of the Mississippi trial were announced in September 2021. Subsequent to the post hoc analysis and meeting with the U.S. FDA in early 2022, we are now focusing the development of NCX 4251 on dry eye disease. The future development of NCX 4251 in the U.S. will require initial manufacturing scale-up followed by two additional efficacy clinical trials, both evaluating one sign and one symptom of dry eye disease, long term safety data, and certain additional clinical and non-clinical data to support an NDA submission in the U.S. The remaining pharmaceutical, non-clinical and clinical development of NCX 4251 is not yet financed and therefore the Company has not planned yet the start of this last phase of development.

Products

Our product commercialized under license, VYZULTA (latanoprostene bunod ophthalmic solution), 0.024%, represents the first FDA approved drug developed based on our internally-developed NO-donating research platform. In VYZULTA, an NO-donating- group was linked to latanoprost, the active ingredient in XALATAN, a PGA, structurally related to prostaglandins. PGAs are in a class of molecules used in ophthalmology to lower IOP and are believed to do so by activating FP receptors located on the surface of cells. In the U.S., PGAs are the first line and the most commonly prescribed pharmacotherapy class for the lowering of IOP in glaucoma and ocular hypertensive patients. VYZULTA is the first PGA with one of its metabolites being NO approved by the FDA for the reduction of IOP. NO is believed to lower IOP by increasing the outflow of fluid from the eye via activation of sGC, a different mechanism from that of PGAs. Thus, VYZULTA is believed to possess a dual MOA in a single molecule. Prior to the FDA approval of VYZULTA, there were no other NO-donating products approved for the lowering of IOP in the U.S. VYZULTA is exclusively worldwide licensed to Bausch + Lomb, a Bausch Health Companies Inc. company, and is commercialized in the U.S., Canada, Argentina, Hong Kong, Mexico, Taiwan and Ukraine. VYZULTA has been also approved in Brazil, Colombia, Jordan, Qatar, South Korea Singapore, Thailand, Turkey and United Arab Emirates.

ZERVIAE (cetirizine ophthalmic solution), 0.24%, our second FDA approved product, is a novel formulation of cetirizine developed and approved for the first time as an eye drop. ZERVIAE, which is indicated for the treatment of ocular itching associated with allergic conjunctivitis, is the first product for the topical treatment of ocular allergies to use cetirizine, the active ingredient in ZYRTEC, a well-established oral antihistamine which has been marketed for over 20 years. We believe that the proven safety and efficacy of oral cetirizine currently recognized by physicians will encourage the adoption of ZERVIAE ophthalmic solution. In 2017, we granted Eyeavance exclusive rights to commercialize ZERVIAE in the U.S. and transferred the New Drug Application, or NDA, to Eyeavance. ZERVIAE has been commercialized in the U.S. by Eyeavance since March 2020. ZERVIAE has been exclusively licensed for development and commercialization to Ocumension

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in the Chinese and majority of Southeast Asian Region markets. In February 2022 Ocumension successfully completed a Phase 3 clinical trial in China with ZERVIATE. Subject to any additional data requested by the Chinese NMPA, this Phase 3 trial, in addition to the data package used by the FDA for ZERVIATE in the U.S., is expected to be sufficient to support a Chinese NDA. ZERVIATE has also been exclusively licensed to Samil in South Korea and Vietnam, to ITROM in Gulf and Arab markets and to Laboratorios Grin in Mexico.

Ophthalmic Products Market

The current treatment landscape for open-angle glaucoma and ocular hypertension is dominated by two drug classes, topical PGAs and topical beta-blockers, with various combinations introduced over the past 20 years. Since PGAs began to replace topical beta-blockers as the first line of IOP-lowering agents in glaucoma, several have been approved and generic competition in the category is significant. In the U.S., PGAs have now replaced beta-blockers as the first line therapy. At the time of approval in the U.S., VYZULTA was the first eye-drop approved in the past 20 years with a novel approach to reducing IOP. This is a situation which we believe has resulted in a significant demand from eyecare providers for new MOAs to lower IOP in patients with open-angle glaucoma or ocular hypertension.

Allergic conjunctivitis is currently treated by both oral and topical ocular antihistamines, with more serious cases requiring topical, or even oral, corticosteroids. The treatment regimens and molecules are well established and most oral antihistamines, and some topical antihistamines, are now available as generics in the U.S. A number of previously prescription-only products are now available without a prescription. Nevertheless, new products in the field are necessary to expand the choices available to doctors and patients.

The dry eye disease market comprises of pharmaceutical prescription products for both chronic and short term use and a significant part of non-prescription artificial tears. The principal mode of pharmaceutical treatment is anti-inflammatory. Some short term prescription products are used together with the chronic treatments, such as at the initiation stage, when the chronic treatment takes time to act, or as adjunctive therapy in case of exacerbations in patients already on chronic treatments. A significant number of generic steroids are used for short term use, and the lead branded chronic treatment (Restasis) has just become available as a generic.

Worldwide, the sales of pharmaceutical ophthalmic treatments reached \$24.3 billion in 2020 and have grown at an average rate of 6% annually since 2015, according to IQVIA Health Analytics. In the U.S. alone, ophthalmology sales reached \$11.1 billion in 2020, growing also at an average rate of 6% annually since 2015. With respect to our markets of focus, worldwide sales of treatments targeting glaucoma were \$6.0 billion, out of the \$24.3 billion worldwide market for ophthalmic drugs and sales. In the U.S. sales of treatments targeting glaucoma totaled \$3.0 billion in 2020, at an average annual rate of 6% since 2015 or 27% of the \$11.1 billion total of the U.S. ophthalmic drug market. The estimated worldwide market for dry eye disease treatment is over \$5 billion, and the current prescription market in the U.S. at around \$3.8 billion (according to Bloomberg). Additionally, prescription topical treatments for ocular allergies generated approximately \$400 million in the U.S. in 2020, not including substantial sales of non-prescription and over-the-counter products used to alleviate symptoms of ocular allergies.

Our intellectual property portfolio consists of patents and pending patent applications related to composition of matter, pharmaceutical compositions and methods of use for our product candidates. We have patent protection for VYZULTA in the U.S. (through 2025 which may be subject to extension to 2030. Eligibility for a patent term extension has been agreed by the USPTO), for ZERVIATE (in the U.S. until 2030 and 2032, in Europe, Japan and Canada until 2030) and for our product candidates NCX 470 (worldwide protection until 2029 under a composition of matter patent with potential extension up to 5 years in the U.S. and EU and formulation patent until 2039 in the U.S., EU, Japan and China), and NCX 4251 (worldwide protection by patents until 2033 and to 2040 by additional patents granted in the EU and Japan). These dates do not include potential patent extensions which may be available to us.

As of December 31, 2021, we had 30 employees, including personnel supporting our development operations in the U.S. and France, and research and nonclinical development operations in Italy. Our headquarters are located in Sophia Antipolis, Valbonne, France, and we have been listed on Euronext Paris (COX.PA) since 1999.

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5.1.2 Our Competitive Strengths

We believe the following key competitive strengths are core to our ability to develop novel treatment solutions for our patients and become a leader in ophthalmology:

- Our clinical stage pipeline, consisting of novel therapies targeting inadequately met or unmet medical needs within ophthalmology, including glaucoma and dry eye disease;
- Our proven NO-donating research platform, which we believe provides a competitive advantage for the discovery of innovative product candidates for the lowering of IOP, as validated by VYZULTA and further demonstrated by the results of the NCX 470 Dolomites Phase 2 clinical trial, and which has generated NCX 1728;
- Our products commercialized in the U.S., VYZULTA (which is also commercialized in certain other territories outside of the U.S.) and ZERVIAE, both of which may potentially be able to obtain marketing approval in other countries where the data submitted to FDA are sufficient, or new data can be generated, for such approval;
- Our proven ability to enter into successful partnerships with leading biopharmaceutical companies, as demonstrated by our worldwide exclusive licensing agreement with Bausch + Lomb for VYZULTA, to enter into regional collaboration agreements as demonstrated by the exclusive licensee agreements with Ocumension and to enter into commercialization partnerships, as demonstrated by our exclusive licensing agreement with Eyevance and as well by the development and commercialization agreements with Ocumension, Samil, ITROM and Laboratorios Grin;
- Our significant experience in ophthalmic drug discovery and development as well as extensive operational, financial and public company experience across both our management team and our board of directors. Our key executives and board members have held leadership roles within major pharmaceutical ophthalmology companies, including divisions of Alcon, Inc., Allergan, Inc., Novartis AG, and ISTA Pharmaceuticals, Inc.

5.1.3 Our Strategy

We plan to keep the maximum of options open for the company by maintaining rights to our novel therapeutics for eye diseases in key territories, such as the U.S. and Europe, as we create value by advancing their development, maintaining the potential for direct marketing, licensing for certain territories and growth through strategic transactions. The strategy is subject to obtaining sufficient or additional financing where necessary. Key elements of our strategy include:

- ***Rapidly advance our product candidates through clinical development to approvals in the U.S.*** Our pipeline includes NCX 470 in Phase 3 for open-angle glaucoma and ocular hypertension and NCX 4251 for dry eye disease;
- ***Optimize development through partnerships.*** We are seeking to optimize development and commercialization of our product candidates through regional collaborations where appropriate, to leverage the resources of a partner, such as our partnerships with Ocumension on NCX 470 in the Chinese, Korean and Southeast Asian markets and NCX 4251 in the Chinese market. In certain instances, we may partner a program for exclusive development;
- ***Demonstrate value in our early-stage pipeline.*** Nicox plans to advance NCX 1728, an NO-donating PDE5 inhibitor, the first molecule selected from this new class of molecules based entirely on NO-mediated activity, into pre-clinical development;;
- ***Maximize the value of ZERVIAE through partnering.*** ZERVIAE has been commercialized in the U.S. by our exclusive U.S. licensing partner, Eyevance Pharmaceuticals, a wholly-owned subsidiary of Santen Pharmaceutical Co., Ltd, Japan, since March 2020. It is also partnered with

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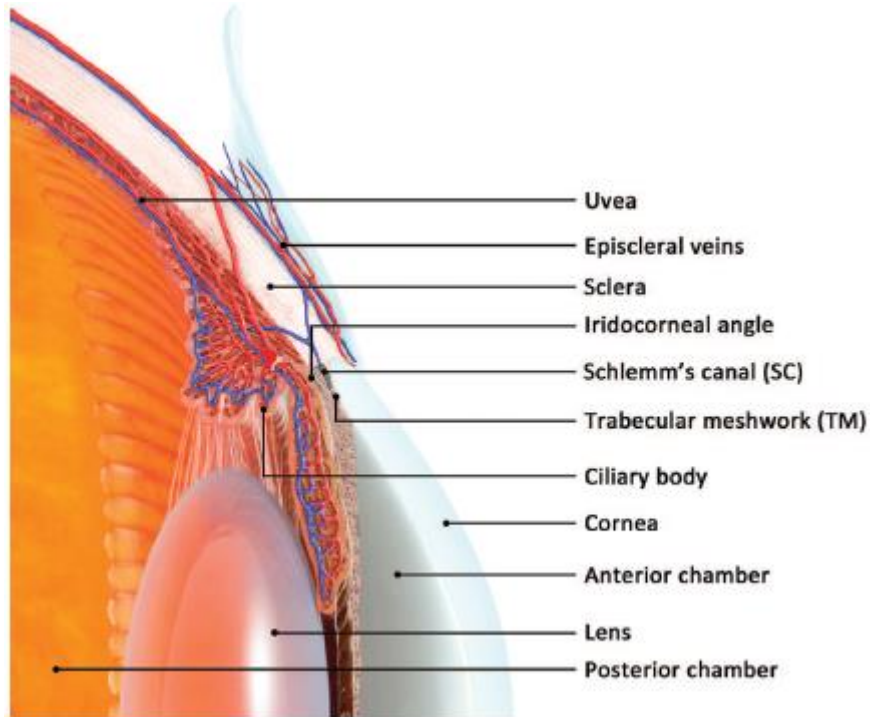
Ocumension for the Chinese and the majority of Southeast Asian markets, with Samil in South Korea and Vietnam, with ITROM in Gulf and Arab markets and with Laboratorios Grin for Mexico. Similar to VYZULTA, we believe this strategy will allow us to efficiently use our internal resources while providing significant financial benefit through milestones and royalty payments. We are currently seeking partners capable of pursuing approval for and marketing ZERVATE in other countries.

5.1.4 Description of the Eye

The eye is a fibrous globe that maintains its spherical geometry by being filled with a fluid called aqueous humor on the front side of the eye adjacent to cornea (also called the anterior segment) and a gel called vitreous humor on the back side of the eye adjacent to retina (also called the posterior segment). Both the front of the eye and the back of the eye are at the proper pressure to maintain the eye's shape and thus maintain an unobstructed and optically clear path for the light through the cornea and the lens to the retina. To maintain the pressure on the front of the eye, and therefore its shape, the aqueous humor is constantly produced inside the front compartment of the eye by a tissue known as the ciliary body and flows forward through the pupil and into the angle defined by the front of the iris and the back of the cornea. Blockages or malfunctions in this drainage system can result in abnormally high IOP often resulting in glaucoma.

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The picture below shows the cross section of the aqueous humor drainage system of the eye.

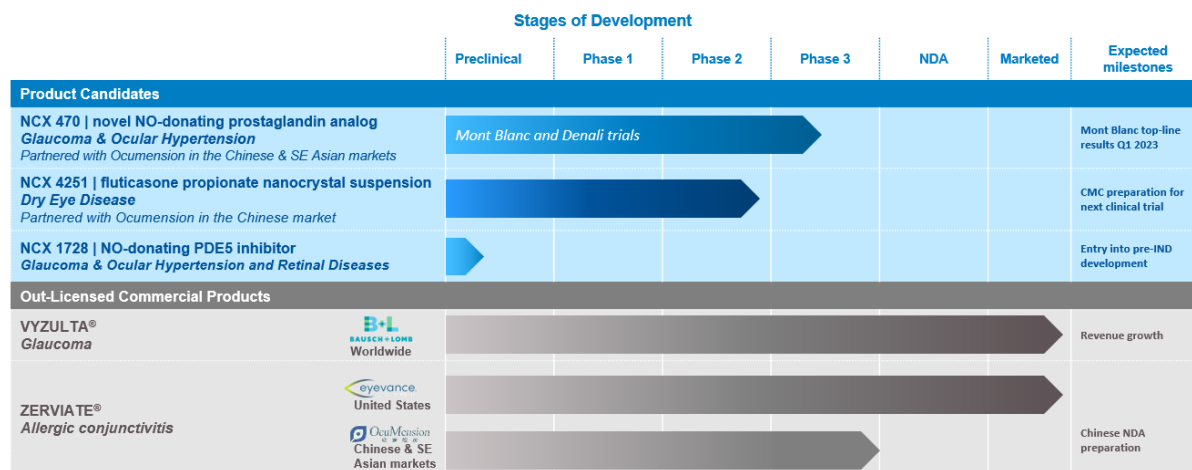


Dry eye disease is a common condition that occurs when the quality and/or quantity of tears are not able to adequately hydrate or lubricate the eyes. This inadequate lubrication can lead to dryness, inflammation, pain, discomfort, irritation, diminished quality of life, and in severe cases, permanent vision impairment.

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5.1.5 Our Pipeline

We believe that our pipeline is strong in glaucoma and broad across eye diseases of the anterior segment (i.e. the front of the eye), with two products commercialized, one product candidate in Phase 3 clinical development, one in Phase 2 clinical development, one preclinical candidate:



Overview

Our product candidate pipeline features clinical and early development stage assets with a potential to offer novel treatments in various eye conditions. Those targeting the lowering of IOP in patients with open-angle glaucoma or ocular hypertension are from our internally-developed NO-donating research platform. We are also targeting dry eye disease with development of a novel and proprietary formulation of a well-established molecule that has previously been used in other indications and therapeutic areas.

In addition, we have two commercialized products; VYZULTA, commercialized in the U.S., Canada, Argentina, Hong Kong, Mexico, Taiwan and Ukraine, and which is also approved in Brazil, Colombia, Jordan, Qatar, Singapore, South Korea Thailand, Turkey and United Arab Emirates, by our exclusive worldwide licensee, Bausch + Lomb, and ZERVIAE, commercialized in the U.S. since March 2020 by our exclusive U.S. partner EyeVance.

Using NO in ophthalmology

We have developed a leading position in the therapeutic application of NO-donating compounds in ophthalmology. Our compounds are designed to release NO with a pharmacological benefit believed to be elicited locally at the tissue level via NO activation of the intracellular enzyme sGC expressed within ocular tissues. Consistent with our strategic positioning in ophthalmology, our research platform is focused on eye conditions where NO has been shown to play an important role.

NO is a well-known small naturally-occurring signaling molecule whose target is an intracellular enzyme, sGC, which converts guanosine triphosphate to the second messenger, cyclic guanosine monophosphate, or cGMP. The cellular machinery, that synthesizes endogenous NO, is present in ocular tissues, together with other components involved in the NO signaling cascade via the activation of sGC. The NO stimulated increase in the concentration of cGMP in the trabecular meshwork leads to the sequestration of intracellular calcium, the relaxation of the trabecular meshwork and, consequently, an increase in the outflow of the aqueous humor from the anterior segment of the eye through the primary or conventional outflow pathway (i.e., via the trabecular meshwork, Schlemm's canal, aqueous veins, and episcleral veins). All of the foregoing events are thought to lead to lowering of IOP. The effect of NO in the sGC signaling cascade may be further increased or prolonged by sGC stimulators, which interact synergistically with NO to increase the production of cGMP. Additionally, the effect of NO on IOP lowering may be further increased and/or prolonged by PDE5 inhibitors, which inhibit the

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degradation of cyclic guanosine monophosphate (cGMP), a key intracellular messenger that is produced as a result of stimulation by NO. Studies have shown that topical administration of traditional NO donors, such as nitroglycerin or isosorbide mononitrate, reduces IOP, reinforcing the role of NO in IOP regulation. Lower plasma levels of NO markers are found in open angle glaucoma patients compared to individuals without glaucoma. Several studies conducted in animal models, as well as in glaucoma patients, have shown that the release of NO activates sGC and lowers IOP.

To date, it has been established that NO plays a key role in the regulation of IOP. An NO-donating moiety can be linked to other pharmaceutical agents to improve IOP-lowering efficacy, as is the case with our lead clinical development candidate NCX 470, a novel NO-donating prostaglandin analog, and our commercialized product with the same mechanism of action, VYZULTA. Release of NO and the subsequent activation of sGC is one of the mechanisms that is believed to lead to IOP lowering- by our novel molecules. By designing our proprietary molecules with a dual MOA, we may be able to achieve increased IOP lowering efficacy compared to the molecules acting by a single mode of action. Based on this approach, our partnered approved product VYZULTA, the only NO-donating molecule approved for an ophthalmic indication in the U.S., and our product candidate NCX 470 currently in clinical development, are comprised of a parent PGA and an NO-donating moiety. NCX 470, a novel NO-donating prostaglandin analog, has demonstrated statistical superiority to latanoprost, based on pre-specified statistical analyses of IOP reduction in the Dolomites Phase 2 trial. We believe that NCX 470 has the potential to become the first approved non-combination product with statistical superiority to a PGA. We also believe that NCX 470 has the potential to lower IOP more than bimatoprost, an FDA approved PGA that is the current U.S. market leader by sales, marketed under the brand LUMIGAN. The results from the Dolomites Phase 2 trial on NCX 470 together with the positive clinical Phase 2 and 3 results obtained with latanoprostene bunod and the subsequent approval of VYZULTA by the FDA demonstrate the potential of such dual MOA approach with our internally-developed NO-donating research platform in ophthalmology.

NO-donating research platform

We have developed a leading scientific and strategic position in the therapeutic application of NO-donating- compounds based on our internally-developed NO-donating research platform. Using this proprietary expertise in generating novel, patentable molecules, are NMEs that release NO, our research center has conducted lead generation and lead evaluation in preclinical studies in ophthalmology, creating a significant patent portfolio.

We have focused our research efforts on ocular disorders in which NO is believed to play a major role in controlling IOP. Our research platform produced the NO-donating compounds, VYZULTA and NCX 470. VYZULTA has demonstrated greater IOP lowering than the parent PGA compound in a randomized clinical trial. This effect is believed to be due to the additional lowering in IOP from the NO-donating moiety. We are applying key learnings, based on Nicox stand-alone NO-donors, to NO-donating moieties attached to other non-PGA therapeutic classes of compounds with the goal of enhancing the NO-mediated effects. NCX 1728, an NO-donating PDE5 inhibitor, is the first in this new class of compounds in which NO-mediated effects are enhanced by concomitant phosphodiesterase-5 (PDE5) inhibition activity within the same molecule. PDE5 inhibition has been shown both to enhance the efficacy and the duration of NO-mediated effects. This class of molecules has the potential for development in IOP lowering and in certain retinal diseases.

Mechanism of action of NO and NO-donating prostaglandin analogs

Evidence suggests that PGAs, which are indicated for reducing elevated IOP in patients with open-angle- glaucoma or ocular hypertension, have a MOA which works via prostaglandin FP receptor activation with a primarily positive impact on the activity of certain enzymes, resulting in a widening of the interstitial spaces of the ciliary muscle and contributing to increased uveoscleral outflow of the aqueous humor. This pathway is referred to as the nonconventional or the secondary pathway. However, the conventional or the primary pathway, wherein aqueous humor exits the eye through the trabecular meshwork into Schlemm's canal, a circumferential vessel in the angle of the eye between the cornea and the iris that collects the aqueous humor from the anterior chamber and delivers it to the venous blood vessels, is believed to be a major limiting factor in aqueous humor outflow, and the flow through the primary or conventional pathway is decreased in glaucoma. PGAs may have only a small impact on this pathway.

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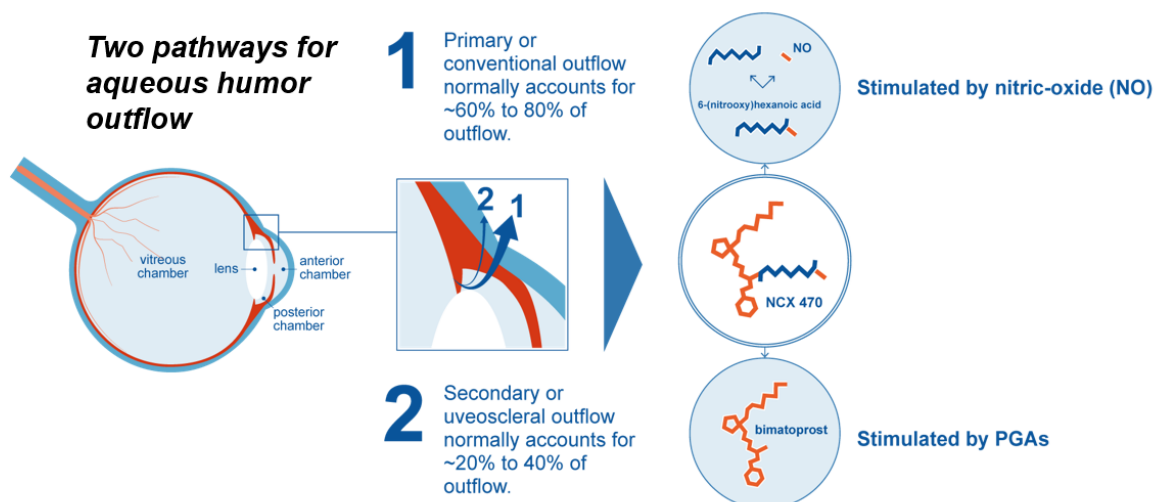
Because the primary or conventional pathway is known to be NO-sensitive, we sought to create a compound that would both release a PGA to target the uveoscleral and secondary pathway by activating FP receptors and, at the same time, release NO to stimulate sGC to target the primary or conventional pathway in order to achieve a novel dual MOA. Through investigating this mechanism, latanoprostene bunod was discovered in our research center in Italy. Latanoprostene bunod (the active ingredient in VYZULTA) is an NO--donating version of an existing drug, latanoprost, which belongs to the category of prostaglandin F2alpha analogs. Latanoprostene bunod- is metabolized, after application on the ocular surface, into latanoprost acid and another moiety which is then further metabolized to release NO.

The preclinical and clinical data demonstrate that latanoprostene bunod lowers IOP to a greater extent than latanoprost alone in multiple animal models and in glaucoma patients. Our partner, Bausch + Lomb, conducted preclinical studies to investigate the effect of latanoprostene bunod on primary human trabecular meshwork cell contractility to determine whether latanoprostene bunod might mediate this additional IOP lowering through the conventional outflow pathway. Results from these preclinical studies support the concept that latanoprostene bunod has a dual MOA and may target both aqueous outflow pathways to lower IOP in patients with glaucoma or ocular hypertension. These data have been further supported by results of a Phase 2 clinical trial of latanoprostene bunod versus latanoprost conducted in glaucoma and ocular hypertension patients.

As mentioned above, NCX 470 is a novel NO-donating prostaglandin analog that we believe has the potential to become the first non-combination product with statistical superiority to a PGA (latanoprost) and to lower IOP more than bimatoprost, an FDA-approved PGA that is the current U.S. market leader by sales marketed under the brand LUMIGAN. Both NCX 470 and VYZULTA are designed to lower IOP via two MOAs. Upon administration to the eye, NCX 470 and VYZULTA are transformed by certain enzymes present in the eye into the PGAs, bimatoprost acid and latanoprost acid, respectively, and the NO-donating moiety. This NO--donating moiety is then further transformed, breaking down into NO and inactive organic compounds. The PGA, one of the active components of NCX 470 and VYZULTA, is released in the eye and is believed to interact with specific receptors (prostaglandin F2 alpha receptors). This interaction is thought to trigger signaling cascades that ultimately lead to rearrangement of the smooth ciliary muscle in the eye's middle layer, called the uvea, which in turn improves the outflow of the fluid present in the eye, or aqueous humor, from the fluid-filled- chamber at the front of the eye backwards through the uvea and sclera (the white fibrous capsule of the eye). This outflow is referred to as the uveoscleral, unconventional or secondary outflow pathway. NO, the second active component released by NCX 470 and VYZULTA, is thought to enhance the outflow of the eye fluid by the conventional or primary outflow pathway, by modulating the eye tissues called the trabecular meshwork and changing the structure of a canal inside the eye known as Schlemm's canal. The released NO is thought to trigger signals leading to a decrease in cell contractility and volume and, thus, allowing an enhancement of the conventional outflow pathway.

The picture below shows the MOAs of NO-donating PGAs: The trabecular meshwork outflow, also known as the primary or conventional outflow pathway, which is NO sensitive and the uveoscleral outflow, the secondary or non-conventional outflow pathway that is PGA sensitive.

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Glaucoma Overview

Glaucoma is a group of ocular diseases in which the optic nerve is injured, leading to peripheral and ultimately central visual field loss. Glaucoma can eventually progress to blindness if not treated and is currently considered to be one of the three leading causes of irreversible blindness worldwide. Glaucoma is frequently linked to abnormally high pressure in the eye, elevated intraocular pressure (IOP) due to blockage or malfunction of the eye's aqueous humor drainage system in the front of the eye. Current medications are targeted at reducing IOP to slow the progression of the disease. It is generally accepted that every mmHg of IOP lowering results in a risk reduction in open angle glaucoma progression of approximately 10% to 20%. Numerous eye drops are available to either decrease the amount of fluid produced in the eye or improve its flow out of the eye. Nearly half of all patients with open angle- glaucoma require more than one medication to lower their IOP to a target level at which visual field loss is likely to be minimized or halted. The requirement for multiple medications to lower an individual patient's IOP to their target level highlights the need for more effective treatments.

High IOP usually does not cause any symptoms, except in cases of acute angle closure in which the IOP may rise to three or four times that of normal IOP and can be painful, but can lead to optic nerve damage and vision loss if left untreated. Optic nerve damage and vision loss can also occur in patients with normal IOP, normotensive glaucoma patients, who are also treated with IOP lowering medications. The Normal Tension Glaucoma Study completed in 1998 showed that lowering IOP slowed the progression of normal tension glaucoma, a form of glaucoma in which the patient's IOP is within normal ranges.

In 2020, worldwide sales of treatments targeting glaucoma were \$6.0 billion, out of the \$24.3 billion worldwide market for ophthalmic drugs. In the U.S., sales of treatments targeting glaucoma totaled \$3.0 billion in 2020 or 27% of the \$11.1 billion U.S. market for ophthalmic drugs. Of the U.S. sales of treatments targeting glaucoma, \$1.4 billion, or approximately 50%, were sales of prostaglandin analogs, of which almost 90% were branded products led by LUMIGAN and TRAVATAN Z. Over 70% of the PGA prescriptions are for generic latanoprost. PGAs are currently used as the first line standard of care pharmacotherapy in the U.S.

While not derived from head-to-head trials, the table below provides a summary of the U.S. FDA labeling information for the currently used first-line pharmacotherapies.

Summary of the U.S. FDA Labeling Information for the Currently Approved First-line Pharmacotherapies for the Reduction of IOP in Patients with Open-Angle of Glaucoma or Ocular Hypertension.

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	XALATAN¹ (latanoprost 0.005%)	LUMIGAN¹ (bimatoprost 0.01%)	TRAVATAN Z¹ (travoprost 0.004%)	VYZULTA² (latanoprostene bunod 0.024%)	ROCKLATAN¹ (latanoprost 0.005% and netarsudil 0.02%)
IOP reduction.....	6 to 8 mmHg	Up to 7.5 mmHg (7 to 8 mmHg for 0.03% bimatoprost)	7 to 8 mmHg	Up to 7 to 9 mmHg	6.8 to 9.2 mmHg 1 to 3 mmHg greater than latanoprost or netarsudil (1.58 mmHg greater than latanoprost 0.005% at 3 months) ³
Patient mean baseline IOP	24 to 25 mmHg	23.5 mmHg (26 mmHg for 0.03% bimatoprost)	25 to 27 mmHg	26.7 mmHg	23.6 mmHg ⁴
Adverse reactions	Foreign body sensation 13%; punctate keratitis 10%; stinging 9%; conjunctival hyperemia 8%	Conjunctival hyperemia 31% (45% for 0.03% bimatoprost)	Conjunctival hyperemia 30% to 50%	Conjunctival hyperemia 6%; eye irritation 4%; eye pain 3%; instillation site pain 2%	Conjunctival hyperemia 59%; instillation site pain 20%; corneal verticillata 15%; conjunctival hemorrhage 11%

- (1) Indicated for the reduction of elevated intraocular pressure in patients with open angle- glaucoma or ocular hypertension.
- (2) Indicated for the reduction of intraocular pressure in patients with open angle- glaucoma or ocular hypertension.
- (3) See Section 14, Clinical Studies, Figure 1 and 2 of ROCKLATAN package insert for diurnal IOP at Day 90 for ROCKLATAN vs. Latanoprost including both Mercury-1 and Mercury-2 IOP values (1.5; 1.7; 1.3; 1.5;2.0; and 1.5 mmHg).
- (4) See Section 14, Clinical Studies, Figure 1 and 2 of ROCKLATAN package insert for baseline IOP for ROCKLATAN including both Mercury-1 and Mercury-2 IOP values (24.8; 23.7; 22.6; 24.7; 23.3; 22.4 mmHg).

For patients whose glaucoma is not well-controlled- on a single PGA eye drop, adjunctive therapies are added on the top of PGAs as second, third and fourth eye drops. The adjunctive therapies include beta blockers, alpha agonists, carbonic anhydrase inhibitors, rho kinase inhibitors, or their fixed dose combinations. As the number of medications increases, compliance decreases and hence the opportunity for more effective single-drop treatments remain. The total sales of adjunctive therapies accounted for approximately \$1.6 billion of the \$3.0 billion U.S. sales of treatments targeting glaucoma in 2020. Currently, it is estimated that 3.5% of the worldwide population between 40 and 80 years of age are affected by the most common forms of glaucoma, and it is estimated that, in 2020, around 34.5 million prescriptions were written in the U.S. annually for glaucoma drugs.

Product Candidates in our Pipeline

NCX 470—Our Lead Product Candidate

NCX 470, an NME, is formulated as an ophthalmic solution for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension. NCX 470 has been evaluated in the Dolomites safety and efficacy Phase 2 clinical trial and is currently in two multi-regional (U.S. – China) Phase 3 trials, Mont Blanc and Denali. NCX 470 is designed to release both bimatoprost and NO following instillation into the eye. Bimatoprost, marketed under the brand name LUMIGAN by Allergan, Inc., is the leading product by sales in the class of PGAs, the most widely used class of drugs for the treatment of elevated IOP in patients with open-angle glaucoma and ocular hypertension. Bimatoprost is generally considered to be slightly better at lowering IOP than latanoprost. Whilst no head-to-head trials have been carried out with NCX 470, we believe that, through the contribution of NO, NCX 470 has the potential for greater IOP lowering efficacy than bimatoprost.

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In December 2018 we entered into an exclusive licensing agreement with Ocumension for the development and commercialization of NCX 470 in the Chinese market. In March 2020 Ocumension's exclusive rights were extended to Korea and Southeast Asian markets.

Top line Results of the Dolomites Phase 2 NCX 470 Clinical Trial

We completed the randomized, double-masked, dose-response Dolomites Phase 2 trial to determine a concentration of NCX 470 for lowering IOP in patients with open-angle glaucoma or ocular hypertension to advance into further clinical development. The trial enrolled 433 patients across 25 sites in the U.S. Patients were randomized to receive either NCX 470 (0.021%, 0.042% or 0.065%) or latanoprost ophthalmic solution, 0.005% once a day in the evening for 28 days.

All three doses of NCX 470 (0.021%, 0.042%, and 0.065%) met the pre-specified primary efficacy endpoint of non-inferiority to latanoprost for reduction from baseline in mean diurnal IOP at Day 28. In a pre-specified secondary efficacy analysis for reduction from baseline in mean diurnal IOP at Day 28, the mid and high doses of NCX 470 (0.042% and 0.065%) met the secondary efficacy endpoint of statistical superiority to latanoprost based on the trial's pre-specified statistical analysis plan. Specifically, IOP reduction from baseline in mean diurnal IOP at Day 28 was 7.8 mmHg for the 0.021% dose of NCX 470 (p-value for NCX 470 vs. latanoprost not statistically significant); 8.2 mmHg for the 0.042% dose of NCX 470 (p-value for NCX 470 vs. latanoprost=0.0281); and 8.7 mmHg for the 0.065% dose of NCX 470 (p-value for NCX 470 vs. latanoprost=0.0009), compared with 7.4 mmHg for latanoprost 0.005%. The dose-dependent IOP reduction from baseline in mean diurnal IOP at Day 28 showed improved IOP lowering with each incremental concentration of NCX 470 tested, thus creating the potential for additional IOP lowering with a higher concentration of NCX 470.

In additional pre-specified secondary efficacy analyses for reduction from baseline in mean diurnal IOP, NCX 470 (0.065%) met the secondary efficacy endpoint of statistical superiority to latanoprost at Day 7 (p=0.004) and Day 14 (p=0.0174), in addition to Day 28 (p=0.0009; described above). In pre-specified secondary efficacy analyses, the 0.065% dose of NCX 470 showed statistical superiority in IOP lowering as a reduction from baseline at all three time points (8 AM, 10 AM and 4 PM IOPs) on Day 28 compared with latanoprost, with the difference reaching up to 1.4 mmHg (p=0.0214 at 8 AM, p=0.0008 at 10 AM, and p=0.0015 at 4 PM). The IOP lowering effect as reduction from baseline at the three time points (8 AM, 10 AM and 4 PM IOPs) across Day 7, Day 14 and Day 28 ranged from 7.6 to 9.8 mmHg for the 0.065% concentration of NCX 470 compared with 6.3 to 8.8 mmHg for latanoprost. Additionally, at Day 28, 44% of patients dosed with NCX 470 (0.065%) had a 1 mmHg or greater mean diurnal IOP reduction from baseline compared with the mean of 7.4 mmHg for the latanoprost group (p-value not significant); 37% of patients had 2 mmHg or greater reduction (p-value not significant); 27% had a 3 mmHg or greater reduction (p=0.0175); 16% had a 4 mmHg or greater reduction (p-value not significant); and 12% had a 5 mmHg or greater reduction (p=0.0150); compared with the mean for the latanoprost group. Furthermore, greater proportion of patients dosed with NCX 470 (0.065%) achieved a mean diurnal IOP reduction at Day 28 of 40% or greater (p=0.0287), 35% or greater (p=0.0393), 30% or greater (p-value not statistically significant), 25% or greater (p=0.0479) and 20% or greater (p=0.0115), compared with those dosed with latanoprost.

NCX 470 was well tolerated when dosed once daily for 28 days in patients with open-angle glaucoma or ocular hypertension. Only three out of the 433 patients in the trial discontinued due to an adverse event. The majority of adverse events in the trial were mild. The most frequently reported adverse event was conjunctival hyperemia, the majority of which were mild, in 16.8% of patients who dosed with the 0.065% dose of NCX 470 compared with 6.5% of patients who dosed with latanoprost. Notably, adverse events for conjunctival hyperemia plateaued at the 0.042% concentration, for which it was reported for 22.2% of patients. There were no treatment-related serious adverse events, and no evidence of treatment-related systemic side effects.

Mont Blanc and Denali Phase 3 Clinical Trials Ongoing

Nicox successfully completed an End-of-Phase 2 meeting with the U.S. FDA and agreed on the design for the NCX 470 Phase 3 program, as well as nonclinical and CMC plans supporting submission of a New Drug Application (NDA) in the U.S.

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In June 2020 Nicox initiated the first Phase 3 clinical trial in the U.S., Mont Blanc, evaluating NCX 470 for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension. Mont Blanc is a multi-regional, double-masked, 3-month, parallel group trial evaluating the efficacy and safety of NCX 470 ophthalmic solution, 0.1% compared to latanoprost ophthalmic solution, 0.005% in patients with open-angle glaucoma or ocular hypertension. The 0.1% dose of NCX 470 was selected through an initial adaptive design portion of the trial, which also included the 0.065% dose. The primary efficacy evaluation of the Mont Blanc trial is based on time-matched IOP at 8 AM and 4 PM at Week 2, Week 6 and Month 3. The Mont Blanc trial is expected to randomize approximately 670 patients at approximately 50 clinical sites, in the U.S. and at one clinical site in China. Top-line results from the Mont Blanc trial are currently expected in Q1 2023.

In November 2020 Nicox initiated the second Phase 3 trial in the U.S., Denali, financed jointly and in equal parts by Nicox and Ocumension, our exclusive Chinese licensed partner. The Chinese part of the trial was initiated in December 2021. Denali is a 3-month Phase 3 trial evaluating the safety and efficacy of NCX 470 ophthalmic solution, 0.1% versus latanoprost ophthalmic solution, 0.005%, for the lowering of IOP in patients with open-angle glaucoma or ocular hypertension. The Denali trial, which includes a long-term safety extension, is expected to randomize approximately 670 patients, at approximately 60 clinical sites in the U.S. and China, with approximately 80% of the patients to be recruited in the U.S and the remaining 20% of the patients to be recruited in China. The Denali trial, together with the Mont Blanc trial, are designed to fulfill the regulatory requirements to support NDA submissions in the U.S. and China and will also provide data for countries accepting the same clinical data package for approval. The topline results will not be available by the end of 2023 as previously communicated due to several hurdles (including the COVID-19 pandemic situation in the U.S. and China). The Company will announce a new date for availability of the results when we have more visibility on the overall timelines of the trial. *NCX 470 Market Research*

In order to understand the potential clinical adoption of NCX 470 for glaucoma and to assess its reimbursement and revenue potential, an independent third party market research agency with extensive experience in the ophthalmology market assessment conducted an initial primary market research trial in the U.S. in the first half of 2019. The market research was comprised of 40 interviews with U.S. ophthalmology key opinion leaders, high volume prescribers including ophthalmologists and optometrists, and third party payers.

Multiple target product profiles of NCX 470 were tested with differentiation from each other by increasing superiority in IOP reduction compared to latanoprost 0.005%, based on a hypothetical statistically significant outcome in a head-to-head Phase 3 clinical trial. The varying levels of efficacy in the three target product profiles tested were chosen based on the current U.S. FDA-approved therapies. Specifically, statistical superiority to latanoprost similar to VYZULTA's published Phase 2 VOYAGER trial was selected for the first profile but with a superior U.S. FDA label based on head-to-head Phase 3 trials vs. a PGA for NCX 470, a statistical superiority to latanoprost similar to the published ROCKLATAN Phase 3 Mercury-1 clinical trial at Month 3 but with improved safety and tolerability vs ROCKLATAN was selected for the second profile and finally a 2 mmHg or better statistical superiority to latanoprost was selected for the third profile. For all three profiles, the safety and tolerability were identical and based on existing PGAs.

Based on our market research, we concluded that there was an opportunity for an impactful product with any of the three profiles tested and that the market potential increased with the size of the improved reduction in IOP. More specifically, the results indicated that the VYZULTA-based product profile had peak U.S. net revenue potential of \$230 million (25% market share of the U.S. first-line therapy branded market); the Mercury-1 ROCKLATAN-based product potential but with improved safety and tolerability to ROCKLATAN had peak U.S. net revenue potential of \$310 million (35% market share of the U.S. first-line therapy branded market); and the profile based on 2 mmHg superiority to latanoprost had peak U.S. net revenue potential of \$540 million (60% market share of the U.S. first-line therapy branded market). The above forecasts include estimations about the future growth of the market and assume an appropriate level of reimbursement is available.

A confirmatory market survey was carried out in 2021 by a different independent third party market research agency. This market research was comprised of 28 interviews with U.S. ophthalmology key opinion leaders, high volume prescribers including ophthalmologists and optometrists, and third party payers. The findings from this market research confirms that NCX 470, with a superiority in IOP reduction of 1.5 to 1.7 mmHg (equivalent to the second profile used in the 2019 market research) compared to latanoprost, could have peak U.S.

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net revenue potential of between \$200 million and \$300 million, taking similar assumptions for the glaucoma market as were used for the market research above in 2019

NCX 470 nonclinical studies

In rabbit, dog and nonhuman primate nonclinical models of IOP, our data demonstrate that NCX 470 is able to lower IOP more than bimatoprost alone, with up to 3.5 mmHg greater lowering of IOP with NCX 470 as compared with bimatoprost 0.03% in a non-human primate model when tested with equimolar solutions (or solutions containing equivalent numbers/concentrations of molecules). Additionally, and notably, in the nonclinical model of ocular hypertension in rabbits in which bimatoprost is known not have an effect on IOP, NCX 470 appeared to lower IOP, with up to 8.4 mmHg IOP lowering due to NO alone, suggesting that its NO-donating part of the molecule produces an IOP lowering- action.

NCX 470 exploratory non clinical studies

Exploratory studies on NCX 470 in a nonclinical model of retinal cell damage induced by endothelin-1 (ET-1) investigated the potential protective effects of NCX 470 on the retina and the optic nerve head. The results suggest that NCX 470 improves ocular perfusion and retinal function in damaged eyes compared to vehicle and therefore may have therapeutic properties in addition to lowering of IOP.

Nonclinical experiments were performed to determine the effect of NCX 470 on ocular vascular reactivity and retinal function after repeated topical ocular dosing in a well-defined model of ischemia/reperfusion injury to the optic nerve in rabbits induced by ET-1. ET-1 alone was administered twice-weekly for 2 weeks, followed by concomitant dosing with NCX 470 or vehicle for a further 4 weeks. Twice-weekly dosing with ET-1 increased ophthalmic artery resistivity after 2 weeks ($p < 0.05$ vs. baseline), and the resistivity continued to increase during the next 4 weeks up to approximately 40% of baseline at week 6 in animals treated with ET-1 and vehicle. This detrimental effect was significantly reversed in eyes where ET-1 was co-administered with NCX 470 0.1% twice daily ($p < 0.05$ vs. vehicle at week 6). In addition, ET-1 dosing resulted in a marked decline in photoreceptor responses, which continued in eyes treated with vehicle. The decline was almost completely reversed by week 6 in eyes treated with NCX 470 ($p < 0.05$ vs. vehicle).

NCX 4251

Our second product candidate in clinical development, which leverages an established molecule, is NCX 4251, a novel patented ophthalmic suspension of fluticasone propionate nanocrystals which is in development as a topical treatment for patients with dry eye disease. NCX 4251 has been evaluated in a Phase 2 trial, Danube, and a larger Phase 2b trial, Mississippi, both of which studied patients with blepharitis. The primary outcome measure in the Mississippi trial was the proportion of patients achieving complete cure in all three hallmark signs and symptoms of blepharitis, eyelid redness, eyelid debris and eyelid discomfort, at Day 15, with two secondary outcome measures focused on signs and symptoms of dry eye disease. The trial did not meet the primary or secondary efficacy endpoints, however a post hoc analysis of the data suggests that NCX 4251 is effective in reducing dry eye symptoms in patients with higher severity (moderate to severe) of key signs and symptoms of dry eye. Subsequent to the post hoc analysis and meeting with the U.S. FDA in early 2022 we are now focusing the development of NCX 4251 on dry eye disease. NCX 4251 is being developed for application to the eyelid margins via an applicator, minimizing potential steroid exposure through the cornea which can lead to damaging side effects such as intraocular pressure increase found with current topical steroids.

In July 2019, we entered into an exclusive license agreement with Ocumension for the development and commercialization of NCX 4251 for blepharitis in the Chinese market. **It**

Dry eye disease

Dry eye disease is a common condition that occurs when the quality and/or quantity of tears aren't able to adequately hydrate or lubricate the eyes. This inadequate lubrication can lead to dryness, inflammation, pain, discomfort, irritation, diminished quality of life, and in severe cases, permanent vision impairment.

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The dry eye market consists of both chronic and short-term use prescription products and a significant part of non-prescription products, principally artificial tears. The estimated worldwide market for dry eye disease treatment is over \$5 billion. The U.S. prescription market for dry eye products in 2021 was estimated to be 8.4 million prescriptions for a value of \$3.8 billion (Bloomberg).

Fluticasone propionate, the active ingredient in NCX 4251, which has not been approved previously for topical ophthalmic use, has an affinity for the glucocorticoid receptor which is approximately ten times greater than dexamethasone, a corticosteroid commonly used in ophthalmology. Fluticasone is a glucocorticoid with potent anti-inflammatory properties that has been approved in numerous drug products over the past 20 years for the treatment of various indications including dermatology, rhinitis and asthma.

Similar to ZERVIAE, we intend to seek regulatory approval for NCX 4251 using the FDA's Section 505(b)(2) regulatory pathway, which enables us to rely, in part, on the FDA's prior findings of safety and efficacy for fluticasone propionate, or published literature, in support of our NDA.

Top-line Results of the Danube Phase 2 Clinical Trial

In December 2019 we completed the U.S. multi-center, randomized, double-masked, placebo-controlled, first-in-man administration, dose-escalation, 14-day Phase 2 clinical trial, Danube, aimed to evaluate the safety and tolerability of NCX 4251 compared to vehicle in patients with acute exacerbations of blepharitis. The trial enrolled 36 patients in clinical sites in the U.S. The Danube Phase 2 trial met the primary objective of selecting the dose of NCX 4251 for further development.

NCX 4251 0.1% once daily (QD) treatment was selected to advance into a larger Phase 2 clinical trial.

The selected dose also demonstrated promising efficacy against exploratory endpoints in the study in reducing the signs and symptoms of dry eye disease.

Danube Phase 2 Clinical Trial Summary

All patients in the once daily (n=10 for NCX 4251 and n=5 for vehicle) and twice daily (n=10 for NCX 4251 and n=11 for vehicle) cohorts successfully completed the 14-day dosing period followed by a 14-day safety evaluation period.

Both once daily (QD) and twice daily (BID) NCX 4251 0.1% were well tolerated. There were no serious adverse events, no treatment related systemic adverse events, and no adverse events of IOP elevation, the most common side effect of topical ophthalmic steroids.

Although the study was not powered for efficacy, in the prospectively defined pooled analysis of QD and BID dosing of NCX 4251 0.1%, there was a statistically significant reduction in the composite score of eyelid redness, eyelid debris and eyelid discomfort at the Day 14 study endpoint (n = 20 for NCX 4251 0.1% and n = 16 for vehicle with p = 0.047 for study eyes and p = 0.025 for the combined study eyes and contralateral eyes). Twenty percent of patients on QD dosing of NCX 4251 achieved complete cure, compared to 0% in patients treated with placebo. Due to the small sample size, these results were not statistically significant. Complete cure was defined as a score of zero in eyelid redness, eyelid debris and eyelid discomfort, also referred to as a Composite Score of zero.

Exploratory analyses of signs and symptoms of dry eye disease, including symptom evaluation using visual analog scale and sign evaluation based on corneal and conjunctival fluorescein staining, revealed encouraging reduction from pre-study baselines.

Mississippi Phase 2b Clinical Trial

Top-line results of the Mississippi Phase 2b Clinical Trial

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Nicox completed the Mississippi Phase 2b clinical trial which evaluated the QD dosed NCX 4251, fluticasone propionate ophthalmic suspension 0.1%, against vehicle in patients with acute exacerbations of blepharitis. 224 patients were recruited from 8 clinical sites in the U.S. Patients completed 2 weeks of treatment and two weeks of follow-up. The primary outcome measure was the proportion of patients achieving complete cure in all the three hallmark signs and symptoms of blepharitis, eyelid redness, eyelid debris and eyelid discomfort, at Day 15, with two secondary outcome measures focused on signs and symptoms of dry eye disease. The results were announced end of September 2021. The future development of NCX 4251 in the U.S. will require initial manufacturing scale-up followed by two additional efficacy clinical trials, both evaluating one sign and one symptom of dry eye disease, long term safety data, and certain additional clinical and non-clinical data to support an NDA submission in the U.S. The remaining pharmaceutical, non-clinical and clinical development of NCX 4251 is not yet financed and therefore the Company has not planned yet the start of this last phase of development

Mississippi Phase 2b Clinical Trial results in Blepharitis

The Mississippi clinical trial results were announced in September 2021. The Mississippi Phase 2b clinical trial did not meet the primary or secondary efficacy endpoints. However, a signal of NCX 4251's potential efficacy was seen in the trial with NCX 4251 0.1% showing a numerical improvement over vehicle in the primary outcome measure of complete cure in eyelid redness, eyelid debris and eyelid discomfort at Day 15. NCX 4251 also showed a statistically significant difference against placebo in the exploratory endpoint of change from baseline in the composite score of the same key signs and symptoms at Day 8 (p=0.03), Day 11 (p=0.01) and Day 15 (p=0.01). NCX 4251 was found to be safe and well-tolerated over 14 days' treatment, with no serious adverse events, and all of the adverse events for the NCX 4251 treatment arm were mild. There were no discontinuations in the study due to an adverse event.

Mississippi Phase 2b Post-Hoc Results in dry eye disease

Positive post hoc results from the Mississippi Phase 2b clinical trial suggest that QD dosed NCX 4251, fluticasone propionate ophthalmic suspension 0.1%, is effective in reducing dry eye symptoms in a subgroup of patients. The post hoc analyses identified a subgroup of patients (123 of 224 patients) with baseline scores ≥ 2.0 on a scale of 0 (none) to 4 (severe) for inferior cornea fluorescein staining, a key sign of dry eye disease. In this patient group, the analysis demonstrated a statistically significant difference against vehicle for change from baseline in eye dryness scores as assessed on a Visual Analog Scale at Day 8 (p=0.0085), Day 11 (p=0.0020) and Day 15 (p<0.0016). Statistically significant differences against placebo were also observed in other symptoms of dry eye disease (photophobia, blurred vision, burning/stinging, foreign body sensation, ocular itching, pain) at all timepoints during treatment (Day 8, Day 11 and Day 15). In some symptoms the effects persisted up to two weeks after the end of treatment. At Day 15, the difference in reduction from baseline in inferior cornea fluorescein staining reached a p-value of 0.0524, which we believe could reach statistical significance with a larger patient population.

A path forward to develop NCX 4251 as a treatment for dry eye disease has been decided following a Q1 2022 meeting with the United States Food and Drug Administration.

NCX 1728 - Lead compound in a new class of molecules based NO-mediated activity.

We are focusing our research efforts on ocular disorders where NO is believed to play a major role in controlling IOP. Our research platform produced the NO-donating compounds, VYZULTA and NCX 470. VYZULTA demonstrated greater IOP lowering than the parent PGA compound in a randomized clinical trial. This effect is believed to be due to the additional lowering in IOP elicited by the NO-donating MOA. We are applying key learnings, based on Nicox stand-alone NO-donors, to NO-donating moieties attached to other non-PGA therapeutic classes of compounds with the goal of enhancing the NO-mediated effects. NCX 1728, an NO-donating PDE5 inhibitor, is the lead compound of this new class (non-PGA related) with NO-mediated IOP-lowering effects that are enhanced and prolonged by concomitant phosphodiesterase-5 (PDE5) inhibition activity within the same molecule. PDE5 inhibition has been shown to enhance the efficacy and the duration of NO-mediated effects. This class of compounds has the potential for development in IOP lowering and in certain retinal diseases. Optimization of ophthalmic formulations of NCX 1728 are underway prior to initiating nonclinical testing required for the filing of an IND application. In non-human primates, NCX 1741, an analog of Nicox's development candidate NCX

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1728, demonstrated reduction of IOP to a similar extent to that of travoprost, with faster onset of activity. Travoprost is a PGA, a class of molecules which are considered standard of care for IOP lowering in humans.

Our Out-Licensed Commercial Products

VYZULTA

Overview

VYZULTA (latanoprostene bunod ophthalmic solution), 0.024% is a PGA with one of its metabolites being NO. At the time of its approval, VYZULTA was the first eye drop approved in twenty years with a novel approach to reduce IOP. VYZULTA was approved by the FDA in November 2017 for the reduction of IOP in patients with open angle- glaucoma or ocular hypertension. Bausch + Lomb, a leading eye health company, has exclusive worldwide rights to develop and market VYZULTA which is commercialized in the U.S., Canada, Argentina, Hong Kong, Mexico, Taiwan and Ukraine and has been also approved in Brazil, Colombia, Jordan, Qatar, Singapore, South Korea Thailand, Turkey and United Arab Emirates.

VYZULTA has demonstrated greater IOP lowering at many of the trial's timepoints and a comparable safety profile compared with two currently available medications for the lowering of IOP in open angle- glaucoma or ocular hypertension in one Phase 2 clinical trial (compared to latanoprost), and two Phase 3 clinical trials (compared to timolol), respectively.

We believe there is an inadequately met or unmet medical need for products with increased IOP lowering in the glaucoma market. We believe that VYZULTA offers a differentiated treatment based on:

- **Increased IOP Lowering**— In the Phase 3 clinical trials, VYZULTA dosed once daily demonstrated statistically significantly greater IOP lowering than twice daily dosed timolol maleate ophthalmic solution 0.5% throughout the day at three months of treatment. Based on analysis of the pooled results of these trials, the IOP lowering from baseline was in the range of 7.5-9.1 mmHg -across three months of treatment. Additionally, in the open-label safety extensions for both Phase 3 trials, VYZULTA demonstrated sustained IOP-lowering effect without any loss of efficacy over 12 months (12-month duration of treatment in first Phase 3 trial and 6-month duration of treatment in the second Phase 3 trial). In the 413 subject Phase 2 randomized trial, VYZULTA demonstrated statistically significantly greater IOP lowering than latanoprost ophthalmic solution, 0.005% after four weeks of treatment. VYZULTA, the 0.024% dose (N=83), showed statistically significant $p < 0.01$ greater day time IOP lowering from baseline compared with latanoprost at a dose of 0.005% at day 28, with the difference for VYZULTA reaching greater than 1 mmHg (statistical significance: $p < 0.01$).
- **Novel Dual Mechanism of Action**—VYZULTA is the first PGA approved by the FDA for the lowering of IOP with one of its metabolites being NO and the only QD single agent IOP- lowering- product to provide activity through two potential distinct MOAs that are mediated by a prostaglandin and NO.
- **Established Tolerability Profile**—In the Phase 3 clinical trials, 562 patients were exposed to the drug. VYZULTA administered once a day in the evening was well tolerated with no serious adverse events. The most common ocular adverse reactions with incidence $\geq 2\%$ are conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%).

With VYZULTA, increased pigmentation of the iris and eyelid can occur with iris pigmentation likely to be permanent. Gradual changes to eyelashes, including increased length, increased thickness and number of eyelashes, can occur and are usually reversible upon discontinuation of treatment. The most common ocular adverse reactions are conjunctival hyperemia, eye irritation, eye pain and instillation site pain.

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ZERVIATE

Overview

ZERVIATE, the brand name for our cetirizine ophthalmic solution, 0.24%, is a novel formulation of cetirizine developed and approved for the first time for topical application in the eye. Cetirizine, the active ingredient in ZYRTEC, is a second generation antihistamine (H1 receptor antagonist) that binds competitively to histamine receptor sites. Cetirizine, in approved oral formulations, has a well characterized- systemic efficacy and safety profile with world-wide exposure resulting from 20 years of oral use. ZERVIATE is the first and only eye drop formulation of the antihistamine cetirizine. In May 2017, the U.S. FDA approved the NDA for ZERVIATE for the treatment of ocular itching associated with allergic conjunctivitis.

In September 2017, we entered into an exclusive licensing agreement with Eyevance for the commercialization of ZERVIATE in the U.S. which is commercialized there since March 2020.

In March 2019 we entered into an exclusive licensing agreement with Ocumension for the development and commercialization of ZERVIATE in the Chinese market. The exclusive rights were expanded to the majority of Southeast Asian markets in March 2020. Ocumension successfully completed a Phase 3 clinical trial of ZERVIATE in China in February 2022. ZERVIATE was found to be statistically non-inferior to emedastine difumarate, an antihistamine marketed under the brand name EMADINE®. Subject to any additional data requested by the Chinese NMPA, this Phase 3 trial, in addition to the clinical data package used by the FDA for ZERVIATE in the United States, is expected to be sufficient to support a Chinese NDA.

In December 2019 we entered into an exclusive licensing agreement with Samil for the development and commercialization of ZERVIATE in South Korea. This agreement was expanded to include Vietnam in February 2022.

In August 2020 we entered into an exclusive licensing agreement with ITROM for the registration and commercialization of ZERVIATE in Gulf and Arab markets.

In May 2021, we signed an exclusive license agreement with Laboratorios Grin for the registration and commercialization of ZERVIATE in Mexico.

The efficacy of ZERVIATE was established in three Phase 3 trials that were randomized, double-masked, placebo--controlled-, conjunctival antigen challenged trials in patients with a history of allergic conjunctivitis. Onset and duration of action were evaluated in two of these trials, and patients treated with ZERVIATE demonstrated statistically and clinically significantly less ocular itching compared to its vehicle at 15 minutes and eight hours after treatment ($p < 0.05$).

Regulatory approval for ZERVIATE was obtained via the FDA's Section 505(b)(2) regulatory pathway, which enabled us to rely, in part, on the FDA's prior findings of safety and efficacy for cetirizine and the published literature in support of our NDA.

In seven clinical trials conducted in patients with allergic conjunctivitis or those at risk of developing allergic conjunctivitis, the most commonly reported adverse reactions occurred in approximately 1% to 7% of patients treated with either ZERVIATE or vehicle. These reactions were ocular hyperemia, instillation site pain and reduced visual acuity.

Allergic Conjunctivitis Overview

Allergic conjunctivitis occurs when an allergic reaction causes conjunctivitis, an inflammation of the thin layer of tissue that lines the outside of the white surface of the eye and the inner surface of the eyelids. It may affect one or both eyes. The signs and symptoms may include eye redness, excessive watering, itchy burning eyes, discharge, blurred vision and increased sensitivity to light.

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It is estimated that more than 75 million people suffer from allergic conjunctivitis in the U.S. and the estimated prevalence of allergic conjunctivitis may be between 15% and 40%. The annual U.S. market for prescription treatment of allergic conjunctivitis totals approximately \$400 million according to IQVIA Health Analytics, which does not include substantial sales of over-the-counter eye drops. Branded prescription products represent around 70% market share by value.

Non-core partnered program

Naproxcinod

Naproxcinod is a Cyclooxygenase-Inhibiting Nitric-Oxide Donating, or CINOD, anti-inflammatory product candidate, which is partnered with Fera Pharmaceuticals in the U.S. Fera have been reviewing opportunities for the development of naproxcinod in a number of indications and have conducted non clinical development work on naproxcinod in models of both COVID-19 infections and sickle cell disease.. Efforts will continue focusing on sickle cell disease and other undisclosed therapeutic indications in which the properties of naproxcinod may be beneficial. In February 2022, Fera received an Orphan Drug Designation (ODD) from the FDA for the use of naproxcinod in sickle-cell disease.

We had previously completed a broad clinical program for naproxcinod in osteoarthritis, including three Phase 3 trials with over 2,700 patients. We submitted an NDA for naproxcinod for osteoarthritis in 2009 and received a Complete Response Letter in 2010 in which the FDA requested substantial additional long-term safety data on the product. We do not plan to further develop naproxcinod- for osteoarthritis.

5.2 Commercial, Industrial and financial contracts and Intellectual Property

5.2.1 Our Collaboration Agreements

Bausch + Lomb

In March 2010, we signed an exclusive worldwide licensing agreement with Bausch + Lomb, a leading eye health company and wholly owned subsidiary of Bausch Health Companies Inc., granting Bausch + Lomb exclusive worldwide rights to develop and market latanoprostene bunod. Latanoprostene bunod is commercialized by Bausch + Lomb under the brand name VYZULTA which is commercialized in the U.S., Canada, Argentina, Hong Kong, Mexico, Taiwan and Ukraine and has been also approved in Brazil, Colombia, Jordan, Qatar, Singapore, South Korea, Thailand, Turkey and United Arab Emirates.

Bausch + Lomb is responsible for funding development and marketing activities, and we jointly manage the collaboration with them through a joint executive committee. The agreement also grants Bausch + Lomb the exclusive worldwide rights to develop and market other products containing latanoprostene bunod, such as fixed dose- combinations, for the reduction of IOP and/or the treatment of glaucoma.

Under the terms of the agreement signed in 2010, Bausch + Lomb made an initial license payment of \$10 million to us upon execution of the agreement. Bausch + Lomb made an additional \$10 million milestone payment to us in April 2012 following the decision to pursue further development of latanoprostene bunod after the Phase 2 clinical trial completion in late 2011.

As a result of the FDA's approval of VYZULTA in November 2017, we received a \$17.5 million milestone payment from Bausch + Lomb and we made a \$15 million milestone payment to Pfizer under the 2009 agreement. In March 2018, we and Bausch + Lomb amended the agreement signed in 2010. The amendment provides that, from January 1, 2019 the royalties due to us according to the original agreement will increase by 1% over the original royalty on net sales above \$300 million per year. Royalties will now be 10% to 16% over four tiers, reaching the maximum tier if and when global net sales exceed \$500 million annually. Taking into account our royalty payments to Pfizer, the net royalties to us will be 6% to 12%, compared to 6% to 11% originally. These royalties could continue to 2030 in the U.S., subject to a Patent Term Extension, and beyond 2030 in other countries, depending on the date of launch of VYZULTA. In addition, the potential milestones payable to us by Bausch + Lomb have been increased by \$20 million, added to and split among three existing milestones at

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increasing annual net sales levels. The first additional amount payable will be added to the milestone on achievement of \$300 million annual net sales and the last additional amount payable will be added to the milestone on achievement of \$700 million annual net sales. The total potential milestones due to us have therefore been increased from \$145 million to \$165 million. We are eligible to receive a \$5 million net (\$20 million before deductions to Pfizer) milestone on VYZULTA net sales reaching \$100 million and are receiving tiered net royalties from Bausch + Lomb of 6% to 12%, after deduction of payments due to Pfizer under the 2009 agreement whereby we regained the rights to latanoprostene bunod.

Pursuant to our agreement with Bausch + Lomb, we had an option to co-promote latanoprostene bunod products in the U.S. In August 2014, we informed Bausch + Lomb of our decision to exercise the option. However, we have since agreed with Bausch + Lomb that we will not co-promote latanoprostene bunod in the U.S.

Additionally, Bausch + Lomb had the option, pursuant to our agreement, to develop additional NO-donating compounds for the reduction of IOP and/or the treatment of glaucoma, including other NO-donating prostaglandin F2-alpha analogs from our research. During the third quarter of 2013, Bausch + Lomb decided to forego this option.

Our licensing agreement with Bausch + Lomb will remain in effect until all royalty payment obligations from Bausch + Lomb expire or unless terminated earlier by either us or Bausch + Lomb pursuant to the early termination provision in the agreement. The duration of royalty obligations under the agreement exists on a country-by-country and licensed product-by-licensed product basis, and commences on the date of first commercial sale for the particular country and the particular licensed product and terminates on the latest of (i) the date on which there exists no subsisting claim of an unexpired patent or collaborative patent covering latanoprostene bunod or a licensed product; (ii) the date of expiration of any period of marketing exclusivity, data protection or data exclusivity applicable to such licensed product in the relevant country; and (iii) ten years after the date of first commercial sale date. If there has been no launch date for a licensed product prior to the expiration of (i-) and (ii), the royalty obligation terminates on the later expiring of (i-) and (ii).

We may terminate the agreement on a country-by-country- basis if Bausch + Lomb fails to use commercially reasonable efforts to develop and commercialize the licensed products. We may also terminate the agreement in its entirety in the event that Bausch + Lomb challenges or causes a third party to challenge the validity or ownership of any of our licensed patents or fails or becomes unable to meet its payment obligations under the agreement. Bausch + Lomb may terminate this agreement without cause upon 90 days' notice. In the event of termination, except in the event of expiration of the payment obligations of Bausch + Lomb, licenses granted by us to Bausch + Lomb will terminate and any sublicenses granted by Bausch + Lomb will either be assigned to us or terminated.

Eye Vance Pharmaceuticals

In September 2017, we entered into an exclusive license agreement with Eye Vance, a wholly-owned subsidiary of Santen Pharmaceutical Co., Ltd, for the commercialization of ZERVATE in the U.S.

Under the agreement, Eye Vance made a onetime nonrefundable upfront payment to us of \$6.0 million in 2017 and a milestone payment \$3.0 million in July 2019 resulting from the achievement by us of certain manufacturing and regulatory objectives. We are eligible to receive up to an additional \$37.5 million in future milestones payable on -Eye Vance achieving predefined sales targets, with \$30 million of these milestones being triggered by annual sales targets of \$100 million and above. In addition, we will also receive tiered royalties of 8% to 15% based on future net sales of ZERVATE. We also are committed to paying -Eye Vance- \$469,000 related to manufacturing costs that resulted from a delay in the completion of certain manufacturing activities. This amount will be directly deducted from royalty payments.

Eye Vance has the exclusive right to commercialize ZERVATE in the U.S. where it has been marketed since March 2020. In February 2021, Eye Vance entered into a partnership with Hikma Pharmaceuticals for promoting ZERVATE to U.S. healthcare professionals working outside the eyecare specialty, with all sales continuing to be booked by Eye Vance, on which Nicox will receive royalties.

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The license agreement with Eyevance will remain in force until the later of the fifteenth anniversary of the commercial launch of ZERVIATE or until the expiry of the last licensed patent in the U.S. Eyevance has the right to renew the agreement for two additional five-year periods with three months' advance notice. Additionally, with 90 days' prior written notice, Eyevance can terminate the agreement for convenience and either party can terminate the agreement upon a material breach by the other party following a 90-day cure period. In the event of expiry or termination of the agreement, Eyevance and certain related parties may complete and sell any work-in-process and product inventory that exists as of the date of termination. Upon termination, all rights granted to Eyevance- terminate.

Fera Pharmaceuticals

In November 2015, we entered into an exclusive license agreement with Fera, granting Fera exclusive rights to develop and commercialize naproxcinod in the United States. The agreement was amended in September 2018 and in December 2020. Under the terms of the amended agreement, we may be eligible to receive up to \$40 million in a single, onetime only, sales-based milestones if annual sales of naproxcinod reach \$1 billion (in any indication), plus 7% royalties based on net sales of naproxcinod in the U.S. Fera will be responsible for, and will fully finance, all clinical development, manufacturing and commercialization activities. The agreement covers all indications excluding ophthalmology- related conditions and Duchenne Muscular Dystrophy, or DMD, and we will retain all rights for naproxcinod outside of the U.S. Fera is eligible to receive an undisclosed royalty should we sell or license rights to sell naproxcinod or related products in any ex-U.S. territory to a third party if the third party uses any Fera intellectual property, regardless of the therapeutic indication and territory. A joint steering committee will be put in place with representation from both companies to ensure that development of naproxcinod- proceeds in accordance with the agreement.

The contract remains in force until the later of the tenth anniversary of the commercial launch or the expiration of the last patent included in the agreement. Upon termination of the agreement due to expiration of the term or our material breach, the licenses become fully paid and irrevocable and Fera will have all rights to the product in the U.S. In the case where Fera, despite having used commercially reasonable efforts, has not submitted an NDA for the product before December 31, 2027, Fera must present a plan for such submission, otherwise we may terminate the agreement. Fera may terminate the agreement at any time by giving one month's notice. In such case (or in the case of material breach by Fera), all the rights concerning regulatory authorizations, intellectual property rights concerning the product and all data (including clinical, preclinical, regulatory, formulation and commercial data) shall be assigned or licensed (if assignment is not possible) to us.

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ITROM Pharmaceutical Group

In August 2020 we entered into an exclusive license agreement with ITROM Pharmaceutical Group for the registration and commercialization of ZERVIAE for the treatment of ocular itching associated with allergic conjunctivitis in Gulf and Arab markets including the Kingdom of Saudi Arabia, the United Arab Emirates and Qatar. ITROM is a regional, Dubai-based, internationally recognized pharmaceutical marketing and distribution group of companies specializing in the introduction and representation of breakthrough ophthalmology products since 1999.

Under the terms of the agreement ITROM is granted exclusive rights to develop and commercialize ZERVIAE in Bahrain, Egypt, Iraq, Jordan, Kuwait, Libya, Oman, Qatar, the Kingdom of Saudi Arabia, the United Arab Emirates and Yemen. Nicox is eligible to receive 15% royalties on net sales of ZERVIAE in certain key countries, and 10% in other countries. Nicox will also receive a license fee on signature and may receive a future milestone payment upon product launch. ITROM will be responsible, at its own cost, for development and commercialization of ZERVIAE in the countries of the agreement. ZERVIAE is expected to require only the existing approved U.S. New Drug Application (NDA) package to support approval.

Laboratorios Grin

In May 2021 we entered into an exclusive license agreement with Laboratorios Grin, for the registration and commercialization of ZERVIAE™ (cetirizine ophthalmic solution), 0.24% for the treatment of ocular itching associated with allergic conjunctivitis in Mexico. Grin, a wholly-owned subsidiary of Lupin Limited, is a Mexican specialty pharmaceutical company engaged in the development, manufacturing and commercialization of branded ophthalmic products.

Grin is granted rights to develop and commercialize cetirizine ophthalmic solution, 0.24% in Mexico. Nicox will receive an undisclosed license fee and potential milestone payments linked to regulatory approval and sales, and is eligible to receive double digit royalties on net sales of ZERVIAE. Grin will be responsible, at its own cost, for the development, manufacturing and the commercialization of ZERVIAE in Mexico.

Ocumention Therapeutics

In December 2018 we entered into an exclusive license agreement with Ocumention Therapeutics for the development and commercialization of Nicox's product candidate, NCX 470, targeting patients with glaucoma or ocular hypertension for a territory comprising mainland China, Hong Kong, Macau, and Taiwan, or the Chinese market. NCX 470 is currently in two Phase 3 trials, Mont Blanc and Denali, designed to fulfill the regulatory requirements for Phase 3 safety and efficacy trials to support NDA submissions of NCX 470 in the U.S. and China and will also provide data for countries accepting the same clinical data package for approval. All development activities are overseen by a Joint Governance Committee comprising representatives of both companies, with Ocumention responsible for undertaking all the activities at its own cost. Ocumention received exclusive rights to develop and commercialize NCX 470, at its own cost, in the agreed territory. Under the terms of the agreement, we received a onetime upfront payment of €3 million from Ocumention and Nicox was eligible to receive a further €2.5 million when we initiate a Phase 3 clinical trial with NCX 470 outside the territory of this agreement. Nicox is also eligible to receive up to an additional €14.5 million in milestones associated with Ocumention's progress with NCX 470, up to and including regulatory approval, and up to €16.25 million split over three separate sales milestones associated with potential sales in the territory of up to € 200 million, as well as tiered royalties from 6% to 12% on sales. However, the agreement was amended in March 2020. Ocumention paid Nicox €15 million (in replacement of the totality of the milestones in the original agreement), gained additional exclusive rights to NCX 470 for Korea and Southeast Asia and will pay 50% of the costs of the second glaucoma Phase 3 clinical trial of NCX 470, Denali, or the Joint Trial. No future NCX 470 milestones will be due from Ocumention to Nicox. In the case that the Joint Trial would not take place, partial or limited refunds of this payment may be made and in certain situations the original milestones of the agreement would again apply. The tiered royalties of 6% to 12% of the original agreement remain unchanged and will apply to sales in the original and the additional territories.

In March 2019 we entered into an exclusive license agreement with Ocumention for the development and commercialization of Nicox's product ZERVIAE for the treatment of allergic conjunctivitis for the Chinese market. Ocumention received exclusive rights to develop and commercialize ZERVIAE, at its own cost, in the agreed territory. The agreement was amended in March 2020 granting Ocumention additional exclusive rights of ZERVIAE in the majority of the Southeast Asian region. Under a new amendment in July 2021, Ocumention

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paid Nicox \$2 million in full advance payment of the future development and regulatory milestones for ZERVIAE. Nicox remains eligible to receive the same sales milestones of up to US\$17.2 million together with tiered royalties of between 5% and 9% on net sales of ZERVIAE by Ocumension. Other terms of the original agreement remain unchanged. All development activities will be overseen by a Joint Governance Committee comprising representatives of both companies, with Ocumension responsible for undertaking all the activities at its own cost. ZERVIAE has completed a confirmatory Phase 3 clinical trial in China to support a Chinese New Drug Application.

In June 2019, we entered into an exclusive license agreement with Ocumension for the development and commercialization of Nicox's product candidate, NCX 4251, for blepharitis in the Chinese market. Ocumension is responsible, at its own cost, for all development activities necessary for the approval of NCX 4251 in the territory, overseen by a Joint Governance Committee comprising representatives of both companies. Ocumension received exclusive rights for the agreed territory to develop and commercialize NCX 4251 in blepharitis. Under the terms of the agreement, Nicox received an upfront payment of US\$ 2.3 million and may potentially receive development and sales milestones of up to US\$ 11.3 million together with tiered royalties of between 5% and 10% on sales of NCX 4251.

Pfizer

In August 2009, we signed an agreement with Pfizer terminating our previous collaboration agreements dated August 2004 and March 2006. Under the terms of the 2009 agreement, we recovered all the development and marketing rights for latanoprostene bunod, and in particular the right to sublicense, as well as all the data and development information. This compound is currently outlicensed to Bausch + Lomb (see above). Moreover, we also have access to certain information regarding development of XALATAN (latanoprost ophthalmic solution) 0.005% belonging to Pfizer, in particular the regulatory files for XALATAN (latanoprost ophthalmic solution) 0.005%. In return, we are obligated to pay Pfizer two milestone payments of \$15 million each linked to approval of VYZULTA in the U.S. (or a lower amount if approved only in Europe or Japan) and \$15 million linked to reaching predefined sales levels. The first milestone payment was made in December 2017. Pfizer is also entitled to receive royalties on potential future sales. Pfizer's royalties are in the low single digit percentages for sales in the U.S. and sales made directly by us outside the U.S. For sales made by our licensees outside the U.S., Pfizer's royalty is the greater of our royalty rate for sales outside the U.S. or a low double-digit percentage of the income that we receive from such licensee. We also recovered the rights to a certain number of new NO donors at the research stage for the potential treatment of diabetic retinopathy and glaucoma.

Samil Pharmaceutical

In December 2019 we entered into an exclusive license agreement with Samil Pharmaceutical Co., Ltd, or Samil, for the development and commercialization of ZERVIAE (cetirizine ophthalmic solution), 0.24% for the treatment of ocular itching associated with allergic conjunctivitis in South Korea. Samil received exclusive rights to develop and commercialize ZERVIAE in South Korea and the agreement was expanded in February 2022 to include Vietnam. Samil is considered as one of the leading Korean companies specialized in the field of ophthalmic medicines including the research and development of drugs in the field of ophthalmology.

Nicox is eligible to receive 10% royalties on net sales on ZERVIAE in South Korea and a milestone payment of 5% of net sales for each calendar year in which net sales exceed approximately US \$900,000 (at current exchange rates). Nicox will also receive a license fee, and may receive approval and launch milestone payments which, together with the license fee, may total almost US \$250,000. Samil will be responsible, at its cost, for development and commercialization of ZERVIAE in South Korea and in Vietnam. ZERVIAE is expected to require only manufacturing transfer and associated pharmaceutical development to support approval in South Korea, in addition to the existing approved U.S. NDA package.

5.2.2 Other Partnerships

We have other partnerships that are not active at this time. For instance, under our collaboration with Portola Pharmaceuticals, Inc., we have exclusive rights to jointly develop certain of their preclinical small molecules for topical ophthalmic indications, but no compound has been selected for development under this agreement. Under our collaboration with Merck, Merck can elect to develop certain of our NO-

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donating- compounds in the cardiovascular field. We do not expect these partnerships to impact our future financial status at this time.

5.2.3 Manufacturing and Supply

We do not have any in-house manufacturing facilities or logistics platforms. Therefore, we need to secure agreements with third parties for the manufacturing and supply of our product candidates under development. These third parties either manufacture and assemble in-house or outsource one or more processes to other external service providers.

Our business is subject to risks associated with our reliance on third-party suppliers. These risks are discussed more fully in the section of this prospectus titled "Risk Factors."

5.3 Patents

5.3.1 Intellectual property protection policy

Intellectual property is of vital importance to the Company's businesses. Nicox takes all possible measures to protect intellectual property, including by obtaining and maintaining patent protection in different territories (particularly in the United States) for its products under development and other inventions important for its business. The Group must also use of trade secrets to protect and ensure the confidentiality of proprietary information to protect those aspects of its business operations that do not lend themselves to patent protection or considered by Nicox as not appropriate for patent protection. The Company must also have recourse to the filing of trademarks, copyrights and contractual obligations to establish and protect its intellectual property rights.

Nicox's activities are dependent on its intellectual property and as such are subject to risks linked to the uncertain protection offered by patents and other intellectual property rights. The position of pharmaceutical companies like Nicox with respect to patents is highly uncertain and involves extremely complex legal, scientific and factual circumstances. In addition, the protections sought in patent applications may be significantly reduced before the patent is issued and its scope may be reinterpreted after it is issued. For that reason, the possibility cannot be excluded that Nicox might not be successful in obtaining or maintaining a patent protection for one of its products under development. The Company cannot anticipate if the patent applications currently pending will result in the issuance of patents in all the targeted territories, or if the claims of the patents issued will offer sufficient protection against the competition. Any patent held by the Company may be challenged, circumvented or invalidated by third parties. The reader is invited to refer to section 3 "risk factors" of the universal registration document that describes the risk factors related to the uncertain protection provided by patents and other intellectual property rights.

The Group has a patent department within its Italian subsidiary Nicox Research Institute Srl. The Group's patent department regularly uses intellectual property law firms in several countries around the world.

Nicox also relies on trade secret protection for its confidential and proprietary information. Even though the Group takes measures to protect its proprietary information and trade secrets, including through contractual provisions with its employees and consultants, third parties may develop independently information and proprietary techniques substantially equivalent or gain access to its trade secrets or disclose its technology. For those reasons, Nicox might not be able to effectively protect its trade secrets. The company's policy requires staff, consultants, external scientific staff and other consultants to sign confidentiality agreements at the start of their employment or relations as consultants with Nicox. The agreements thus concluded with employees also provide that all inventions designed by an employee in the course of his or her term of employment within the Company or based on the use of confidential information of the Company remain the exclusive property of Nicox.

5.3.2 Nature and coverage of patent families owned by the company

As of December 31, 2021, our patent portfolio included 358 issued patents and 96 pending patent applications and 8 patent applications under the Patent Cooperation Treaty, or PCT. In the U.S., our patent portfolio includes 46 issued patents and 9 pending patent applications. We also have 18 patents granted by the European

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Patent Office, which have been validated in the principal European countries, and 8 pending European patent applications.

Latanoprostene bunod (the active ingredient of VYZULTA) is protected in the United States by four granted patents which expire in 2025. A patent term extension (PTE) application was filed in December 2017. In March 2021 the United States Patent and Trademark Office (USPTO) issued a communication confirming that the patent covering VYZULTA is eligible for PTE. The USPTO will take about two years to make the final determination and issue of a PTE certificate. The PTE could provide additional protection until 2030.

In Europe, a patent covering latanoprostene bunod (the active ingredient of VYZULTA) was issued in February 2016 and validated in 36 countries of the EPC (European Patent Convention) and will provide protection until 2024. An application could be made for a Supplementary Protection Certificate (SPC) to extend the term of the patent to a maximum of 5 years.

On November 23, 2016, Teva Pharmaceutical Industries Ltd. filed a notice of opposition against the grant of the European patent covering latanoprostene bunod. On July 13, 2018, the Opposition Division rejected the opposition and decided to maintain the patent as granted. On September 12, 2018, Teva Pharmaceutical Industries Ltd. filed an appeal against the decision of the Opposition Division. In March 2019, Nicox filed its statement of appeal. The Appeal oral proceedings before the Board of Appeal are scheduled on July 5, 2022

In Japan, latanoprostene bunod (the active ingredient of VYZULTA) is protected by a patent which expires in 2024.

ZERVIAE is protected in the United States by four patents expiring in 2030 and 2032. On January 5, 2022, The European Patent Office (EPO) publishes the grant of the European patent covering Zerviate. This patent will offer protection until 2030.

In Japan, ZERVIAE is covered by three patents expiring in March 2030.

NCX 4251 is protected in the United States and in Europe by patents which expire in 2033.

In July 2020, Nicox filed a PCT application and national patent applications in the U.S., Europe (EPC), China, Japan, Taiwan and Argentina covering the process for the preparation of the NCX 4251 formulation under development and the NCX 4251 formulation as product. The European and the Japanese patents were granted, these patents provide protection until 2040 as well as the other members of this patent family which, if granted, will provide worldwide patent coverage until 2040.

NCX 4240 is protected in the United States, Japan and Mexico by granted patents covering the NCX 4240 eyedrop formulation and its therapeutic use for treating specific viral infections of the eye. In Canada the patent application is under review. These patents will provide protection until 2035.

NCX 470 is covered by a patents family which includes the granted patent US 8,101,658 expiring in 2029 and the European patent EP 2 274 279 which was validated in France, Germany, Italy, Spain and the United Kingdom. The product patent family also includes patents granted in Canada, Japan, China, Hong Kong, Argentina and India which are in force until 2029. Patent US 8,101,658 is eligible for a patent term extension which, if granted, may extend the expiration date for a period of up to five years.,

In July 2019, Nicox filed a PCT application and national patent applications in USA, Europe (EPC), China, Japan, Taiwan and Argentina covering the NCX 470 formulation under development. The U.S., the European, the Japanese and the Chinese patents were granted extending patent coverage of the NCX 470 formulation to 2039.

In February 2018 Nicox filed an European patent application and, in February 2019, a correspondent PCT application covering an industrial process of synthesis of NCX 470. In Europe the patent was granted in September 30, 2020 and it was validated in 16 member States of the European Patent Convention (EPC); this patent provides protection for the process and the product prepared by the process until 2038. The national patent applications deriving from the PCT application, if granted, will provide worldwide patent coverage for NCX 470 until 2039. In 2021 Nicox filed a new PCT application covering a process improvement in the synthesis of NCX 470, the patent family deriving from this PCT application, if granted, will provide additional protection for NCX 470 until 2041.

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The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch--Waxman- Act permits a patent term extension of up to five years beyond the expiration of the patent.

The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other foreign jurisdictions. In the future, if our products receive FDA approval or other regulatory authorities, we expect to apply for patent term extensions on patents covering one or more of those products. However, there is no guarantee that the applicable authorities will agree with our assessment of whether such extensions should be granted and, if granted, the length of such extensions.

The following tables summarize the status of our current patent portfolio for Nicox products and key product candidates as of December 31, 2021. For each family of patents, a table shows the different members of the family in force, by country, with the maximum possible expiration date subject to regular payment of maintenance fees and the absence of questioning of the validity of the patent concerned.

VYZULTA (latanoprostene bunod)

Patent title: PROSTAGLANDIN DERIVATIVES

This patent family covers nitrooxy-derivatives of prostaglandin F2 α analogues having improved pharmacological activity and enhanced tolerability and their use for the treatment of glaucoma and ocular hypertension.

Latanoprostene bunod, its use for the treatment of glaucoma and ocular hypertension and its pharmaceutical formulations are specifically disclosed and claimed.

Patent owner: Nicox SA

Patent status	Territory	Filing Date	Issue Date	Expiry date*	
Granted	Europe#	EP 1 704 141	27-Dec-2004	24-Feb-2016	27-Dec-2024
		United States	US 7,273,946 [^]	05-Jan-2005	25-Sep-2007
	Japan	US 7,629,345 [^]	05-Jan-2005	08-Dec-2009	05-Jan-2025
		US 7,910,767 [^]	05-Jan-2005	22-Mar-2011	05-Jan-2025
		US 8,058,467 [^]	05-Jan-2005	15-Nov-2011	05-Jan-2025
		JP 3 984 283	27-Dec-2004	13-July-2007	27-Dec-2024
39 other countries		Dec-2004 - Jan-2005	Aug-2006 - Feb-2016	Dec-2024 - 5-Jan-2025	
Pending	Europe	EP3643702 A1	9-sep-2019	—	27-Dec-2024
	7 other countries		27-Dec-2004	—	27-Dec-2024

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.

(#) EP 1 704 141 was validated in 36 member States of the European Patent Convention (EPC). On November 23, 2016, TEVA Pharmaceutical Industries Ltd, or TEVA, filed a Notice of Opposition at the EPO. On July 13, 2018, the Opposition Division decided to reject the Opposition and to maintain the patent as granted. A notice of appeal against the decision of the Opposition Division was filed by TEVA Pharmaceutical Industries Ltd on September 12, 2018. On March 2019, Nicox filed a reply to the grounds of appeal. The Appeal oral proceedings before the Board of Appeal are scheduled on July 5th, 2022.

([^]) U.S. 7,273,946, U.S. 7,629,345, U.S. 7,910,767 and U.S. 8,058,467 are listed in the Orange Book for VYZULTA.

In December 2017, Nicox filed requests for PTE for U.S. 7,273,946, U.S. 8,058,467 and U.S.7,629,345 at the USPTO.



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In April 2021 the United States Patent and Trademark Office (USPTO) issued a communication confirming that the patents covering VYZULTA are eligible for PTE.

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ZERVIA TE (cetirizine)

Patent title: OPHTHALMIC FORMULATIONS OF CETIRIZINE AND METHOD OF USE

This patent family covers topical ophthalmic formulations comprising cetirizine and its salts wherein cetirizine is present in an amount of 0.1% to 0.25% (w/v), and method for alleviating signs and symptoms of allergic conjunctivitis by topical administration of the ophthalmic formulations.

ZERVIA TE, 0.24% cetirizine hydrochloride formulation and its use in the treatment of ocular itching associated with allergic conjunctivitis are specifically claimed.

Patent owner: Nicox Ophthalmics Inc.

<u>Patent status</u>	<u>Territory</u>	<u>Filing Date</u>	<u>Issue Date</u>	<u>Expiry date*</u>	
Granted	United States	US 9,254,286 [^]	15-March-2010	9-Feb-2016	09-July-2032
		US 8,829,005 [^]	21-May-2013	9-Sep-2014	15-March-2030
		US 9,750,684 [^]	29-Dec-2015	05-Sept-2017	15-March-2030
		US 9,993,471 [^]	10-Mar-2017	12-June-2018	15-March-2030
	Japan	JP 6033677	15-March-2010	04-Nov-2016	15-March-2030
		JP 6144393	12-Aug-2016	19-May-2017	15-March-2030
	Japan	JP 6893573	13-May-2020	3-June-2021	15-March-2030
	Europe	EP 2408453	15-March-2010	5-Jan-2022	15-March-2030
CA 2,755,679		15-March-2010	12-Sept-2017	15-March-2030	
Pending	United States	US2020/0405711	11-Sept-2020	—	15-March-2030

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.

([^]) U.S. 9,254,286, U.S. 8,829,005, U.S. 9,750,684 and U.S. 9,993,471 are listed in the Orange Book for ZERVIA TE.

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NCX 470 (NO-donating bimatoprost)

Patent title: NITRIC OXIDE DONATING PROSTAMIDES

This patent family covers nitrooxyderivatives of bimatoprost and their use for treating glaucoma and ocular hypertension.

NCX 470 is specifically disclosed and claimed.

Patent owner: Nicox SA

<u>Patent status</u>	<u>Territory</u>	<u>Filing Date</u>	<u>Issue Date</u>	<u>Expiry date*</u>	
Granted	Europe#	EP 2 274 279	11-May-2009	31-July-2013	11-May-2029
	United States	US 8,101,658	11-May-2009	24-Jan-2012	11-May-2029
	Japan	JP 5 401 540	11-May-2009	01-Nov-2013	11-May-2029
	China	CN102099330	11-May-2009	30-Apr-2014	11-May-2029
	4 other countries		11-May-2009	2015 - 2019	11-May-2029

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.

(#) EP 2 274 279 was validated in the five main European countries.

NCX 470 eye drop formulation

Patent title: OPHTHALMIC COMPOSITIONS CONTAINING A NITRIC OXIDE RELEASING PROSTAMIDE

This patent family covers aqueous ophthalmic compositions in the form of solution containing NCX470 and macrogol 15 hydroxystearate as the only solubilizing agent, and a method for their preparation.

Patent owner: Nicox SA

<u>Patent status</u>	<u>Territory</u>	<u>Filing Date</u>	<u>Issue Date</u>	<u>Expiry date*</u>	
Granted	Europe#	EP 3 583 788#	10-July-2019	28-Oct-2020	10-July-2039
	United States	US 10,688,073	10-July-2019	23-June-2020	10-July-2039
	United States	US 11,020,368	11-Mar-2020	01-June-2021	10-July-2030
	Japan	JP 6672512	10-July-2019	6-March-2020	10-July-2039
	China	CN 110237031	10-July-2019	11-Feb-2022	10-July-2039
	Pending	Europe	EP 3718535	29-Apr-2020	-
United States		US 2021-0128458	11-Jan-2021	-	10-July-2039
China		CN 111249228A	4-Mar-2020	-	10-July-2039
Japan		JP 2020-105201 A	4-Mar-2020	-	10-July-2039
18 other countries			10-July-2019	-	10-July-2039

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.

(#) EP 3 583 788 was validated in 38 States of the European Patent Convention (EPC) and in Bosnia-Herzegovina, Montenegro, Cambodia, Moldova, Morocco, Tunisia and Hong Kong

In February 2019, Nicox filed a PCT application and national patent applications in Taiwan and Argentina covering an industrial process of synthesis of NCX 470. This patent family, if granted, will provide worldwide patent coverage until 2039. In Europe a patent was granted in September 30, 2020 and it was validated in 16 contracting States of the European Patent Convention (EPC).

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In 2021 Nicox filed a new PCT application covering process improvement in the synthesis of NCX 470, the patent family deriving from this PCT application, if granted, will provide additional protection for NCX470 until 2041.

NCX 4251 (Fluticasone propionate nanocrystals)

Patent title: PREPARATION OF HYDROPHOBIC THERAPEUTIC AGENTS, METHOD OF MANUFACTURE AND USE THEREOF

This patent family covers nanocrystals of fluticasone propionate (Form A) wherein the nanocrystals have the c-axis crystallographic direction substantially normal to the surfaces that define the thickness of the nanocrystals and an average particle size of 100 nm to 1000 nm.

This patent family also covers: nanosuspensions containing nanocrystals of fluticasone propionate (Form A), methods for treating or alleviating symptoms of blepharitis, postoperative ocular inflammation, dry eye or eye allergy and the sono-crystallization- process for preparing the fluticasone propionate nanocrystals.

Patent owner: Nicox Ophthalmics Inc.

<u>Patent status</u>	<u>Territory</u>	<u>Filing Date</u>	<u>Issue Date</u>	<u>Expiry date*</u>	
Granted	United States	US 8,765,725	07-Jan-2013	01-July-2014	7-Jan-2033
	United States	US 10,174,071	26-July-2018	8-Jan-2019	6-May-2033
	United States	US 10,954,263	29-Nov-2018	23-Mar-2021	6-May-2033
	Japan	JP 6285419	06-May-2013	09-Feb-2018	6-May-2033
	Japan	JP 6564891	01-Feb-2018	2-Aug-2019	6-May-2033
	Japan	JP 6752940	17-June-2019	21-Aug-2020	6-May-2033
	Europe	EP 2 847 207 [^]	06-May-2013	27-March-2019	6-May-2033
	Europe	EP 3517541 [#]	11-Feb-2019	15-July-2020	6-May-2033
	China	CN 107880091	23-Nov-2017	18-Dec-2020	6-May-2033
	8 other countries		06-May-2013	2018-2020	6-May-2033
Pending	Europe	EP 3741772A1	29-May-2020	—	6-May-2033
	United States	US 2021/300963	17-Feb-2021	—	6-May-2033
	4 other countries				

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.

([^]) EP 2 847 207 was validated in 12 member States of the European Patent Convention (EPC)

([#]) EP 3 517 541 was validated in 24 member States of the European Patent Convention (EPC)

NCX 4251 (Fluticasone propionate nanocrystals)

Patent title: PROCESS FOR THE PREPARATION OF STERILE OPHTHALMIC AQUEOUS FLUTICASONE PROPIONATE FORM A NANOCRYSTALS SUSPENSIONS

This patent family covers the preparation of aqueous suspensions containing nanocrystals of fluticasone propionate (Form A) having an average particle size of 100 nm to 1000 nm.

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This patent family also discloses the nanosuspension containing nanocrystals of Fluticasone propionate under development and method for treating blepharitis, posterior blepharitis, Meibomian gland dysfunction or dry eye disease wherein the method comprises topically applying to eyelids, eyelashes or eyelid margin the ophthalmic aqueous nanosuspension.

Patent Owner: Nicox Ophthalmics Inc.

<u>Patent status</u>	<u>Territory</u>	<u>Filing Date</u>	<u>Issue Date</u>	<u>Expiry date*</u>	
Active	PCT [§]	WO2021/014348	21-July-2020	NA	
Granted	Europe	EP3769753 [#]	21-July-2020	17-Nov-2021	21-July-2040
	Japan	JP7021301	21-July-2020	16-Feb-2022	21-July-2040
Pending	United States	US2021/023001	21-July-2020	—	21-July-2040
	China	CN111821261A	21-July-2020	—	21-July-2040
	3 other countries			—	21-July-2040

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.

(§) PCT WO2021/014348 will enter the national/ regional phases in January 2022

(#) EP 3 769 753 will be validated in all the States of the European Patent Convention (EPC) and in Bosnia-Herzegovina, Montenegro, Cambodia, Moldova, Morocco and Tunisia.

NCX 4280 (formerly AC-120)

Patent title: METHOD FOR THE TREATMENT AND PREVENTION OF EYELID SWELLING

This patent family covers the use of a composition comprising oxymetazoline and glycerine for treating eyelid swelling.

This patent family also discloses topical pharmaceutical compositions comprising an osmotically active agent and a vasoconstrictor agent. The preferred osmotically active agent is glycerin and the vasoconstrictor agent is selected from oxymetazoline or naphazoline.

Patent owner: Nicox Ophthalmics Inc.

<u>Patent status</u>	<u>Territory</u>	<u>Filing Date</u>	<u>Issue Date</u>	<u>Expiry date*</u>	
Granted	United States	US 8,685,439	26-Apr-2007	01-Apr-2014	09-July-2030
Pending	United States	US 2021/0177807	07-Dec-2020	—	26-Apr-2027

(*) Expiry dates given prior to any potential extensions in accordance with local patent regulations.

Protection for other NO-donating compounds

Our novel NO-donating PDE5 inhibitors have potential patent protection in the United States, Europe and other main countries until 2039. Additional novel molecules combining NO-donation and other non-PGA MOAs compounds are protected in the United States, Europe and other main countries by patents and patent applications that provide patent protection until 2034.

5.4 Important events

5.4.1 Important events since January 1st, 2021

January 5, 2021 **Nicox Highlights Successful 2020 Development Progress and Clinical Milestones for 2021**

https://www.nicox.com/assets/files/EN_Update-PR_20200105_F.pdf

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- January 6, 2021 **Nicox's Licensee Bausch + Lomb Launches VYZULTA® in Mexico**
https://www.nicox.com/assets/files/EN_VYZULTA-Launch-Mexico-PR_20210206_F.pdf
- January 20, 2021 **Nicox Provides Fourth Quarter 2020 Business Update and Financial Highlights**
https://www.nicox.com/assets/files/EN_Q4-2020-Results-PR_20210120_F1.pdf
- January 22, 2021 **Nicox Analyst Coverage Initiated by Edison Investment Research**
https://www.nicox.com/assets/files/EN_Edison-Nicox-Initiation-PR_20210122_F1.pdf
- January 29, 2021 **Nicox Amends Bond Financing Agreement with Kreos to Provide Financial Flexibility in 2021**
https://www.nicox.com/wp-content/uploads/EN_Kreos-Amendment-PR_20210129_F.pdf
- February 9, 2021 BAUSCH HEALTH ANNOUNCES VYZULTA® (LATANOPROSTENE BUNOD OPHTHALMIC SOLUTION), 0.024%, IS NOW APPROVED IN SOUTH KOREA**
https://www.nicox.com/wp-content/uploads/EN_-Joint-PR_VYZULTA-approval-South-Korea_20210209_-F2.pdf
- February 15, 2021 Nicox's U.S. Licensee Eyevance Expands U.S. Promotion of ZERVIAE® In Agreement with Hikma**
<https://www.nicox.com/wp-content/uploads/Nicoxs-U.S.-Licensee-Eyevance-Expands-U.S.-Promotion-of-ZERVIAE%C2%AE-In-Agreement-with-Hikma-Nicox.pdf>
- February 23, 2021 Nicox Announces the Publication in Leading Scientific Journal of Pre-Clinical Efficacy Results on a New Class of Non-PGA NO-donating IOP-Lowering Compounds**
https://www.nicox.com/wp-content/uploads/EN_NCX1741-JOPT-PR_20210223_F.pdf
- March 1, 2021 Nicox Announces 2020 Financial Results and 2021 Key Milestones
https://www.nicox.com/wp-content/uploads/EN_FY2020Results_PR_20210301_F-3.pdf
- March 4, 2021 Nicox's NCX 470 Receives Approval by Chinese Authorities for Local Start of Denali Phase 3 Trial
https://www.nicox.com/assets/files/EN_NCX470DenaliChineseINDApproval_PR_20210304_F.pdf
- March 23, 2021 Nicox's NCX 470 Mont Blanc Phase 3 Glaucoma Trial Reaches 50% Enrollment Milestone
https://www.nicox.com/assets/files/EN_NCX470MontBlanc50PercentEnrollment_PR_20210323_F.pdf
- April 16, 2021 **BAUSCH HEALTH ANNOUNCES VYZULTA® (LATANOPROSTENE BUNOD OPHTHALMIC SOLUTION), 0.024%, IS NOW APPROVED IN BRAZIL**
https://www.nicox.com/wp-content/uploads/EN_VYZULTA-approved-Brazil-PR_20210416_F.pdf
- April 19, 2021 Nicox Provides First Quarter 2021 Business Update and Financial Highlights
https://www.nicox.com/wp-content/uploads/EN_Q1-2021-Results-PR_20210419_F.pdf

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- April 22, 2021 U.S. Patents for Nicox's Latanoprostene Bunod, Commercialized as VYZULTA®, Eligible for Patent Term Extension
https://www.nicox.com/wp-content/uploads/EN_LBN-USPTO-InitialDecision_PR_20210422_F.pdf
- April 23, 2021 Nicox's NCX 4251 Mississippi Phase 2b Blepharitis Trial Reaches 50% Enrollment
https://www.nicox.com/wp-content/uploads/EN_NCX4251Mississippi50PercentPR_20210423_F.pdf
- April 27, 2021 U.S. Patent Office Issues Notice of Allowance for Nicox's Latanoprostene Bunod in Normal Tension Glaucoma
https://www.nicox.com/wp-content/uploads/EN_VYZULTANormotensivePatentGrant_PR_20210427_F.pdf
- April 30, 2021 Nicox Updates on Fera Pharmaceuticals' Continuing Evaluation of Naproxcinod
https://www.nicox.com/wp-content/uploads/EN_FeraUpdate_PR_20210430_F.pdf
- May 4, 2021 Nicox's Licensee Bausch + Lomb Launches VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024% in Taiwan and Receives Approval in Qatar
https://www.nicox.com/wp-content/uploads/EN_VYZULTALaunchTaiwan_PR_20210504_F.pdf
- May 5, 2021 Nicox partners with Laboratorios Grin to bring ZERVIAATE to Mexico
https://www.nicox.com/wp-content/uploads/EN_ZERVIAATEGrinMexico-PR_202105_F1.pdf
- June 1, 2021 Nicox's Completes Pre-Defined Enrollment of NCX 4251 Mississippi Phase 2b Blepharitis Trial
https://www.nicox.com/wp-content/uploads/EN_NCX4251Mississippi100PercentPR_20210601_F.pdf
- June 25, 2021 Nicox's Licensee Bausch + Lomb Receives Approval for VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024% in the United Arab Emirates
https://www.nicox.com/wp-content/uploads/EN_VYZULTAUnitedArabEmiratesApprovalJune2021PR_20210625_F.pdf
- July 1, 2021 Nicox's NCX 470 Demonstrates Significant Intraocular Pressure Lowering in Dolomites Phase 2 Glaucoma Trial
https://www.nicox.com/wp-content/uploads/EN_NCX-470-Dolomites-WGC-June-2021PR_20210701_F1.pdf
- July 2, 2021 Nicox Announces Last Patient Completed NCX 4251 Mississippi Phase 2b Blepharitis Trial
https://www.nicox.com/wp-content/uploads/EN_NCX-4251-Mississippi-LPLV-PR_20210702_F.pdf
- July 5, 2021 Nicox to Receive \$2 Million from Ocumension Therapeutics as Advance Milestone Payment under ZERVIAATE® Agreement

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- https://www.nicox.com/wp-content/uploads/EN_OCUMENSIONAmendment3_PR_20210705_F.pdf
- July 13, 2021 Nicox Appoints Robert N. Weinreb, M.D. and Sanjay G. Asrani, M.D. to its Glaucoma Clinical Advisory Board
- https://www.nicox.com/wp-content/uploads/EN_CABUpdateJuly2021PR_210713F.pdf
- July 16, 2021 Nicox Provides Second Quarter 2021 Business and Financial Highlights and Strategic Update
- https://www.nicox.com/wp-content/uploads/EN_Q2-2021-Results-PR_20210716_F.pdf
- September 24, 2021 Nicox Announces Results from the NCX 4251 Phase 2b Mississippi Blepharitis Trial
- https://www.nicox.com/wp-content/uploads/EN_NCX-4251-Mississippi-results-PR_F_20210923.pdf
- September 27, 2021 Nicox First Half 2021 Financial Results and Business Update
- https://www.nicox.com/wp-content/uploads/EN_H1_2021Results-PR_20210927_F.pdf
- September 29, 2021 Nicox's NCX 470 Shows Retinal Cell Protection in a Nonclinical Model
- https://www.nicox.com/wp-content/uploads/EN_NCX-470RetinalCellProtection-PR_20210929_F.pdf
- October 4, 2021 Nicox Launches New Corporate & Investor Website
- https://www.nicox.com/wp-content/uploads/EN_Website-launch_20211004_F.pdf
- October 19, 2021 Nicox Provides Third Quarter 2021 Business and Financial Highlights
- https://www.nicox.com/wp-content/uploads/EN_Q3_2021-Results-PR_20211019_F.pdf
- November 17, 2021 Nicox is Granted Patent for Blepharitis Product Candidate NCX 4251 in Europe
- https://www.nicox.com/wp-content/uploads/EN_NCX-4251-EU-patent-grant-2040_PR_20211117_F.pdf
- November 24, 2021 Nicox's Positive Post Hoc Results from NCX 4251 Phase 2b Mississippi Trial Suggest Path Forward in Dry Eye Disease
- https://www.nicox.com/wp-content/uploads/EN_MississippiDry-Eye-PR_20211130_F.pdf
- December 13, 2021 Nicox Appoints Doug Hubatsch as new Chief Scientific Officer to lead Clinical and Nonclinical Development
- https://www.nicox.com/wp-content/uploads/EN_AppointmentDHubatsch-PR_20211213_F.pdf
- December 16, 2021 Nicox Announces First Patient in China screened in the ongoing NCX 470 Denali Phase 3 Trial in Glaucoma
- https://www.nicox.com/wp-content/uploads/EN_NCX-470Denali-FPFV-ChinaPR_20211216_F2.pdf

5.4.2 Important events since January 1st, 2022

- January 5, 2022 Nicox European Patent Seals ZERVIATE Major Market Coverage to 2030

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	https://www.nicox.com/wp-content/uploads/EN_ZERViate-Patent-EU-PR_20220105_F1.pdf
January 16, 2022	Nicox Provides Fourth Quarter 2021 Business and Financial Highlights https://www.nicox.com/wp-content/uploads/EN_Q4-2021-Results-PR_20220121_F.pdf
January 27, 2022	Nicox to Participate in Financial, Pharmaceutical Industry and Scientific Events in H1 2022 https://www.nicox.com/wp-content/uploads/EN-PR-conferences-H1-2022_20220127_F.pdf
February 8, 2022	Nicox's Positive FDA Meeting Shows Clear Path for NCX 4251 in Dry Eye https://www.nicox.com/wp-content/uploads/EN_NCX-4251-DryEyePostFDAMeeting-PR_20220208_F.pdf
February 21, 2022	Nicox Granted New Patent for NCX 470 in China, Extending Coverage to 2039 https://www.nicox.com/wp-content/uploads/EN_NCX-470-New-Formulation-Patent-China-PR_20220221_F.pdf
February 22, 2022	Nicox Granted New Patent for NCX 4251 in Japan https://www.nicox.com/wp-content/uploads/EN_NCX-4251-Japanese-Patent-PR_20220222_F1.pdf
February 23, 2022	Nicox Announces VYZULTA Now Commercialized in 7 Territories and Approved in Further 9 Countries https://www.nicox.com/wp-content/uploads/EN_VYZULTA-Recap-PR_20220223_F.pdf
March 1, 2022	Nicox's Partner Ocumension Obtains Positive Phase 3 Clinical Trial Results for ZERViate® in China https://www.nicox.com/wp-content/uploads/EN_ZERViate-China-Phase3-Results-PR_20220301_F.pdf
March 2, 2022	Nicox's Partner Fera Pharmaceuticals Obtains Orphan Drug Designation from the U.S. FDA for Naproxinod for the Treatment of Sickle Cell Disease https://www.nicox.com/wp-content/uploads/EN_Naproxinod-ODD-Sickle-Cell-PR_20220302_F.pdf
April 11, 2022	Nicox's NCX 470 Dolomites Phase 2 Results Published in Journal of Glaucoma https://www.nicox.com/wp-content/uploads/EN_NCX-470-Dolomites-Results-Publication PR_20220411_F.pdf

5.5 Competition

5.5.1 Overview

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We believe that our internally-developed NO-donating- research platform, knowledge, experience and scientific resources provide us with competitive advantages. However, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and

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public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Our potential competitors include large pharmaceutical and biotechnology companies, and specialty pharmaceutical and generic drug companies. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Many of our potential competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient recruitment for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of each of our product candidates, if approved for marketing, are likely to be its efficacy, safety, method of administration, convenience, price, the level of generic competition and the availability of coverage and adequate reimbursement from government and other third-party payors.

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. In addition, our ability to compete may be affected in many cases by insurers or other third party payors seeking to encourage the use of generic products.

Our product candidates target markets that are already served by a variety of competing products based on a number of active pharmaceutical ingredients. Many of these existing products have achieved widespread acceptance among physicians, patients and payors for the treatment of ophthalmic diseases and conditions. In addition, many of these products are available on a generic basis, and our product candidates may not demonstrate sufficient additional clinical benefits to physicians, patients or payors to justify a higher price compared to generic products. In many cases, insurers or other third-party payors, particularly Medicare, seek to encourage the use of generic products. Given that we are developing products based on FDA approved therapeutic agents, our product candidates, if approved, will face competition from generic and branded versions of existing drugs based on the same active pharmaceutical ingredients that are administered in a different manner, such as biodegradable drug product formulations.

Because the active pharmaceutical ingredients in some of our product candidates are available on a generic basis, or are soon to be available on a generic basis, competitors may be able to offer and sell products with the same active pharmaceutical ingredient as our products so long as these competitors do not infringe our patents. For example, our patents covering our NO-donating compounds largely claim new composition of matter. However, intellectual property covering certain other products such as ZERVATE and NCX 4251 relate to the formulation and method of use of these compounds. As such, if a third party were able to design around the formulation and process patents that we hold and to create a different formulation using a different production process not covered by our patents or patent applications, we would likely be unable to prevent that third party from manufacturing and marketing its product.

5.5.2 Reduction of IOP in patients with glaucoma and ocular hypertension

Prostaglandin analogs are used as first line IOP lowering therapy and account for more than 50% of prescriptions for IOP lowering drugs in the U.S., where the leading branded product by sales is LUMIGAN (bimatoprost ophthalmic solution) 0.03% from Allergan, the other leading branded product is TRAVATAN Z (travoprost ophthalmic solution) 0.004% from Novartis, and the leading generic product is latanoprost. Generic travoprost has also recently become available. ROCKLATAN (netarsudil and latanoprost ophthalmic solution)

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0.02%/0.005%, a fixed dose combination of netarsudil and latanoprost, was also approved by FDA and subsequently launched in the U.S. by Aerie Pharmaceuticals, or Aerie, in 2019. It was also approved in Europe in January 2021, under the brand name ROCLANDA. XELPROS (latanoprost ophthalmic emulsion) 0.005% was recently approved for IOP lowering in patients with open-angle- glaucoma or ocular hypertension and was launched in the U.S. by a subsidiary of Sun Pharmaceutical Industries Ltd in 2019. Allergan, Inc., an Abbvie company, launched DURYSTA, a bimatoprost extended release biodegradable implant for IOP lowering, in the U.S. in 2020. The other products in the market, currently used mostly as adjunct therapies added on the top of PGAs, are alpha agonists, beta blockers and carbonic anhydrase inhibitors, most of which are available as generic as well as branded forms. Another adjunct therapy, Rhopressa (netarsudil ophthalmic solution) 0.02%, a rho kinase inhibitor, was approved by FDA and launched in the U.S. by Aerie in 2018, and was approved under the brand name Rhokiinsa in Europe in 2019.

Several competitors are developing new formulations, novel chemical compounds and other sustained drug release products for the same ophthalmic indications as our current NO-donating compounds for IOP lowering. The list below sets out the principal programs in Phase 3 (excluding generics of existing, approved products):

- *Glaukos* is conducting Phase 3 clinical development of the iDose implant, which is a nonbiodegradable metal insert that releases travoprost- and is placed in the eye during a surgical procedure.
- *Laboratorios Sophia S.A.de C.V.* is conducting Phase 3 clinical development of PRO-067, a cyclodextrin containing formulation of latanoprost that is aimed at improving the stability of currently available latanoprost formulations.
- *Ocular Therapeutix, Inc.* has conducted Phase 3 clinical development of OTXTP, a sustained release travoprost punctal- plug formulation that is aimed at lowering IOP, which did not meet its primary endpoint. Other clinical studies are ongoing.
- *Santen* is developing DE117, an EP2 agonist for the lowering of IOP. It has been launched in Japan under the brand name EYBELIS and the U.S. FDA accepted the NDA for review in February 2021. A Complete Response letter was received in November 2021.

5.5.3 Competitors to our other pipeline product candidates

We may also be exposed to potentially competitive products which may be under development for our other indications.

Allergic conjunctivitis

The allergic conjunctivitis market is dominated by Alcon Laboratories, Inc.'s PAZEO, PATANOL and PATADAY, three products based on olopatadine at different concentrations, together with generic olopatadine products. Olopatadine is now also available as a non-prescription drug in the U.S. The supplemental NDA for Ocular Therapeutix' DEXTENZA, a dexamethasone insert, for the treatment of ocular itching associated with allergic conjunctivitis, was approved in October 2021. The list below sets out the principal programs in Phase 3 (excluding generics of existing, approved products):

- *Aldeyra Therapeutics, Inc.*, is in Phase 3 clinical trials with reproxalap (ADX102) for allergic conjunctivitis.
- *Faes Pharma*, has completed a Phase 3 clinical trial in the U.S. with bilastine for allergic conjunctivitis.

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Dry Eye Disease

The principal prescription treatments for dry eye disease are RESTASIS (cyclosporine ophthalmic emulsion), 0.5%, from Allergan for which a generic has recently become available, XIIDRA (lifitegrast ophthalmic solution), 5%, from Novartis and CEQUA (cyclosporine ophthalmic solution), 0.09%, from Sun Pharmaceutical Industries. Products recently launched include EYSUVIS (loteprednol etabonate ophthalmic suspension), 0.25%, from Kala Pharmaceuticals and TYRVAYA (varenicline solution) nasal spray from Oyster Point Pharmaceuticals. The condition is also treated with non-prescription products, principally artificial tears

The list below sets out the principal programs in Phase 3 (excluding generics of existing, approved products):

- *Palatin Technologies* is developing PL9643 ophthalmic solution, currently in a Phase 3 clinical trial for dry eye disease.
- *RegenTree* is developing RGN-259 ophthalmic solution, containing Thymosin beta 4, currently in a Phase 3 clinical trial for dry eye disease.
- *Hanal BioPharma Co., Ltd.* and *Daewoong Pharmaceutical Co. Ltd* are developing tanfanercept (HL036) ophthalmic solution 0.25%, currently in a Phase 3 clinical trial for dry eye disease.
- *Aldeyra Therapeutics* is developing Reproxalap Ophthalmic Solution (0.25%), a RASP inhibitor, currently in multiple clinical trials including Phase 3 for dry eye disease.
- *Novaliq GmbH* is developing both CyclASol Ophthalmic Solution (cyclosporine) and NOV03 for dry eye disease and both are in Phase 3.
- *Mitotech* has completed a Phase 3 trial on SkQ1 ophthalmic solution for dry eye disease.

5.5.4 Other NO-delivery and NO--donating- technologies

As far as we are aware, there are at nine pharmaceutical companies working in the field of NO-donating- drugs:

- *AntiRadical Technologies* is developing caged NO molecules for the treatment of life threatening disruption of blood flow.
- *Bellerophon Therapeutics, Inc.* is currently developing the INOpulse, an NO device system product in the U.S. for the treatment of various conditions related to pulmonary hypertension.
- *Edixomed* is developing *in--situ* generation of NO for application in wound care, dermatology, critical care, respiratory and transdermal drug delivery
- *Kowa Pharmaceutical Europe Co. Ltd.* markets HYPADIL Kowa Ophthalmic Solution 0.25% in Japan for the treatment of glaucoma and intraocular hypertension. The active ingredient of this drug is nipradilol, an alpha and beta--adrenergic blocker with NO--releasing- action.
- *Mallinckrodt PLC* markets INOmax in the United States, a gaseous NO product for the treatment of persistent pulmonary hypertension of the newborn.
- *Novan Therapeutics* is developing NO donors for the treatment of acne, viral infections, onychomycosis and inflammatory skin disease. Their most advanced program is in Phase 3.
- *Topadur* is developing an NO-releasing PDE5 inhibitor to accelerate chronic wound closure.

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- *Vast Therapeutics* is developing controlled and local delivery of NO via macromolecules for treatment of severe respiratory infections in patients with cystic fibrosis.
- *Zylo Therapeutics* is developing transdermal drug delivery systems including NO.

It is important to note that once marketed (subject to obtaining marketing approvals on an ad hoc- basis), the products developed by us will be competing with a number of products that are already commercially available. In addition, research conducted by the pharmaceutical industry and by public and private institutions will continue to generate new products that could compete with our existing or future commercial products.

5.6 Investments

The Company has not made any investments since January 1st, 2021.

5.6.1 Historical investments

The Company subcontracts its research, development and production activities for the active ingredient of its drugs and therefore the tangible fixed assets are not significant compared to the overall research and development expenses of the Company. The gross value of property, plant and equipment amounts to € 3 755 000 as of December 31, 2021.

The Company's intangible assets mainly break down as follows:

- A portfolio of unlicensed patents acquired in April 2009 from the Nitromed Company, covering nitric oxide donor compounds with a gross value of €2,000,000.
- The late-stage drug pipeline targeting major segments of the ophthalmology market of Nicox Ophthalmics Inc. (formerly Acix Therapeutics Inc.) for a gross amount of €66,580,000.

5.6.2 Ongoing investments

The Company has no significant investments in progress

5.6.3 Environmental information that may influence the use made by the Company of its property, plant and equipment

In accordance with the MiddleNext corporate governance code updated in September 2020 to which the company refers and the internal regulations of the Board of Directors, the Corporate Governance Committee and then the Board of Directors examined the social, societal and environmental consequences, of the Company's activities and strategy. The Board of Directors considered that the activities and strategy of the Company do not have significant consequences which would require specific action.

The Group only has offices with limited environmental impact. In addition, the Group's subcontracted activities are, for the most part, intellectual activities with a moderate impact on the environment, the other subcontracted activities (in particular research and development activities) being limited in terms of their impact on the environment. terms of financial flows at the date of publication of this report.

The Group is not subject to specific environmental certification procedures.

There are no provisions and guarantees for environmental risks.

The Group did not pay any compensation during the financial year in execution of a court decision in environmental matters.

Press Release

Nicox Reports 2021 Financial Results and First Quarter 2022 Financial Highlights and Provides Update on Key Programs and Milestones

- **NCX 470 Mont Blanc Phase 3 clinical trial in glaucoma at over 98% recruitment**
- **Development pathway for NCX 4251 in dry eye disease confirmed following meeting with the U.S. FDA**
- **First quarter 2022 U.S. prescriptions for VYZULTA® increased by 43% over first quarter 2021**
- **Cash position of €42.0 million as of December 31, 2021 and €35.1 million as of March 31, 2022, confirming the Company is financed to Q4 2023**

April 28, 2022 – release at 7:30 am CET
Sophia Antipolis, France

Nicox SA (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced the financial and operating results for Nicox and its subsidiaries (the “Nicox Group”) for the year ended December 31, 2021, as approved by the Board of Directors on April 27, 2022, along with a business update and financial highlights for the first quarter 2022, and provided an update on key upcoming milestones.

“We are very pleased by the rapid progress of the NCX 470 Mont Blanc phase 3 trial and are eagerly expecting its completion which will mark a major inflexion point for our Company and a turning point in the development of drugs for the treatment of patients with open-angle glaucoma and ocular hypertension.” said **Michele Garufi, Chief Executive Officer of Nicox.**

Key Upcoming Milestone

- **Mont Blanc Phase 3 clinical trial on NCX 470 in glaucoma:** recruitment advances more quickly than anticipated and thus topline results fully on track.

First Quarter 2022 and Recent Events and Pipeline Updates

Product candidates

NCX 470

- **NCX 470** is a novel nitric oxide (NO)-donating prostaglandin analog currently in a Phase 3 clinical program for the lowering of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.
- Owing to a better than expected enrollment rate in recent months, over 98% of the patients required to complete the **NCX 470** Mont Blanc Phase 3 clinical trial have been enrolled.
- Patient enrollment is continuing in both the United States (U.S.) and China in the ongoing Denali Phase 3 clinical trial on **NCX 470** in patients with open-angle glaucoma or ocular hypertension. Denali, which also includes a long-term safety extension, has been recruiting patients in the U.S. since November 2020. Approximately 670 patients are expected to be randomized at approximately 60 clinical sites in the U.S. and China, with approximately 80% of the patients to be

recruited in the U.S. and the remaining 20% of the patients to be recruited in China. The topline results will not be available by the end of 2023 as previously communicated due to several hurdles (including the COVID-19 pandemic situation in the U.S. and China). The Company will announce a new date for availability of the results when we have more visibility on the overall timelines of the trial.

- The Chinese National Intellectual Property Administration has granted Nicox a formulation patent for **NCX 470** in China to 2039. With the equivalent U.S. and European patents already granted, the formulation is now covered in most major global territories. NCX 470 is also covered by granted composition of matter patents.

NCX 4251

- **NCX 4251** is a novel, patented, ophthalmic suspension of fluticasone propionate nanocrystals in clinical development stage for dry eye disease.
- Following the encouraging *post hoc* results from the Mississippi Phase 2b clinical trial and a subsequent meeting with the U.S. Food and Drug Administration (FDA), the future development of **NCX 4251** will be focused on dry eye disease. The Mississippi *post hoc* results, [reported](#) on November 30, 2021, suggest that once-daily dosed NCX 4251, fluticasone propionate ophthalmic suspension 0.1%, is effective in reducing dry eye symptoms in patients who score more highly for a key sign of dry eye disease. The Company is currently exploring how to best advance the development of NCX 4251 in dry eye disease and will communicate its strategy at a future date.
- The Japanese Patent Office has granted a new patent expiring in 2040 for **NCX 4251**. Patent JP.7021301 covers ophthalmic suspensions comprising a specific form of fluticasone propionate nanocrystals and the method for manufacturing the ophthalmic suspensions. It complements the recent granting of a patent from the same family in Europe. Corresponding patent applications are under examination in the U.S., China and other territories.

Commercial Out-licensed Products

- **VYZULTA**[®] (latanoprostene bunod ophthalmic solution), 0.024% U.S. prescriptions¹ increased by 43% in the first quarter of 2022 compared to first quarter 2021, however revenue remained unchanged due to an increased level of rebates. As of December 31, 2021, VYZULTA, exclusively licensed worldwide to Bausch + Lomb, was commercialized in 7 territories: United States (2017), Canada (2019), Argentina (2020), Mexico (2020), Hong Kong (2020), Taiwan (2021) and Ukraine (2021). VYZULTA is also approved in 9 other countries, namely Brazil, Colombia, Jordan, Qatar, Singapore, South Korea, Thailand, Turkey and United Arab Emirates. VYZULTA is indicated for the reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.
- Our partnership with Samil Pharmaceutical concerning **ZERVIAE** in South Korea has been expanded to include Vietnam.
- Our Chinese partner Ocumension Therapeutics successfully completed a Phase 3 clinical trial of **ZERVIAE** (cetirizine ophthalmic solution), 0.24% in Chinese patients with allergic conjunctivitis in which ZERVIAE was compared to emedastine difumarate ophthalmic solution, 0.05%, an antihistamine marketed under the brand name EMADINE[®]. ZERVIAE was found to be non-inferior to emedastine difumarate in the primary efficacy endpoint of change from baseline in the itching score in the 24 hours prior to the Day 14 visit. ZERVIAE was safe and well-tolerated with no difference in the proportion of patients with adverse events compared to emedastine difumarate. This Phase 3 clinical trial was required for Ocumension to be able to submit a New Drug Application (NDA) for approval to commercialize ZERVIAE in China.

¹ Bloomberg data, comparing the period of the weeks ending 7 January 2022 to 1 April 2022 with the period of the weeks ending 8 January 2021 to 2 April 2021

Other partnerships

- The U.S. FDA has granted Orphan Drug Designation for **naproxcinod** for the treatment of sickle cell disease, which affects an estimated 100,000 Americans. Naproxcinod is a nitric oxide (NO)-donating naproxen combining the cyclooxygenase (COX) inhibitory activity of naproxen with that of nitric oxide developed by Nicox and exclusively licensed to Fera in the U.S. Nicox has tested naproxcinod in over 2,700 patients in osteoarthritis, generating a significant package of clinical safety data which is available to support Fera's development of naproxcinod, and ultimately an NDA submission for sickle cell disease.

Management and Advisors

In December 2021, we announced the appointment of Doug Hubatsch as Chief Scientific Officer to lead all of the Company's non-clinical and clinical development activities. Based in Nicox's U.S. subsidiary Nicox Ophthalmics Inc., he is responsible for setting the research and development strategy of the Group and is a member of the Nicox Executive Committee.

In July 2021, we announced that two internationally recognized experts in glaucoma, Robert N. Weinreb, M.D., Distinguished Professor and Chair, Ophthalmology and Director, Shiley Eye Institute, University of California San Diego, and Sanjay G. Asrani, M.D., Professor of Ophthalmology, Duke University, joined the Nicox Glaucoma Clinical Advisory Board.

2021 Financial Summary

Net revenue² for the full year 2021 was €7.2 million (€2.4 million in net royalties, €4.8 million in license payments), compared to €12.9 million (€2.4 million in net royalties, €10.5 million in license payments) for the full year 2020. The principal difference in revenue is due to an IFRS treatment of a licensing payment received from our partner Ocumension Therapeutics in 2020.

Operating expenses for the year 2021 increased to €25.1 million from €19.5 million for the previous year among which €5.2 million comes from non-clinical and development expenses due to the advancement and progress of the Phase 3 trials on NCX 470.

Net loss of the Nicox Group for the full year 2021 was €43.8 million against €18.1 million for the full year 2020. However, the 2021 net loss includes €27.8 million of non-recurring, non-cash items due to a reduction in the estimated fair value of ZERVIAE (of €12.7 million) and of NCX 4251 (of €15.1 million) reflecting, respectively, the changes in the allergic conjunctivitis market in the U.S. and the changes in the development plan and timeline for NCX 4251.

As of December 31, 2021, the Nicox Group had cash and cash equivalents of €42.0 million, as compared with €47.2 million at December 31, 2020, and as previously announced, the Company is financed until Q4 2023, assuming the development of NCX 470 alone.

As of December 31, 2021, the Nicox Group had financial debt of €20.5 million, consisting of €18.5 million in the form of a bond financing agreement with Kreos Capital signed in January 2019 and a €2 million credit agreement guaranteed by the French State, and granted in August 2020 in the context of the COVID-19 pandemic.

First Quarter 2022 Financial Highlights

As of March 31, 2022, the Nicox Group had cash and cash equivalents of €35.1 million as compared with €42.0 million at December 31, 2021. Net revenue² for the first quarter of 2022 was €0.7 million (entirely composed of net royalty payments). Net revenue² for the first quarter of 2021 was €1.7 million (including €0.7 million of net royalty payments).

² Net revenue consists of revenue from collaborations less royalty payments which corresponds to Net profit in the consolidated statements of profit or loss

As of March 31, 2022, the Nicox Group had financial debt of €20.5 million consisting of €18.5 million in the form of a bond financing agreement with Kreos Capital signed in January 2019 and a €2 million credit agreement guaranteed by the French State, and granted in August 2020 in the context of the COVID-19 pandemic.

Only the figures related to the cash position, revenue and debt of the Nicox Group as of December 31, 2021 and December 31, 2020 are audited; all other figures of this press release are non-audited.

About Nicox

Nicox S.A. is an international ophthalmology company developing innovative solutions to help maintain vision and improve ocular health. Nicox's lead program in clinical development is NCX 470, a novel nitric oxide-donating prostaglandin analog, for lowering intraocular pressure in patients with open-angle glaucoma or ocular hypertension. The Company is also developing NCX 4251, a proprietary formulation of fluticasone, for dry eye disease. Nicox generates revenue from VYZULTA® in glaucoma, licensed exclusively worldwide to Bausch + Lomb, and ZERVIAE® in allergic conjunctivitis, licensed in multiple geographies, including to Eyevance Pharmaceuticals, LLC, in the U.S. and Ocumension Therapeutics in the Chinese and in the majority of Southeast Asian markets.

Nicox is headquartered in Sophia Antipolis, France, is listed on Euronext Paris (Compartment C: Mid Caps; Ticker symbol: COX) and is part of the CAC Healthcare, CAC Pharma & Bio and Next 150 indexes.

For more information on Nicox, its products or pipeline, please visit: www.nicox.com.

Analyst coverage

Bryan, Garnier & Co	Dylan van Haaften	Paris, France
Edison Investment Research	Pooya Hemami	London, UK
H.C. Wainwright & Co	Yi Chen	New York, U.S.
Kepler Cheuvreux	Damien Choplain	Paris, France



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Forward-Looking Statements

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CONSOLIDATED STATEMENTS OF PROFIT OR LOSS (DRAFT)

	As of December 31:	
	2021	2020
Revenue from collaborations	8,583	14,423
Royalty payments	(1,350)	(1,516)
Net profit	7,233	12,907
Research and development expenditures	(17,910)	(12,728)
Administrative expenses	(7,000)	(6,677)
Other income	843	1,083
Other expenses	(211)	(93)
Operating loss before amortization and impairment of intangible assets	(17,045)	(5,508)
Amortization of intangible assets	(1,205)	(1,252)
Impairment of intangible assets (1)	(27,760)	-
Operating loss	(46,010)	(6,760)
Finance income	3,456	1,168
Finance expense (2)	(4,851)	(12,478)
Net financial income, (expense)	(1,395)	(11,310)
Loss before tax	(47,405)	(18,070)
Income tax (expense) / benefit	3,644	(28)
Loss after tax	(43,761)	(18,098)
Loss for the period	(43,761)	(18,098)

- (1) Includes two non-cash adjustments on US ZERVIAE estimated fair value decreasing by €(12.7) million, due to changes in the United States allergic conjunctivitis market, and on NCX 4251 estimated fair value, decreasing by €(15.1) million, reflecting the changes made to the development plan and timeline for NCX 4251.
- (2) Includes in 2021 a net loss of €(3.3) millions related to the restructuring of the Kreos debt and in 2020 a net loss of €(6.9) millions following the divestment of VISUfarma shareholding and loan.

CONSOLIDATED STATEMENTS OF FINANCIAL POSITION (DRAFT)

	As of December 31:	
	2021	2020
ASSETS		
Non-current assets		
Goodwill	25,637	23,663
Intangible assets	39,974	64,848
Property, plant and equipment	1,023	1,166
Non-Current financial assets	237	68
Total non-current assets	66,871	89,745
Current assets		
Trade receivables	1,086	1,723
Government grants receivables	1,452	736
Other current assets	377	237
Prepayments	2,853	2,630
Cash and cash equivalents	41,970	47,195
Total current assets	47,738	52,521
TOTAL ASSETS	114,609	142,266
EQUITY AND LIABILITIES		
Shareholders' equity		
Issued capital	43,138	37,030
Share premium	536,200	528,595
Cumulative translation adjustment	5,953	2,959
Treasury Shares	(847)	(605)
Accumulated deficit	(508,892)	(467,144)
Total equity	75,552	100,835
Non-current liabilities		
Non-current financial liabilities	21,160	13,429
Deferred taxes liabilities	9,236	11,868
Provisions	661	730
Total non-current liabilities	31,057	26,027
Current liabilities		
Current financial liabilities ⁽³⁾	346	5,646
Trade payables	3,649	2,421
Deferred income	1,970	5,174
Other current liabilities	2,035	2,163
Total current liabilities	8,000	15,404
TOTAL LIABILITIES AND EQUITY	114,609	142,266

Press Release

Nicox at ARVO 2022: Presentation of clinical Phase 2 results on NCX 4251 and new non-clinical evidence of improved hemodynamic and retinal cell physiology on NCX 470

May 2, 2022 – release at 7:30 am CET
Sophia Antipolis, France

Nicox SA (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced poster presentations highlighting the effect of NCX 4251 in patients with dry eye disease as well as new non-clinical evidence of neuroprotective activity on NCX 470 at the Association for Research in Vision and Ophthalmology (ARVO) 2022 Annual Meeting, one of the key scientific events in vision research, being held in person on May 1-4, 2022 in Denver, CO, United States and virtually on May 11-12.

Details of the poster presentations (all U.S. local times):

Title: Eyelid application of NCX 4251 for treatment of signs and symptoms of dry eye disease

Session title: Dry Eye, Clinical

Date: May 2, 2022 from 12:30 PM to 2:30 PM MDT

Presentation number: 1542 – A0267

Presenter: Gary Foulks MD, Emeritus Professor, University of Louisville Department of Ophthalmology and Vision Sciences, Louisville, KY, United States.

NCX 4251 is a novel and patented ophthalmic suspension of fluticasone propionate nanocrystals currently in Phase 2 development in the U.S. for patients with dry eye disease.

Title: NCX 470, a nitric oxide (NO)-donating prostaglandin analog, restores ocular hemodynamic and photoreceptor function after endothelin-1-induced ischemia/reperfusion injury in rabbits

Session title: Neuroprotection and Neuroregeneration

Date: May 2, 2022 from 12:30 PM to 2:30 PM MDT

Presentation number: 1606 – A0429

Presenter: Francesco Impagnatiello, PhD, Nicox Research Institute, Milan Italy

Title: NCX 470, a nitric oxide (NO)-donating prostaglandin analog, elicits sustained IOP-lowering and modifies aqueous humor dynamic in non-human primates

Session Title: Pharmacology/cellular Mechanisms

Date: May 3, 2022 from 1:00 PM to 3:00 PM MDT

Presentation number: 2839 – A0362

Presenter: Elena Bastia, PhD, Nicox Research Institute, Milan, Italy

Nicox's lead product candidate, NCX 470 is a novel nitric oxide (NO) donating prostaglandin analog being studied in two multi-regional Phase 3 clinical trials, Mont Blanc and Denali, for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

About Nicox

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Eyevance Pharmaceuticals, LLC, in the U.S. and Ocumension Therapeutics in the Chinese and in the majority of Southeast Asian markets.

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Analyst coverage

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Press Release

Nicox Announces a New Governance Structure

- **New governance structure with a separation of the functions of Chief Executive Officer and Chairman of the Board**
- **Andreas Segerros to be appointed as Chief Executive Officer of Nicox as of June 1st, 2022**
- **Jean-Francois Labbé, current Board member of Nicox, to become the future Chairman of the Board**
- **Co-Founder Michele Garufi will remain as a Board member of Nicox**

May 16, 2022 – release at 7:30 am CET
Sophia Antipolis, France

Nicox SA (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced that its Board of Directors appointed Andreas Segerros as Chief Executive Officer of Nicox S.A on May 13th, 2022, effective from June 1st, 2022, following the Board's decision to end the mandate of Michele Garufi, who has been Chairman, Chief Executive Officer and Co-Founder of the Company since its creation in 1996. Michele Garufi will remain as Board member of Nicox SA.

The Board has also decided to separate the roles of Chief Executive Officer and Chairman of the Board. Current Board member and Chairman of the Audit Committee, Jean-Francois Labbé has been proposed by the Board to become the future Chairman of the Board. This nomination is subject to the approval of an amendment to the Company's by-laws to increase the age limit for the Chairman of the Board, which will be the subject of a resolution to be voted at the Company's next Extraordinary General Meeting. During the interim period, the Board of Directors has nominated Michele Garufi as interim Chairman of the Board, effective from June 1st, 2022.

Michele Garufi, Chairman of the Board of Nicox SA said *"Having led Nicox from its foundation to becoming one of the most promising European Ophthalmic R&D Companies, I am pleased that the Board has decided to hand over the leadership of the company to Andreas Segerros. I am very confident that Andreas and the team will continue to successfully develop Nicox as a major player in the ophthalmic field through the last phase of development of NCX 470. I will be honored to support Andreas as a Board member and I wish him all the best in his new endeavor. At the same time, I would like to heartily thank all of my collaborators, the Board members and all of our business partners during the years of my Presidency who have largely contributed in making Nicox a leader in its therapeutic field."*

*"Working to bring novel and innovative ophthalmic treatments to market has been an important part of my professional life, and renewing that commitment with Nicox is indeed an honor," said **Andreas Segerros, Chief Executive Officer of Nicox SA.** "With its rich pipeline, near term development of NCX470, and the hard work and vision of a talented and passionate team, we can look forward to delivering products to treat some of the world's most prevalent and serious ophthalmic disorders, with the potential to make a meaningful difference in the lives of patients."*

Andreas Segerros

Andreas Segerros has spent most of his career in global pharma, with executive positions (R&D, Marketing and Business Development) in the U.S., Europe and Japan, at Pharmacia, Pharmacia & Upjohn and Ferring, with the focus on specialty Pharma, ophthalmology in particular. As Global Head of Ophthalmology at Pharmacia, Andreas launched XALATAN® (latanoprost), making it the industry's first billion-dollar ophthalmic drug. His venture capital experience comes from being Partner at the Scandinavian group Sunstone Capital, and also co-founded Eir Ventures. Andreas has made numerous

investments in successful companies in Europe and the U.S. Andreas holds an MSc in Organic Chemistry from The Royal Institute of Technology in Stockholm, Sweden, and an MBA in International Financing from The University of Uppsala, Sweden.

Jean-Francois Labbé

Jean-François Labbé has served as a member of Nicox' Board of Directors since 2010 and has been the Chairman of the Audit Committee of Nicox since 2013. M. Labbé is the Founder and Chief Executive Officer of SpePharm Holding BV, a pan-European specialty pharma company. Prior to founding SpePharm, M. Labbé served as Chief Executive Officer of OTL Pharma SA from 2001 to 2004 and as Chief Operating Officer of ProStrakan UK from 2004 to 2005. He began his career at Roussel Uclaf in 1974, then Hoechst Roussel and HMR, where he served in various positions in Europe, the United States and was a member of the HMR's Executive Committee before its merger with Aventis in 1999. M. Labbé received an MBA from the Ecole des Hautes Études Commerciales (HEC), Paris, France.

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Press Release

Nicox Accelerates Topline Results from NCX 470 Mont Blanc Phase 3 Glaucoma Trial to November 2022

- **Phase 3 Mont Blanc clinical trial approaches study completion with screening closed**
- **These Phase 3 results will be a key milestone for the Company**

June 3, 2022 – release at 7:30 am CET
Sophia Antipolis, France

Nicox SA (Euronext Paris: FR0013018124, COX), an international ophthalmology company, today announced that it has closed screening for additional patients in its Phase 3 Mont Blanc clinical trial of NCX 470 0.1% in patients with open-angle glaucoma or ocular hypertension. Therefore, the Company now expects to advance the announcement of the Mont Blanc topline results to November this year, as opposed to Q1 2023. NCX 470 0.065% has already demonstrated a statistically significant greater reduction of intraocular pressure compared to latanoprost 0.005% in a Phase 2 trial and is being evaluated in Phase 3 at a higher concentration than was tested in Phase 2.

“Thanks to the efficiency of Nicox’s clinical team and the tremendous effort of our clinical sites we now expect to be able to announce topline results from Mont Blanc ahead of schedule in November of this year. These first Phase 3 results for NCX 470 will be a key milestone for Nicox, defining what we expect to be a best-in-class intraocular pressure lowering profile, and potentially opening up multiple opportunities for this program and the Company.” said **Andreas Segerros, Chief Executive Officer of Nicox**. *“The Phase 2 efficacy results showed up to 1.4 mmHg superior intraocular pressure lowering with NCX 470 compared to latanoprost 0.005%. The Mont Blanc trial is testing a higher concentration of NCX 470, and so could potentially demonstrate even greater efficacy. In addition, the NCX 470 results on retinal cell protection in animal models recently presented at ARVO 2022 also open the way to a further differentiated product profile.”*

NCX 470 Phase 2 results and Phase 3 trial design

In the earlier Dolomites Phase 2 clinical trial, NCX 470 0.065% [demonstrated](#) statistical superior lowering of intraocular pressure of up to 1.4 mmHg compared to latanoprost 0.005% at Day 28. The results of the Dolomites trial were recently [published](#) in the *Journal of Glaucoma*. Mont Blanc is a Phase 3 clinical trial in patients with elevated intraocular pressure due to open-angle glaucoma or ocular hypertension. The Mont Blanc Phase 3 trial had an initial adaptive design period during which NCX 470 0.065% was evaluated together with the higher concentration of NCX 470 0.1%. Following the adaptive design period, the NCX 470 0.1% concentration was chosen to continue in the Mont Blanc Phase 3 trial, and was used to initiate the second Phase 3 clinical trial, Denali. Mont Blanc continued after the adaptive design period as a multi-regional, double-masked, 3-month, parallel group trial evaluating the efficacy and safety of NCX 470 ophthalmic solution 0.1% compared to latanoprost ophthalmic solution, 0.005%. Latanoprost is the most widely prescribed first-line therapy for open-angle glaucoma or ocular hypertension. The primary efficacy evaluation in Mont Blanc is based on time-matched IOP at 8 AM and 4 PM at Week 2, Week 6 and Month 3.

Nicox retains 100% of the rights to NCX 470, notably in U.S., Europe and Japan, other than those licensed to its partner Ocumension Therapeutics in China and elsewhere in the Far East. Nicox intends to continue developing NCX 470 itself in the U.S., and to partner in other key territories, particularly in Japan, as a key market opportunity. The Denali topline results are expected after 2023 and the Company will announce a new date for availability of the results when we have a more firm estimate of the overall timelines of the trial.

About Glaucoma and NCX 470

Glaucoma is a disease of the optic nerve which, if left untreated, can lead to irreversible vision loss. Glaucoma is frequently linked to elevated intraocular pressure (90% of patients) and is often due to blockage in the drainage system located in the front of the eye. Currently, reducing intraocular pressure remains the only way to slow the progression of the disease. About 3 million people in the United States between 40 and 80 years of age are affected by the most common form of glaucoma, open-angle glaucoma.

NCX 470 is a novel, potential best-in-class, nitric oxide (NO)-donating prostaglandin analog eye drop designed to release bimatoprost and NO following instillation into the eye. Bimatoprost, marketed under the brand name LUMIGAN® by AbbVie, Inc., is one of the leading branded products in the class of prostaglandin analogs. Prostaglandin analogs are the most widely used class of drugs for IOP-lowering in patients with open-angle glaucoma or ocular hypertension. NCX 470 is in development to reduce IOP in patients with open-angle glaucoma or ocular hypertension. Nitric oxide brings additional IOP-lowering efficacy by enhancing aqueous humor drainage from the eye via a different mechanism of action than that engaged by prostaglandin analogs.

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REQUEST FOR DOCUMENTS

Extraordinary Shareholder Meeting of July 11, 2022.

I,
LAST Name :

First Name:

Address :
.....

Email:

Owner of registered shares*
And/ or bearer shares,

Of **NICOX SA**

Hereby acknowledge that I have received the documents pertaining to the aforementioned General Meeting pursuant to article R.225-81 of the Code de Commerce.

request that the documents and information pertaining to the General Shareholder Meeting of July 11, 2022, as provided for under article R.225-83 of the same Code be addressed to my attention.

Signed in, on 2022

Signature

* Pursuant to article R.225-88 paragraph 3 of the Code de Commerce, holders of registered shares may submit a request to the company for a copy of all documents and information stipulated in article R.225-81 and R.225-83 of of the Code de Commerce for each subsequent general meeting. The shareholder must mention her/his desire to exercise this right in the present request.